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Cardiac Rehab for Functional Improvement

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Abstract

Purpose of Review Cardiac Rehabilitation (CR) was originally designed to return patients to their prior level of functioning after myocardial infarction (MI). Research has since revealed the mortality benefit of CR, and CR has been given a class 1A recommendation by the American Heart Association/American College of Cardiology (AHA/ACC). In this review, we shift our focus back to function and highlight the most recent research on the functional benefits of CR in a broad range of cardiac diseases and conditions.

Recent Findings Currently, CR is indicated for patients with coronary artery disease (CAD), heart failure with reduced ejection fraction (HFrEF), peripheral arterial disease (PAD), transcatheter aortic valve replacement (TAVR), left ventricular assist devices (LVADs), and cardiac transplant. Among patients with those conditions, CR has been shown to improve exercise capacity, cognition, mental health, and overall quality of life.

Summary As survival of cardiac diseases increases, CR emerges as an increasingly important tool to lend quality to patients' lives and therefore give meaning to survival.

Keywords Cardiac rehabilitation · Secondary prevention · Exercise training · Post-myocardial infarction care

Introduction

At the start of the twentieth century, there was no expectation for patients to recover after myocardial infarction (MI). As physicians in the 1950s began to realize the benefits of early mobilization, the treatment of choice for patients after MI went from strict bedrest and presumed long-term convalescence to cardiac rehabilitation with the expectation that patients would return to their work and prior level of activity [1]. This shift can be attributed to physicians such as Dr. Herman Hellerstein, who developed a revolutionary understanding of the myriad lifestyle factors that influence cardiovascular risk and subsequently created the first multidisciplinary program designed to target those lifestyle factors and improve functioning. Hellerstein urged physicians to recognize their essential role in rehabilitation beyond just diagnosis and treatment of disease, writing that "the practice of rehabilitation should not be below the dignity of the physician" [2].

Despite the evolution in technology and pharmacotherapy for the treatment of cardiovascular disease (CVD) since the 1950s along with education about proper lifestyle habits, CVD has remained the leading cause of death worldwide for the past decade. In 2016, CVD alone was responsible for over 9.5 million deaths worldwide [3, 4]. As a result, the importance of CR has become increasingly clear. Although Hellerstein's approach was once considered radical, in 1994 the American Heart Association (AHA) emphasized that CR should be standard of care and integrated into the treatment plan for all patients with CAD [5]. The AHA also defined the goals of CR: to improve functional capacity, alleviate or lessen activity-related symptoms, reduce disability, and identify and modify coronary risk factors in an attempt to reduce subsequent morbidity and mortality due to cardiovascular illness. A year later, the Agency for Healthcare Policy and Research released *Cardiac Rehabilitation*, which pioneered a framework of comprehensive healthcare guidelines regarding medical management, exercise, and education for those living with CVD in the USA. These emphasized exercise-training, physical activity, risk reduction, and pharmacotherapy [6].

Although from its inception the goals of CR were centered around patient function, there has since been an accumulation of

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outcomes data revealing the mortality benefit of CR [7–9]. As a result, the AHA/American College of Cardiology (ACC) has given CR a class 1A recommendation. Despite this accumulation of incredible outcomes data, however, it is important to honor the original purpose of CR and recognize the growing data on improved patient function and quality of life, which has demonstrated a benefit for a broad range of indications beyond CVD (Table 1).

Overview of Programs

Traditional Cardiac Rehabilitation (TCR)

The earlier models of CR align closely to what is now referred to as Traditional Cardiac Rehabilitation (TCR). TCR follows a 36-session model with a general outline of 3 sessions per week for 12 weeks. These sessions are comprised of moderate-intensity aerobic exercises and education on CVD and lifestyle modifications [6, 10]. Importantly, TCR encourages maintenance of independent exercise beyond the clinical setting. The current AHA/ACC guidelines suggest 30–60 min of moderate-intensity aerobic activity including brisk walking and household chores for 5–7 days out of the week whether that be within a clinical setting or independently. For further risk reduction, TCR includes education which emphasizes cessation of substances such as tobacco and alcohol. TCR includes comprehensive evaluation of patient cardiometabolic risk factors, including lipid panels, diabetes, blood pressure, and weight [11].

Table 1 Current and future indications for cardiac rehabilitation and the corresponding functional benefits

Disease/ condition	Potential functional benefits from cardiac rehabilitation (CR)
CAD	• Increased health-related quality of life • Improved mental health and cognitive function • Increased exercise tolerance • Improved sleep quality
HFrEF	• Increased health-related quality of life • Decreased shortness of breath and fatigue • Increased peak oxygen consumption
PAD	• Improved ambulatory function • Increased health-related quality of life
LVAD	• Increased peak oxygen consumption • Increased health-related quality of life • Increased independence • Improved mental health and cerebrovascular function
Cardiac Transplant	• Improved exercise capacity • Increased health-related quality of life
TAVR	• Increased independence • Improved functional status • Increased health-related quality of life
HFpEF	• Improved exercise capacity • Increased health-related quality of life • Improved mental health
POTS	• Decreased resting heart rate • Improved heart rate recovery after exercise • Increased health-related quality of life

Intensive Cardiac Rehabilitation (ICR)

Intensive cardiac rehabilitation (ICR) is a novel approach to CR that involves comprehensive lifestyle changes and incorporates stress management, group therapy, and nutrition counseling. Two widely-accepted models of ICR in the United States are the Pritikin Program and the Ornish Reversal Program [12].

The Pritikin Program divides the 72 recommended hours of ICR into 36 h of exercise and 36 h of educational sessions consisting of instructional videos [13]. A low-fat diet emphasizing intake of vegetables, grains, and fruit is recommended. Saturated fats and cholesterol-rich foods such as egg yolks and red meat are discouraged. The exercise portion consists of aerobic exercises as well as strength and flexibility training, given studies have shown that the combination yields increased peak oxygen consumption, a measure of cardiorespiratory fitness [14]. Although the program does encourage mental health practices, there are no specific classes or requirements regarding stress management, yoga, or meditation.

The Ornish Reversal Program emphasizes the four key components of nutrition, fitness, stress management, and group support [15]. The Lifestyle Heart Trial investigated the outcomes of CAD patients with sustained adherence to the program. After 1 year in the study, patients demonstrated a 37.2% reduction in low-density lipoprotein (LDL) cholesterol. Additionally, the frequency of anginal episodes was reduced by 91% and average percent diameter stenosis of coronary lesions was reduced by 2.2% [16]. Another randomized trial ($n = 93$) compared patients in the Ornish Program ($n = 46$) with patients on a TCR program ($n = 47$), assessing several cardiovascular disease risk factors. The study found that patients on the Ornish program had significantly greater improvements ($p < .001$) in weight, dietary habits, and body mass index (BMI) [17]. The program recommends consumption of healthy, monounsaturated fats and plant-based proteins and limitation of alcohol, sugars, and sodium. The exercise-training component involves 30-min sessions of monitored, moderate-intensity aerobic exercise such as light walking on the treadmill, elliptical use, or stationary biking [18]. Yoga and meditation are encouraged for stress management. Yoga has been shown to have anti-inflammatory effects on the body in favor of stress modulation [19, 20]. Beyond stress management, the Ornish program highlights the importance of group support and psychosocial counseling as a part of a strong foundation for mental health.

Mechanisms of Functional Improvement

Several studies have investigated the mechanisms underlying the myriad beneficial effects of CR on cardiovascular function [21]. Exercise is antiatherogenic via two mechanisms. First, it increases blood flow and shear stress on arterial walls, thereby improving endothelial function. Second, it enhances synthesis and release of nitric oxide, which in turn inhibits processes involved in atherogenesis [22, 23]. Similar to percutaneous coronary intervention (PCI), exercise training increases myocardial perfusion; however, contrary to PCI, exercise has a broader effect on all arteries [24]. Exercise has been shown to reduce plasma levels of C-reactive protein, a biomarker of inflammation in the body [25]. Physical activity has also been shown to decrease platelet aggregation and enhance fibrinolytic activity, decreasing risk of clot formation [26]. Further, exercise reduces the risk of arrhythmias by improving cardiac autonomic function, increasing vagal tone, and decreasing sympathetic activity [27, 28]. All of these protective effects of exercise increase patients' independence from medications, hospitalizations, and procedures and therefore increase patient functionality.

Perhaps the most obvious effect of exercise is its promotion of healthy skeletal muscle and inhibition of atrophy. Sarcopenia or muscle wasting occurs with increasing age and with deconditioning; however, it also specifically affects chronic heart failure (CHF) patients via modulation of genes in the ubiquitin-proteasome system [29–31], autophagy [32, 33], and myostatin-mediated signaling [34, 35]. In CHF patients, exercise training has been shown to decrease expression of MuRF-1 and Rnf28, genes for enzymes that trigger protein degradation in skeletal muscle [36]. Myostatin, a member of the transforming growth factor-β family, modulates muscle growth and differentiation and is associated with cachexia in advanced heart failure patients; however, exercise training results in decreased expression of myostatin in these patients [37, 38]. Exercise training in both coronary artery disease (CAD) patients and CHF patients has been shown to increase insulin-like growth factor-1, which promotes increased muscle mass and inhibits muscle wasting [39]. Exercise training also results in decreased contractile protein modification, thereby increasing force production [38]. CHF and CAD patients have also been shown to have decreased ability of the mitochondria to generate ATP, which in turn interferes with the ability of skeletal muscle to maintain long-lasting muscle contraction [40]. Exercise training resulted in increased surface density of mitochondria and improved mitochondrial respiration, which correlated with increased ATP production and peak oxygen consumption in heart failure patients [41, 42].

Another muscle influenced by exercise training is the diaphragm. The ability to breathe has a major impact on patients' functional status. In Ayurveda, breath or "prana" is a synonym for life force. Indeed, dyspnea frequently limits the daily activities of heart failure patients in particular. Breathing is carried out by the musculature and respiratory tract, which moves air in and out of the lungs (ventilation), as well as the lung parenchyma, which exchanges oxygen for carbon dioxide across a capillary membrane (respiration). Beyond the impact of pulmonary edema, respiratory muscle dysfunction contributes to dyspnea in both systolic and diastolic heart failure patients [43–46]. CHF impacts respiratory muscle function through several mechanisms. First, it causes a shift in fiber type from type II (high force production) to type I (low force production) [47, 48]. Further, it causes muscle fiber atrophy [42]. Carbonylation of contractile proteins as well as oxidation of mitochondria have also been shown to impair respiratory muscle function [49–51]. In animal studies, exercise training has been shown to prevent carbonylation of proteins, improve the integrity of the neuromuscular junction, and prevent mitochondrial and functional impairments of the diaphragm [51–53].

Indications for Cardiac Rehabilitation (CR)

As cardiovascular medical technology has evolved over time, CR has correspondingly evolved to care for the increasing number of patients that are now surviving and living with heart disease that would have previously been fatal. Thus, over time the indications for CR have broadened from its initial focus on coronary artery disease (CAD) to encompass systolic heart failure, heart transplant, transcatheter aortic valve replacement (TAVR), and most recently peripheral arterial disease (PAD).

Coronary Artery Disease (CAD)

About 18.2 million adults are currently living with CAD [54]. CR has been aimed at improving functioning in the growing number of CAD patients since its infancy, and it is now understood to play a key role in secondary prevention as well. Anderson et al. conducted a systematic review which examined randomized control trials of exercise-based CR programs in patients mostly post-MI or post-revascularization and found that CR reduced cardiovascular mortality [7]. However, the body of literature proving the benefit of CR on quality of life has also grown and should not be overlooked (Fig. 1). In the same systematic review, CR was shown to consistently reduce the risk of hospital readmission, thereby freeing patients from dependence on the hospital and allowing them to regain a sense of normalcy. In addition, health-related quality of life (HRQL) and emotional or mental health were improved in patients that underwent CR compared with control [7]. Similar benefits have been demonstrated in home-based CR with telemonitoring [55].

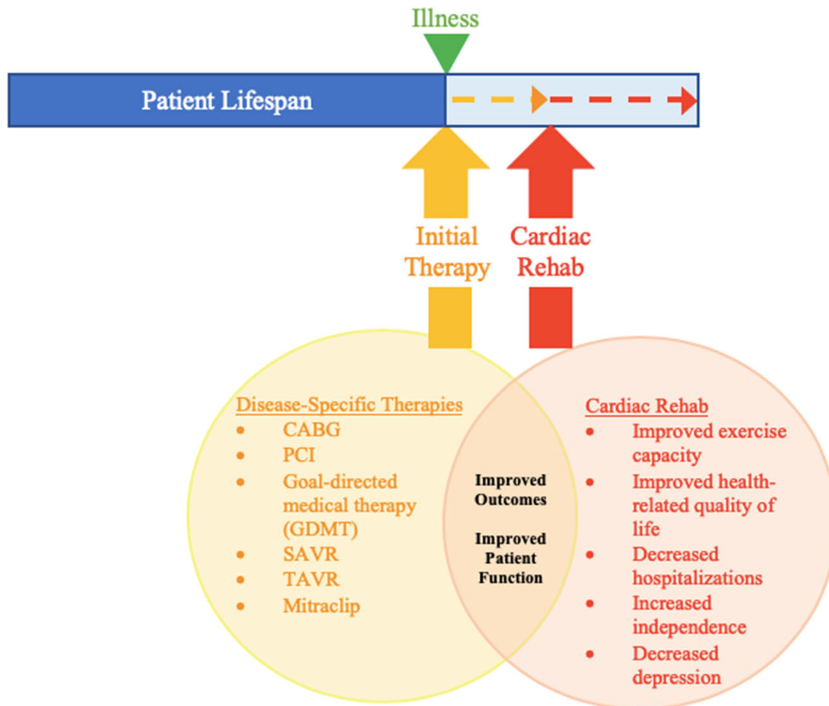

Fig. 1 CR works synergistically with disease specific therapies to improve functional status and life span

The benefits of CR on quality of life are particularly pronounced in the elderly population, who are at a high risk of losing independence and functioning as a result of CAD [56–61]. CR has been shown to decrease submaximal myocardial oxygen demand, making daily activities more feasible [56]. A key benefit of strength training is enhanced ease of daily activities [60]. In one study, elderly patients showed a 39% increase in exercise tolerance after CR compared with 31% in the other age group [61]. Other studies have shown significant improvements in depression, anxiety, and somatization alongside improvements in mental health, general health, energy, pain, function, and physical, social, and total quality of life [57, 60].

CR-mediated improvements in mental health are becoming increasingly recognized and understood. Patients' feelings of helplessness in the face of CAD increase anxiety and depression [62]. Depressive symptoms have been shown to decrease by up to 40% with exercise training alone [63]. However, the educational and social support aspects of CR also empower patients with an understanding of the lifestyle factors that influence their risk and teach them how to make sustainable lifestyle changes, thereby giving patients a sense of control over their health. CR has also been shown to improve cognitive function via better control of baseline autonomic function and neuro-cardiovascular stress reactivity [64, 65]. Interestingly, one study showed that CR in CAD patients with sleep apnea reduced the apnea-hypopnea index by up to 54%, indicating long-term diminishment of sleep apnea, and therefore better sleep quality and overall health and well-being of the individual [66].

Heart Failure with Reduced Ejection Fraction (HFrEF)

Heart failure patients often experience debilitating symptoms. These patients suffer from significant dyspnea and fatigue as well as bothersome lower extremity edema that interferes with daily functioning to such an extent that depression is common [67]. The HF-ACTION trial is a large-scale clinical trial which evaluated health status in 2331 patients primarily with systolic heart failure NYHA class II-III [68]. Importantly, this study used the Kansas City Cardiomyopathy Questionnaire (KCCQ) to evaluate patient-reported health status. This widely accepted self-evaluation tool asks questions that specifically target functional status. It assesses the degree to which each patient is limited by symptoms of heart failure (shortness of breath or fatigue) in his or her daily activities: showering/bathing, walking one block on level ground, and hurrying/jogging. Further, it evaluates how often patients are experiencing symptoms, including swelling, fatigue, and shortness of breath. It delves deeper to elucidate how the patient's symptoms are affecting his or her enjoyment of life, including his or her ability to participate in hobbies and spend time with loved ones. Through the KCCQ tool, this landmark trial found a statistically significant and durable benefit to quality of life for patients who had participated in aerobic exercise training plus evidence-based medical therapy compared with medical therapy alone.

In contrast to studies in CAD patients, a recent systematic review and meta-analysis of 44 clinical trials did not demonstrate a mortality benefit in patients with HFrEF after CR [69]. Instead, the analysis clearly showed reduced hospital admissions and improvement in HRQL. There was evidence of clinically important improvement in Minnesota Living with Heart Failure (MLWHF) scores with exercise. The MLWHF is another reliable and valid patient-oriented measure of the adverse effects of heart failure on a patient's life. This meta-analysis underscores the role of CR in the functional improvement of heart failure patients even without clear evidence of a mortality benefit yet. In the case of HFrEF, the life-saving measures may have already taken place prior to CR, such as a coronary artery bypass graft (CABG), PCI, goal-directed medical therapy (GDMT), left ventricular assist device (LVAD), or heart transplant. CR then plays a role in actually giving that survival meaning by helping him or her return to prior functioning.

Little data exist for patients with advanced, NYHA class IV heart failure. One small study did show that CR improves peak oxygen consumption and health status without any complications in patients both with and without LVADs [70]. Though the benefit of CR on function in NYHA class II-III patients is clear, more studies are needed to further elucidate the safety and effects in NYHA class IV patients.

Peripheral Arterial Disease (PAD)

Peripheral arterial disease (PAD) is a debilitating condition that affects patient mobility and therefore daily functioning. The primary symptom is intermittent claudication (IC), severe lower extremity pain that occurs with exercise and resolves with rest. IC often limits patients to only light physical activity and confines them to short walking distances. Exercise training has been shown to improve several measures of functional capacity: initial claudication distance (ICD), pain-free walking distance (PFWD), and absolute claudication distance (ACD) or maximal walking distance (MWD) [71]. Because of its proven benefits on quality of life as well as the potential to prevent progression of PAD and lower the risk of future cardiovascular events, supervised exercise training is recommended as the initial treatment for patients with IC [72]. According to AHA/ACC recommendations, supervised exercise training may be standalone or within a CR program. CR programs in particular have been evaluated and found to be effective in improving cardiovascular profiles, ambulatory function, and quality of life in PAD patients [73]. Exercise programs of at least 1 month duration have been shown to be effective in assisting patients in making concrete, lasting lifestyle changes that maintain a higher quality of life [74].

Left Ventricular Assist Devices (LVADs)

Left-ventricular-assist devices (LVADs) improve cardiac function in patients with end-stage heart failure for the purpose of prolonging life or providing a bridge to heart transplant. CR can improve the quality of the extra time that LVADs provide. Exercise training in LVAD patients has been shown to improve peak oxygen consumption, decrease NT-proBNP, and trigger myocardial growth factors [75]. The Rehab-VAD study is a randomized clinical trial that examined 26 patients with a recent LVAD implantation and assigned them to either a standard care group or 6 weeks of CR. The results showed improved cardiorespiratory fitness, muscle strength, treadmill time, 6-min walking distance, and KCCQ score in the CR group [76]. Overall, CR has been shown to be beneficial in helping LVAD patients achieve independent home care [77]. These clear functional benefits have rendered CR an indication for LVAD patients [78].

CR also impacts cognition and mental health in LVAD patients. It has been shown that a 12-week exercise training program increases cerebral blood flow responses to incremental exercise and improves cerebrovascular function [78]. Further, another study demonstrated not only benefit to quality of life but also reduced anxiety and depression. The study also showed reduced strain on patients' caregivers with CR [79].

Cardiac Transplant

Due to advancing technology, life expectancy after heart transplant has improved greatly in recent years; however, survival is still reduced compared with the general population [80, 81]. Although heart transplant improves exercise capacity compared with end-stage heart failure, these patients still have reduced exercise capacity and HRQL compared with the general population [82]. Large-scale clinical trials assessing CR programs are difficult to perform in heart transplant patients, as patients often live far from their respective transplant centers. Several studies have consistently reported improvement in exercise capacity with CR [82]. Improvement in QOL has been shown to track with improvement in exercise capacity [83–87]. RCTs have also demonstrated the positive effect of exercise on muscle strength, body composition, endothelial function, some inflammatory biomarkers, and HRQL [88, 89]. Other studies, however, have failed to measure improvement in HRQL [82]. This could be due to the use of generic measures of quality of life that lack sensitivity compared with disease-specific measures. Also, it is possible that the general improvement in QOL post-transplant compared with pre-transplant makes the effect of CR difficult to measure.

Transcatheter Aortic Valve Replacement (TAVR)

Aortic stenosis (AS) is a disease with similar pathophysiology to CAD that causes debilitating symptoms, including dyspnea, angina, and syncope. Valve replacement has been shown to improve those symptoms as well as physical function and disease-specific measures of quality of life [90]. However, studies still show that a large proportion of patients do not improve their NYHA classification, indicating they remain significantly symptomatic even after valve replacement [90]. In addition, AS has been shown to be associated with atherosclerosis, and frequently patients with severe AS requiring valve replacement also have underlying coronary disease [91]. Thus, transcatheter aortic valve replacement (TAVR) patients represent an important population in which lifestyle intervention through CR could not only improve patient functioning but also prevent progression of coronary atherosclerosis.

A systematic review examining 3 observational studies and 3 randomized clinical trials demonstrated increased pooled exercise capacity in patients after TAVR who undergo CR [92]. In one observational study of 60 patients specifically focused on QOL that examined both short-term and long-term outcomes, the majority of patients undergoing CR experienced significant improvement in functional status, autonomy, and QOL [93].

Although surgical valve replacement has been the preferred treatment for younger patients with TAVR being reserved for poor surgical candidates, the PARTNER 3 and EVOLUT trials suggested that TAVR could be used in low-surgical-risk patients as well [94, 95]. PARTNER 3 showed a mortality benefit to TAVR compared with surgical aortic valve replacement (SAVR), while EVOLUT showed non-inferiority of TAVR compared with SAVR. Based on these landmark trials, the number of patients undergoing TAVR can be expected to dramatically increase in the coming years. CR could represent an intervention with a dramatic impact on long-term function in this patient population.

Future Indications for Cardiac Rehabilitation

Although CR programs are not currently indicated as treatment recommendations for some groups, research is emerging to suggest a substantial benefit with CR in patients with HFpEF and POTS. In the future, CR will likely apply to these diseases as well.

Heart Failure with Preserved Ejection Fraction (HFpEF)

Patients with HFpEF experience similar symptoms to patients with HFrEF; however, the treatment of HFpEF has proven challenging, and there are currently no therapies proven to improve morbidity and mortality. Thus, CR could be a key therapy to improve function in these patients. Exercise training has been shown to improve exercise capacity, quality of life, and depression status in HFpEF patients [96–98]. Randomized clinical trials have shown significant improvement in cardiorespiratory fitness (CRF) as well as quality of life with exercise training [99]. A large-scale clinical trial, the Exercise Training in Diastolic Heart Failure (Ex-DHF) trial, is currently ongoing and aims to determine the long-term effects of exercise training on patient-related outcomes in HFpEF [100]. The pilot study of this trial demonstrated improved exercise capacity and quality of life [101]. This benefit was associated with beneficial atrial remodeling and improved left ventricular diastolic function.

The pathophysiology of HFpEF describes a mechanism for the potential benefit of CR in HFpEF patients. Endothelial dysfunction is more prevalent in HFpEF patients than HFrEF patients, and as previously mentioned, exercise has been shown to improve endothelial function [102–104]. Risk factors for HFpEF such as diabetes mellitus, smoking, obesity, hypertension, hyperlipidemia, and chronic kidney disease are known to cause inflammation and endothelial dysfunction [105–107]. It has been suggested that the pathophysiology of HFpEF is actually mediated by a proinflammatory state [108]. CR is particularly suited to target inflammation given that exercise, a Mediterranean diet, and stress-reduction such as yoga have all been shown to reduce inflammation [109–112].

Postural Orthostatic Tachycardia Syndrome (POTS)

Patients with POTS experience often dramatic symptoms that significantly impair their QOL, including orthostatic intolerance, gastrointestinal problems, and dysfunctional sleep [113]. Among treatments for POTS including pharmaceuticals, studies and analysis have shown that exercise is a key component of symptom relief [114, 115]. In a clinical trial in which POTS patients were treated either with short-term exercise or propranolol, exercise training showed greater improvements in adrenal function and POTS symptoms [116]. Exercise training also demonstrated a greater improvement in QOL.

Given the diversity of mechanistic causes of the various subtypes of POTS, there is currently no simple pharmacological solution. Mechanistically, exercise training hastens heart rate recovery after exercise and increases baroreflex sensitivity, thereby decreasing resting heart rate and targeting the primary source of POTS symptoms [117, 118]. A study in 251 POTS patients who participated in exercise training administered through their primary care physicians [119] demonstrated that 71% of patients no longer met criteria for POTS after exercise training. In addition, patient quality of life improved tremendously. This effect persisted at 6–12 months [119]. Thus, exercise is a key element of treatment for POTS regardless of subtype [114].

Beyond exercise training, the psychosocial aspects of CR would also be beneficial to POTS patients. Clinicians have detailed the dynamic, family-centered approach that is the most beneficial to improve QOL [115]. Group and family education is considered to be a crucial tool to improve exercise intolerance. Anecdotally, physicians have reported that POTS patients often feel isolated and seek the social support of other POTS patients and their families [115].

Conclusions

The procedural, pharmaceutical, and technological advances that the field of cardiology has seen in the last decade have given patients a chance at a life that would otherwise have been prematurely taken from them. However, how much meaning can prolonged life have if patients are unable to achieve the level of functioning they enjoyed prior to their cardiovascular illness? CR gives meaning to survival. Incidentally, it has been shown that CR also improves survival in CAD. Perhaps more importantly, though, evidence continues to accumulate in support of CR's positive effects on patient exercise capacity, independence, cognition, mental health, and overall quality of life. It is essential to continue to prioritize patient function as the field of cardiology progresses: to both continue to research the impact of CR on patient function in a variety of cardiac conditions and to educate clinicians on the growing number of recommended indications for CR. As Hellerstein emphasized, rehabilitation is not below the dignity of the physician. In fact, physicians are just as responsible for patients' rehabilitation as for their treatment.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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