

Role and efficacy of cardiac rehabilitation in patients with heart failure

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Abstract

Despite improvements in treatments, the prognosis of heart failure remains poor. Elderly patients with heart failure are burdened with multiple co-morbidities and polypharmacy. Multidisciplinary disease-management programs are recommended as standard care for patients at high risk of hospitalization. Cardiac rehabilitation is defined a coordinated multidimensional intervention that *integrates* the basic elements in multidisciplinary management programs with a continuing program of physical activity and exercise training. Cardiac rehabilitation services can be provided on an inpatient or outpatient basis according to the clinical characteristics and severity of the disease. Data support the usefulness of inpatient cardiac rehabilitation interventions soon after hospitalization for acute decompensated heart failure as a “transition care service” to overcome the particularly high risk “vulnerable” phase. Although in the elderly, physical activity is conditioned by the general clinical conditions, the presence of comorbidities and frailty, several data underscore the importance of improving exercise capacity in the elderly vulnerable patient.

Introduction

Even though the incidence of heart failure (HF) is stable, its prevalence is increasing due to the combined effect of population ageing and prolonged survival of patients with cardiovascular disease. In contrast to younger patients, HF in the elderly is often part of a constellation of chronic conditions that may exacerbate the clinical severity of HF and impact on outcomes. The complexities

of HF management, particularly in the setting of multiple comorbidities and polypharmacy, is highlighted in HF guidelines that recommend multidisciplinary disease-management programs as standard care for patients at high risk of hospitalization [1]. Multidisciplinary management programs generally involve health education with particular emphasis on adherence and self-care, physiologic monitoring, diet promotion and regular follow-up also including telemonitoring or remote monitoring. The evidence supporting multidisciplinary heart failure disease management programs to reduce hospitalizations and mortality is well-established [2-4]. The “complexity” of the multidisciplinary program relates to events rate. A clinical audit in Australia established that those management programs that provided “more” interventions were associated with fewer morbid and fatal events [5]. Specialized heart failure cardiologists and nurses, psychosocial intervention, professional coordination are relevant components required to achieve the best health outcomes [6].

Cardiac rehabilitation that is defined as a “coordinated multidimensional intervention designed to stabilize or slow disease progression, alleviate symptoms, improve exercise tolerance and enhance quality of life, thereby reducing morbidity and mortality” *integrates* the basic elements in multidisciplinary management programs with a continuing program of physical activity and exercise training [7].

This paper will address the role and efficacy of cardiac rehabilitation in heart failure patients, with a particular focus on residential rehabilitation.

The role of cardiac rehabilitation in heart failure

Heart failure is a chronic disease characterized by cyclical progressive clinical instabilities requiring hospitalization. The early post-discharge period – that includes the first 2-3 months immediately following a HF hospitalization - carries particularly high risk of poor clinical outcome and is known as the “vulnerable” phase. In the US approximately 25% of patients hospitalized with HF are readmitted within 30 days of discharge, and mortality during this period can approach 30% [8]. These figures are largely different from the metric observed in the Italian nationwide registry IN-CHF reporting less than 10% for the combined end-point of 30-day readmission and mortality [9]. The underlying pathophysiology is typically related to short-term worsening of hemodynamics, primarily increasing left ventricular filling pressures. Management strategies and interventions specifically applied in the transition phase are now being identified as transition care services. A recent network meta-analysis including 53 RCTs (12,356 patients) found that among services that significantly decreased all-cause mortality compared to usual care, nurse home visits were most effective followed by disease management clinics [10].

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The consolidated practice of working in a multidisciplinary team (involving cardiologist, nurse, physiotherapist, dietician, psychologist) makes cardiac rehabilitation the most suitable and most efficient service to face the multiple problems of the patient with HF in the vulnerable phase, especially the elderly patient often presenting with frailty and comorbidities. The rehabilitation facility provides continuity of care, close surveillance by cardiologists, monitoring of vital parameters and blood samples, optimization of evidence-based therapies, reinforcement of patient motivation and education, promoting adherence and self-efficacy to diet. Rehabilitation services can be provided on an inpatient or outpatient basis according to the clinical characteristics and severity of the disease as defined in the joint-society consensus document ANMCO/GICR/IACPR [11].

The efficacy of in-hospital cardiac rehabilitation in heart failure

Data support the usefulness of inpatient cardiac rehabilitation interventions soon after hospitalization for acute decompensated HF. In a single center study including 275 patients, *Scrutinio et al.* [12] showed that hospitalization in a cardiac rehabilitation facility significantly improved 1-year survival. Patients were treated by cardiologists with expertise in heart failure treatment who also provided individual counseling on monitoring of weight changes, worsening of symptoms, signs of fluid retention and medical adherence. Interestingly, more than 50% of patients required adjustment of evidence-based therapies. Each participant was also given a tailored low-intensity exercise program supervised by a physiotherapist. Functional autonomy was achieved in most patients who had severely limited mobility at entry, and among the patients who could perform a six-minute walking test at entry into rehabilitation the distance walked increased by 26% [12].

Early recovery of physical function is of major importance in older patients. Older patients hospitalized with acute decompensated heart failure have severe and widespread impairments in physical function that persist despite conventional HF treatment and contribute to adverse clinical outcomes. Within this context, the results of the pilot study REHAB-HF (Rehabilitation Therapy in Older Acute Heart Failure Patients) demonstrated that an individually tailored multidomain physical intervention can improve physical function and reduce all-cause hospitalization [13].

Recent data from the administrative database of the Lombardy region highlight the importance of in hospital cardiac rehabilitation as a *transition care service* in HF [14]. The analysis included more than 140,000 subjects with incident HF in the years 2005-2012 of whom 29% received cardiac rehabilitation, and showed that the transition to one of the in-hospital cardiac rehabilitation facilities reduced mortality and readmissions and favored the implementation of the recommended therapies [14]. It is worth noting that patients referred for rehabilitation were more frequently male, and had a greater burden of comorbidities and interventional procedures.

Exercise-based cardiac rehabilitation

The HF-ACTION (Heart Failure: A Controlled Trial Investigating Outcomes of exercise TraiNing) trial definitely estab-

lished the safety of regular exercise in stable, symptomatic outpatients with HF with reduced ejection fraction (HFrEF) [15]. By contrast, the primary efficacy end-point of all-cause mortality and hospitalization differed between the exercise and control group only by 4% at 3 years of follow-up (hazard rate 0.93 [95% CI 0.84-1.02], $p=0.13$). A small statistically significant reduction in the primary end-point resulted after adjustment for several baseline factors (hazard rate 0.89 [95% CI 0.81-0.99], $p=0.03$). The interpretation of the results of the HF-ACTION must be made in the context of its limitation. It is important to note that the control group was not devoid of physical activity and, of major importance, the adherence to the exercise prescriptions in the exercise group was rather poor. Indeed, at 12 months, only 30% of patients in the active arm were adherent. In a study in which supervised exercise was sustained for a period of 10 years, a reduction in cardiovascular mortality and hospitalizations was noted as well as improvements in symptoms and left ventricular ejection fraction [16].

In 2014, a Cochrane review including 33 RCTs (4740 participants predominantly HFrEF and NYHA classes II and III) found that exercise-based rehabilitation compared with no exercise control decreased all-cause and heart failure-related hospitalization to 1 year and improved quality of life but had no significant effect on mortality [17]. These results were further supported by the additional randomized evidence provided by the 2019 update of this Cochrane Review that included 44 trials (5783 participants) with a median of six months' follow-up [18]. Current HF guidelines provide class I, level of evidence A support for regular aerobic exercise to improve symptoms and functional capacity in patients with HF and to reduce the risk of heart failure hospitalization in patients with HFrEF [1]. A recent position paper from the Committee on Exercise Physiology and Training and the Committee of Advanced Heart Failure of the Heart Failure Association of the ESC [19] underscores the benefits of early mobilization and exercise training even in ventricular assist device (VAD) recipients and provides practical advice on its implementation in this special population.

Recent data, however, questioned the value of exercise training in HF patients. The ExTraMATCH II meta-analysis [20] upon individual data from 3912 patients with HF from 18 RCTs, found no impact of exercise-based cardiac rehabilitation in patients with HF on mortality and hospitalization, when compared to no exercise control. However, some differential treatment effects across patient characteristics emerged in secondary analyses. In detail, exercise-based cardiac rehabilitation was associated with a larger reduction in all-cause and HF mortality in older patients ($p=0.034$ and $p=0.017$ respectively), a larger reduction in HF mortality in ischemic patients ($p=0.047$) and a larger reduction in all-cause hospitalization in patients with lower baseline peak VO_2 ($p=0.027$).

Exercise-based rehabilitation in heart failure patients with preserved ejection fraction

Although the evidence base includes predominantly patients with HFrEF, an increasing number of studies include patients with HFpEF that accounts about half of all HF patients. In recent years there has been a paradigm shift with respect to understanding of the pathophysiology of HFpEF. Physical inactivity and low fitness have been recognized as potential modifiable targets for prevention as well as management of HFpEF.

There is a growing body of evidence indicating the improvement in aerobic capacity after exercise training in HFpEF patients. In a meta-analysis including 8 intervention studies providing a

total of 174 exercising subjects and 143 control subjects, peak VO_2 increased by a mean difference of 2.08 mL kg^{-1} min^{-1} (95% C.I. 1.51 to 2.65) in exercise training *versus* sedentary control, equating to a 17% improvement from baseline [21]. Another meta-analysis involving 276 patients with HFpEF enrolled in six RCTs found exercise training was associated with an improvement in physical functioning and quality of life [22] without any significant change in resting diastolic or systolic function.

Exercise-based rehabilitation in elderly heart failure patients

The results of the subgroups in EXTraMATCH II meta-analysis [20] do highlight the relevant clinical implications of exercise training and physical activity in elderly HF patients. In the elderly, physical activity is conditioned by the general clinical conditions, the presence of comorbidities and frailty. In a prospective study on 314 elderly patients (mean age 74±6 years) with advanced HF, usual physical activity performed before HF decompensation was evaluated by the physical activity scale for the elderly (PASE) usually on the second day after hospital admission. It was found that physical activity, whether pursued for its own sake or linked to the activity of daily living, was a predictor of mortality regardless of comorbidities, disability and physical function [23]. The risk of death being inversely related to physical activity levels: the higher the involvement in leisure and in household and occupational activity the lower the mortality. This study underscores the importance of improving exercise capacity in the elderly vulnerable patient.

There is some evidence available on the impact of cardiac rehabilitation in elderly patients with HFpEF. Besides the already quoted REHAB-HF [13], a meta-analysis of seven RCTs including 530 patients above 70 years of age (range 70-81) found that exercise training significantly increased the six-minute walking distance by 50.5 meters (95% CI: 28.4-71.7) and improved quality of life (95% CI: 0.06-0.18) [24]. An impact on mortality or hospital readmissions was not seen. A more recent large trial showed that cardiac rehabilitation confers significant benefits even on the oldest HF patients [25]. In this study, 343 HF patients with both reduced and preserved ejection fraction (mean age 77±6 years) were randomized to exercise therapy (supervised training sessions for 3 months in the hospital followed by home telemonitoring sessions for 3 months) versus usual care [25]. As compared to usual care, trained patients at 6 months showed: significantly increased six-minute walking distance, increased ADL scores, 40% reduced risk of rehospitalization and significantly improved perceived quality of life.

Conclusions

Effective management of heart failure is key to reducing hospitalization and improving survival. Cardiac rehabilitation is a complex multidisciplinary intervention embracing not only the medical but also the social, psychological and behavioral dimensions of the disease that can improve evidence-based practice and patient outcomes to optimize the transition of care across the cyclical trajectory of heart failure. The role of cardiac rehabilitation in heart failure is largely beyond providing supervised exercise training.

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