## **Review Article**

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## **Cardiac Rehabilitation in Heart Failure**

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## ABSTRACT

Heart failure (HF) is a complex clinical syndrome caused by a structural and/or functional cardiac abnormality, resulting in reduced organ perfusion. The goals of treatment in patients with HF are to improve functional capacity and quality of life, and to reduce mortality. Cardiac rehabilitation (CR) including exercise training is one of the treatment options, and current guidelines recommend CR as safe and effective for patients with HF. CR has been known to improve exercise capacity and quality of life, minimize HF progression, and lower mortality in patients with HF. Improvement of vascular endothelial function, activation of the neurohormonal system, increase of mitochondrial oxygen utilization in peripheral muscles, and increase of chronotropic responses are possible mechanisms of the beneficial effects of exercise-based CR in HF. Although CR has been shown to decrease morbidity and mortality, it is underutilized in clinical practice. Despite the existence of concrete evidence of clinical benefits, the CR participation rates of patients with HF range from only 14% to 43% worldwide, with high dropout rates after enrollment. These low participation rates have been attributed to several barriers, including patient factors, professional factors, and service factors. The motivation for participating in CR and for overcoming the patients' barriers for CR before discharge should be provided to each patient. Current guidelines strongly recommend applying a CR program to all eligible patients with HF.

Keywords: Heart failure; Cardiac rehabilitation; Exercise therapy

## INTRODUCTION

Heart failure (HF) is a complex clinical syndrome with a global economic burden and is a leading cause of hospitalizations owing to repeated worsening of the disease.<sup>1)2)</sup> The largest proportion of health-care costs for patients with HF in South Korea was reported to be related to hospitalization, especially admissions through the emergency department.<sup>3)</sup> Appropriate treatment strategies, including modification of risk factors to prevent or decrease hospitalizations, are needed to reduce the economic burden on patients with HF.

Cardiac rehabilitation (CR), which includes disease education, exercise, nutrition counseling, risk factor management, and stress management as components, is a comprehensive, multidisciplinary, long-term intervention offered to patients diagnosed with HF (**Figure 1**).

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## General strategies for CR

- Optimal exercise training
- Counseling on nutrition
- Hypertension management
- Diabetes management
- Smoking cessation
- Psychosocial management
- Physical activity counseling

#### • HF specific strategies for CR

- Precise patient assessment
  - Ventricular function
  - Arrhythmic risk
  - Muscle waisting
  - Baseline functional capacity
  - Volume status
  - Other comorbidities

Figure 1. Core components of cardiac rehabilitation and special considerations in patients with HF. CR = cardiac rehabilitation; HF = heart failure

Exercise training is a core component of CR.<sup>4)</sup> Over the past decades, evidences of the need for CR in patients with HF have accumulated, and the American Heart Association and American College of Cardiology guidelines recommend CR as a class I indication for HF.<sup>5)6</sup> Particularly in patients with HF, several points need to be considered when applying a CR program. When a participant with HF has symptoms or signs of acute decompensated HF, CR is not feasible. Moreover, if a patient has a high burden of fatal arrhythmia, it would be better to initiate CR after the condition has been stabilized. In addition, in the presence of severely reduced muscle mass or function, underlying pulmonary disease, overloaded volume status, and other significant comorbidities, the risk and benefit should be considered before participation in CR.

By considering patients' baseline characteristics and modifying the health behaviors in a comprehensive manner, CR can effectively improve exercise capacity and quality of life, minimize HF progression associated with recurrent hospitalizations, and lower mortality, eventually reducing the health-care costs. This review focuses on the evidence of the beneficial effects of CR on the disease progression and quality of life of patients with HF.

## WHAT ARE THE CLINICAL OUTCOME BENEFITS OF CR IN HF?

Although exercise training is a core component, current guidelines recommend comprehensive CR programs including other components to optimize the reduction of cardiovascular risks.<sup>4)</sup> The benefits of CR in patients with HF have been comprehensively reviewed in several clinical trials and numerous meta-analyses. CR has an important effect in reducing mortality in patients with HF. According to the Exercise Training Meta-Analysis of Trials in patients with Chronic Heart failure (ExTraMATCH) study, the mortality rate in the CR group was reduced by 35% compared with that in the control group during the 2-year follow-up period.<sup>7)</sup> The HF: A Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION) study was a randomized controlled 30-month study of 2,331 patients with HF with reduced ejection fraction (HFrEF).8) The overall mortality or readmission decreased by 11% and the peak  $VO_2$  increased by an average of 4% in the CR group compared with those in the control group, although the results were significant only after adjustment for high prognostic risk factors. In the analysis of the group that more faithfully adhered to exercise, the mortality and readmission rates in the CR group decreased by >30% compared with the control group. Furthermore, there was no death associated with aerobic exercise and only 3% of patients in the exercise-treated group were hospitalized for exercise-related symptoms, a ratio similar to that of the control group (2%). In addition, it was reported that the maximum oxygen intake proportionally increased with the amount of exercise performed

every week (metabolic equivalent of task-hour per week), consequently contributing to improving the clinical aspects of patients with HF. Other meta-analysis results reported by Smart and Marwick also showed that the exercise treatment group had a 39% reduction in mortality.<sup>9)</sup> From these earlier studies about the effectiveness of exercise training, it has been considered that regular exercise in patients with HF contributes to reduce moderate cardiovascular events and mortality.<sup>10</sup> However, it is important to note that there has been heterogeneity among recent studies on the effects of exercise training on the outcomes of HF. The 2014 Cochrane review reported that exercise groups had a reduction in the risk of overall hospitalization and HF-specific hospitalization compared with no-exercise control groups,<sup>11</sup> However, a recent meta-analysis showed contradictory results. In 2018, the ExTraMATCH II Collaboration published a meta-analysis of randomized trial data on exercise training in HF, which included 18 trials comprising 3.912 patients (1.948 in the exercise group, 1.964 in the control group). According to this report, exercise training had no significant effect on mortality or hospitalization in patients with HF.12) In addition, it failed to reveal evidence of a differential effect of exercise training according to patients' characteristics (e.g., age and sex). This result could have several possible explanations, including variations in the exercise training intervention and the patients' adherence across trials. Another potential explanation for the reduced strength of the effect of exercise training on the outcomes could be the inclusion of more recent trials in this updated meta-analysis. More recent trials are more likely to have included patients with up-to-date usual HF treatment, including diseasemodifying drugs (e.g., statins, beta-blockers, renin-angiotensin aldosterone antagonists, angiotensin receptor blocker/neprilvsin inhibitors, etc.) and device therapy (defibrillator or cardiac resynchronization therapy) than earlier studies. However, according to the Cochrane systematic review of exercise training in HF, meta-regression showed no statistical association between the effect of exercise training on mortality or hospitalization and the trial publication date.13)14) Various results of such representative clinical trials and metaanalysis on exercise training in HFrEF are shown in Table 1.

Most studies have included patients with chronic stable HF with left ventricular ejection fraction <40%, classified as New York Heart Association (NYHA) functional class II or III. As the population is getting older, HF with preserved ejection fraction (HFpEF) becomes highly prevalent in the general population aged  $\geq$ 60 years, with a prevalence rate of 4.9%, which is expected to further increase in the future.<sup>19)</sup> CR in patients with HFpEF has also been reported to improve exercise performance and quality of life and to reduce hospitalization rates.<sup>20)</sup> However, most clinical trials that evaluated patients with HF included participants with systolic dysfunction; thus, more randomized controlled studies are needed. A recent study comparing exercise training in patients with HFPEF and HFpEF showed that significantly higher peak VO<sub>2</sub> level was achieved in patients with HFpEF.<sup>21)</sup> Moreover, an ongoing clinical trial, known as REHABilitation therapy in older acute Heart Failure patients (REHAB-HF) trial, is investigating the efficacy of CR in older patients with HFrEF and HFpEF.<sup>22)</sup> This study is expected to provide information on the effectiveness of CR in the extended HF category.

## **BENEFICIAL EFFECTS OF EXERCISE-BASED CR IN HF**

The improvement of vascular endothelial cell function, in part as a result of regular exercise, is known to have the potential to improve the reduced cardiac output and peripheral vasoconstriction in patients with HF. In addition, exercise slows down the secretion of

#### **Cardiac Rehabilitation in Heart Failure**

Study	Year	Method	Size (No.) (exercise, control)	Mean (or median) follow-up duration	Population	Description of training program	n Outcomes
Belardinelli et al. <sup>15)</sup>	1999	RCT	90 (50, 40)	15 months	HFrEF (<40%) and NYHA class II–IV	Supervised cycling, 60 minutes, 3 days a week for 8 weeks, then 2 days a week	Mortality (RR, 0.37; p=0.01), HF hospitalization (RR, 0.29; p=0.02)
Belardinelli et al. <sup>16)</sup>	2012	RCT	123 (63, 60)	10 years	HFrEF (<40%) and NYHA class II or III	Supervised exercise training, three sessions a week for 2 months, then 2 supervised sessions for the rest of the year	Hospital readmission (HR, 0.64; p<0.001), cardiac mortality (HR, 0.68; p<0.001)
Zwisler et al. <sup>17)</sup>	2008	RCT	770 (380, 390)	10.5 months	HFrEF (<45%) and NYHA class II or III	Six-week intensive comprehensive cardiac rehabilitation program including 12 exercise training sessions, patient education	Composite outcome: mortality, myocardial infarction, and acute first readmission for heart disease (RR, 0.96; 95% CI, 0.78–1.26)
O'Connor et al. <sup>®)</sup> (HF-Action)	2009	RCT	2,331 (1,159, 1,172)	30 months	HFrEF (<35%) and NYHA class II-IV	Supervised exercise training (walking, treadmill, or stationary cycling), 36 supervised sessions (three sessions per week) followed by home-based training	Mortality (HR, 0.96; p=0.70), cardiac mortality or cardiac hospitalization (HR, 0.92; p=0.14), cardiac mortality or HF hospitalization (HR, 0.87; p=0.06)
Piepoli et al. <sup>7)</sup> (ExTraMATCH)	2004	Meta- analysis	9 trials including 801 patients (395, 406)	20 months (5–75 months)	HF with left ventricular systolic dysfunction (<50%)	Included types of exercise intervention: exercise training program lasting ≥8 weeks, utilizing at least both legs	Mortality (HR, 0.65; 95% CI, 0.46–0.92), composite of mortality and hospital readmission (HR, 0.72; 95% CI, 0.56–0.93)
Davies et al. <sup>18)</sup> (Cochrane review)	2010	Meta- analysis	19 trials including 3,647 patients	Up to 12 months	HFrEF (<40%) and NYHA class II-IV	Included types of exercise intervention: exercise- based interventions either alone or as a component of a comprehensive cardiac rehabilitation (e.g., health education and psychological interventions)	Mortality (RR, 1.03; 95% CI, 0.70-1.53), HF hospitalization (RR 0.72; 95% CI, 0.52-0.99)
Taylor et al. <sup>11)</sup> (Cochrane review)	2014	Meta- analysis	33 trials including 4,740 patients	Up to 12 months		Included types of exercise intervention: exercise- based interventions either alone or as a component of a comprehensive cardiac rehabilitation (e.g., health education and psychological interventions)	Mortality (RR, 0.93; 95% CI, 0.69–1.27), hospital readmission (RR, 0.75; 95% CI, 0.62–0.92; p=0.005), and HF hospitalization (RR, 0.61; 95% CI, 0.46–0.80; p=0.002)
Taylor et al. <sup>12)</sup> (ExTraMATCH II)	2018	Meta- analysis	18 trials including 3,912 patients (1,948, 1,964)	19 months for mortality outcomes, 11 months for hospitalization outcomes	HFrEF and NYHA class II or III	Included types of exercise intervention: aerobic exercise training performed by the lower limbs, lasting ≥3 weeks either alone or as a component of a comprehensive cardiac rehabilitation (e.g., health education and psychological interventions)	Mortality (HR, 0.83; 95% CI, 0.67-1.04), HF-specific mortality (HR, 0.84; 95% CI, 0.49-1.46), and HF hospitalization (HR, 0.98; 95% CI, 0.72-1.35)

Table 1. Randomized clinical trials or meta-analysis on exercise training in HF

CI = confidence interval; HF, heart failure; HFrEF = heart failure with reduced ejection fraction; HR = hazard ratio; NYHA = New York Heart Association; RCT, randomized clinical trial; RR, relative risk.

cytokines and the activation of neurohormonal systems, improves the utilization of oxygen in mitochondria of peripheral muscle cells, increases muscle mass, increases respiratory efficiency without a deleterious effect on left ventricular remodeling, and ultimately improves the clinical outcome of patients with HF (**Figure 2**).<sup>23)</sup>

Over the past years, the beneficial effects of exercise-based CR for patients with chronic stable HF have been established by several randomized clinical trials.<sup>15)30</sup> Exercise training can decrease the resting heart rate and increase the chronotropic reserve through a beneficial

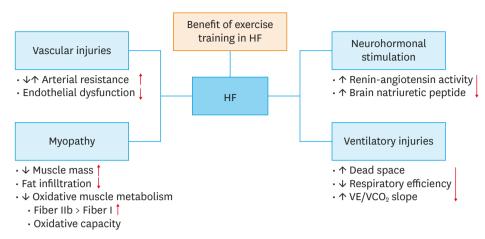


Figure 2. Beneficial effects of regular exercise in HF.<sup>23)</sup>

Exercise training enables the improvement of both endothelial function and endothelium-dependent vasoactivity of skeletal muscle vasculature in patients with HF.<sup>24)</sup> Exercise training leads to an increase in muscle capacities, myofibril cross-sectional area, and mitochondrial/capillary density,<sup>25)</sup> and high-intensity exercise training can result in an increase in type I fiber composition and a decrease in type II fiber composition.<sup>26)</sup> Moreover, it also reduces sympathetic activity and improves heart rate variability with a more balanced sympathetic-vagal tone,<sup>27)</sup> reduces brain natriuretic peptide levels,<sup>28)</sup> and improves the oxygen uptake efficiency slope.<sup>29)</sup> HF = heart failure.

effect on the sympathetic nervous system, even in patients with HF taking a beta-blocker.<sup>23)</sup> The beneficial effects on left ventricular function in patients with HF remain controversial, as previous studies showed either no effect or only a slight improvement.<sup>31)32)</sup> Further, exercise training enhances the vagal tone by decreasing the central sympathetic nerve outflow, and is associated with a significant reduction of tumor necrosis factor-alpha, interleukin 1-beta, interleukin-6, and brain natriuretic peptide levels.<sup>33)34)</sup>

The U.S. and European HF treatment guidelines recommend regular exercise as a class I or IIa indication (**Table 2**). In general, resistance exercise training (other than aerobic exercise) is not recommended in patients with HF and is further limited in HF patients with severe peripheral muscle atrophy. Peripheral muscle abnormalities are another reason for exercise intolerance in patients with chronic HF. Exercise training leads to a significant increase in type I muscle fiber (oxidative fiber) composition with increased muscle aerobic capacity, whereas the type IIb muscle fiber (glycotic fiber) composition is decreased.<sup>25)</sup> Although the exercise intensity range used in patients with HF has generally been 70–80% of peak VO<sub>2</sub>, it

#### Table 2. Summary of current available guidelines

2013 ACCF/AHA guideline for the management of heart failure<sup>35)</sup>

1. Exercise training (or regular physical activity) is recommended as safe and effective for patients with HF who are able to participate, to improve functional status. (Class I, level of evidence: A)

2. Cardiac rehabilitation can be useful in clinically stable patients with HF, to improve functional capacity, exercise duration, health-related quality of life, and mortality. (Class IIa, level of evidence: B)

AHA effectiveness-based guidelines for the prevention of cardiovascular disease in women - 2011 update<sup>36)</sup>

 A comprehensive CVD risk-reduction regimen, such as cardiovascular or stroke rehabilitation or a physician-guided home- or community-based exercise training program, should be recommended to women with current/prior symptoms of heart failure and an LVEF of 35%. (Class I, level of evidence: B)
 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure<sup>37)</sup>

1. It is recommended that regular aerobic exercise is encouraged in patients with HF to improve functional capacity and symptoms. (Class I, level of evidence: A)

2. It is recommended that regular aerobic exercise is encouraged in stable patients with HFrEF to reduce the risk of HF hospitalization. (Class I, level of evidence: A)

3. It is recommended that patients with HF are enrolled in a multidisciplinary care management program to reduce the risk of HF hospitalization and mortality. (Class I, level of evidence: A)

ACCF = American College of Cardiology Foundation; AHA = American Heart Association; CVD = cardiovascular disease; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; LVEF = left ventricular ejection fraction.

depends on the training heart rate or the patients' physical state. The moderate, continuous exercise modality used in the HF-ACTION trial is generally accepted in patients with chronic stable HF; however, some researchers showed that the increase in peak VO<sub>2</sub> was greater with aerobic interval training than with continuous training.<sup>38)</sup> Another substudy from the HF-ACTION trial further supported the benefit of CR by using the Kansas City Cardiomyopathy Questionnaire to show overall improvement between the 2 groups.<sup>39)</sup> The authors found a significant improvement in quality of life in the exercise group.

In addition, one meta-analysis showed that high-intensity exercise training improved the quality of life, and aerobic-only or combined aerobic and resistance training can offer the greatest improvement in the quality of life.<sup>40</sup> However, inconsistent results have also been reported. One recent meta-analysis showed that high-intensity interval training improves peak VO<sub>2</sub> but its superiority over moderate-intensity continuous training was not significant.<sup>41</sup>

Several measures of exercise intensity are available. Compared with the metabolic equivalent of tasks, which is an absolute measurement of the energy expenditure for exercise training, "the talk test," which is a subjective measure, can be a simple and effective method for exercise-intensity measurement.<sup>42)43</sup> As the name suggests, the talk test measures the exercise intensity based on the patient's ability to talk during exercise. This method has the advantage of being easy to measure. Moreover, it can be determined by the patients themselves when they continue to exercise in the community setting.

Along with aerobic exercise, muscle-strengthening exercise as an anaerobic exercise should be added to exercise training at a tolerable intensity. In our study that examined the association of muscular fitness with HF rehospitalization in patients with HFrEF, knee extensor muscle power was a more powerful prognostic factor than knee extensor maximal isometric contraction, the traditional method of measuring knee extensor fitness (unpublished data). In particular, inspiratory muscle training may be beneficial for increasing inspiratory muscle strength, resulting in improved dyspnea in patients with HF.

## CARDIOPULMONARY EXERCISE TESTING (CPET) AND ITS APPLICATION IN PATIENTS WITH HF

CPET is an exercise stress test with concomitant expired gas analysis, which provides objective parameters of exercise capacity. As CPET can assess the integrated exercise responses of the cardiopulmonary, vascular, and skeletomuscular systems, it can reveal abnormalities that are not apparent in a resting state, which may reflect the underlying mechanisms of exertional dyspnea in patients with HF.<sup>44)</sup> HF is a prototype of exercise intolerance and muscle fatigue, and peak VO<sub>2</sub> is related to cardiac output and skeletal muscle blood flow at peak exercise. However, the inability to appropriately increase cardiac output in HF results in insufficient perfusion to skeletal muscles, which can cause muscle fatigue.<sup>44)</sup> Chronotropic incompetence, defined as the inability of heart rate to adequately increase during exercise, has been observed in 20–70% of patients with HF and may contribute to exercise intolerance. Beta-receptor downregulation or myocardial beta-adrenergic receptor desensitization in the state of increased circulating catecholamine is one of reasons for this derangement.<sup>45)</sup> Numerous studies showed that a peak VO<sub>2</sub> of <50% of the predicted value or peak VO<sub>2</sub> <14 mL/kg/min was the strongest predictor of cardiac events in patients with HF.<sup>46)</sup> Taken together, CPET has an important role in the assessment of functional capacity,

disease severity, and prognosis in patients with HF. According to our previous study, CPET is a relatively safe and useful modality for assessing exercise capacity, even for the elderly South Korean population with underlying cardiovascular diseases.<sup>47)</sup>

## **IS EXERCISE-BASED CR SAFE IN HF?**

Patients with HFrEF (left ventricular ejection fraction <35%) have been considered a high-risk group, with risk stratification conducted by doctors before participation in an exercise program for CR. Because of the stereotype that exercise can be dangerous for patients with HF, many physicians still do not recommend exercise-based CR to patients with HF. However, most studies have found no evidence suggesting that exercise training causes harm in terms of an increased risk of all-cause death in patients with chronic stable HF. In the 1980s–1990s, studies on exercise-related deaths or sudden death have shown that exercise-related death or heart attack occurs in approximately 1 in 100,000 exercise hours. Exercises that require long-term high-intensity activity, such as long-distance running, are more dangerous than low-intensity activities, and the risk can be greatly reduced if medical surveillance is performed during exercise, especially with electrocardiogram monitoring. Since the 2000s, most CR centers selected subjects at a high risk for heart attack during exercise and conducted electrocardiogram monitoring during exercise. It was reported that one case occurred per 300,000 exercise hours and the mortality rate was also very small (0 to 1 case per 300,000 exercise hours).<sup>48)</sup> In particular, in elderly people with HF or physical inflexibility, body correction must be performed before exercise through a body design exercise, in which the physical conditions of the body are taken into account to avoid exercise-related accidents. Before exercise, warming up should be performed for at least 5 minutes through stretching and light walking. Exercise training is safe in elderly patients when an adapted protocol is used. Considering each patient's cardiorespiratory function, the physician should select the proper type and sequence of exercise, such as aerobic exercise and resistance training, and determine the intensity and frequency of exercise. Moreover, at the end of the exercise, muscle fatigue should be reduced by facilitating the discharge of lactic acid in the muscle through a cooling-down process.

## **CR FOR SPECIFIC SITUATIONS IN HF**

HF is a very heterogeneous disease entity. Most studies that evaluated CR in patients with HF mainly focused on chronic stable HF of NYHA functional class II or III. Therefore, the effect of exercise training in patients with acute decompensated HF, including patients with severe cardiogenic shock requiring mechanical circulatory support (MCS), also warrants investigation. In addition, a large portion of patients with HF have end-stage disease. These patients may be waiting for heart transplantation or ventricular assist device (VAD) implantation, or have already received a heart transplant or have undergone VAD implantation. As knowledge of these advanced HF management strategies is accumulating, the need for CR in these population is also increasing.

## CR in patients with acute decompensated HF

Performing exercise training during acute decompensated HF is virtually infeasible owing to severely impaired exercise tolerance. The mainstay of management in acute decompensated HF must be within guideline-directed medical therapy. However, a study has evaluated the effect of exercise training performed early after an episode of acute decompensated HF.<sup>49)</sup>

This prospective randomized study with a total of 72 participants with HFrEF showed that early exercise training after acute decompensation improved cardiac performance indices and pulmonary function in patients with HF. Further studies are needed to fully understand the mechanism and proper management with CR in this population.

## CR in patients with implanted VAD

In general, VADs have unique limitations for CR, such as drivelines and console equipment that limit exercise and increase the risk for anatomical alterations (e.g., diaphragm compression).<sup>50)</sup> Data about the impact of CR in patients with implanted VAD are scarce, and no guidelines describing exercise training for VAD-supported patients are available. Although the evidence of the feasibility of exercise training in patients with VAD has been reported, showing improvements in the quality of life or physical capacity,<sup>51)</sup> the effect of long-term training has not been studied. In these population, early mobilization is important because it prevents the complications of muscle deconditioning and facilitates independence.<sup>52)</sup> Thereafter, it is important to rule out any contraindications to exercise and to start exercise only after overcoming troublesome situations.<sup>53)</sup> A randomized trial, the Rehab-VAD trial, showed within-group improvements in functional capacity and life quality questionnaire scores in the CR arm, and the results were significantly different from those in the usual care group.<sup>54)</sup> According to a recent review, exercise training is feasible in patients with VAD, but appropriate screening is crucial to avoid complications.<sup>53)</sup> Nevertheless, more robust data are needed to increase the utility of CR in VAD-supported patients.

## **CR** in patients with MCS

The feasibility and effectiveness of CR in patients with MCS is more uncommon than in patients with implanted VAD. CR during MCS therapy (e.g., venous-arterial extracorporeal membrane oxygenation [ECMO] or central VAD via a sternotomy) is challenging. If possible, early mobilization can be beneficial for selected patients with MCS who are waiting for recovery or heart/lung transplantation. In a case report, early rehabilitation during ECMO was prescribed to facilitate recovery in a patient with chronic thromboembolic pulmonary hypertension.<sup>55)</sup> If the patient can tolerate MCS therapy and is awake without any other disability, exercise training (e.g., bedside cycling) can prevent deconditioning and enhance psychological well-being. Likewise, more promising investigations on CR in this population are awaited.

## CR in patients who had received a heart transplantation

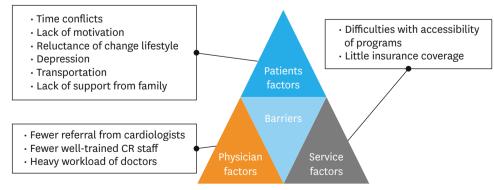
A body of evidence is available on the role of CR in heart transplant recipients. Despite the improvement in hemodynamic status after heart transplantation, the exercise capacity of these patients is still poor when compared with that of their sex- and age-matched healthy counterparts.<sup>56)</sup> Because reduced exercise tolerance in heart transplant recipients is associated with reduced survival,<sup>57)</sup> improving exercise capacity is a major goal after heart transplantation. Among the several evidences, a recent prospective randomized trial demonstrated that high-intensity training was safe and efficient for improving exercise capacity in heart transplant recipients.<sup>58)</sup> Peripheral adaptation was suggested to be the main mechanism of improvement of exercise capacity (e.g., peak oxygen uptake).<sup>59)</sup> However, as chronotropic incompetence due to the cardiac denervation effect after heart transplantation is one of the major limiting factors to poor exercise capacity, transplant recipients with more evidence of cardiac reinnervation (e.g., enhanced maximal heart rate response during exercise) have been demonstrated to respond more to exercise training than those without cardiac reinnervation.<sup>60)</sup> These evidences indicate that both central and peripheral adaptations are important, and that exercise training can improve the and exercise capacity after heart transplantation.

## ALTERNATIVE MODELS OF CR DELIVERY

Rehabilitation programs are usually introduced as "physician-supervised" models. Traditionally, CR consists of 3 phases: inpatient, outpatient, and maintenance phases.<sup>61</sup> Phase I and II are usually executed under supervision, and phase III is considered to be a lifelong phase of CR in which the patient continues regular exercise and self-management. Along with the conventional center-based CR model, there is growing evidence of alternative models of CR delivery, including home-based CR and electronic device- or mobile technology-based models.<sup>4)</sup> Electronic device- or mobile technology-based models are now widely used, and they enable remote monitoring either alone or in combination with center-based CR. Together with these types of models, the home-based CR model can provide patient-centered management; however, the participants need to be educated and encouraged to adhere to the instructions of clinicians and training specialists. As home-based CR has the advantages of accessibility and cost-effectiveness, it is promising that well organized protocols can be applied in this homebased setting. A recent systematic review demonstrated that home-based CR seems to be similarly effective for improving clinical outcomes and quality of life in patients with coronary artery disease or HF.<sup>62</sup> Moreover, a randomized trial in patients with chronic HF showed that home-based CR increased the peak VO<sub>2</sub>, quality of life score, and 6-minute walking distance, and reduced hospital readmission compared with the control group.<sup>63</sup> In this regard, further long-term studies are still needed to provide solid evidence.

## **POSSIBLE BARRIERS TO CR IN HF**

Despite concrete evidence supporting the above-mentioned clinical benefits, the participation rates in CR among patients with HF remain low, ranging from 14% to 43% worldwide with high dropout rates after enrollment,<sup>4)5/740)15)20)2330)</sup> and limited data are available in South Korea. In a recent report on CR in patients who were discharged after treatment in the intensive care unit, patients with HF had lower CR participation rates than patients with atrial fibrillation, acute myocardial infarction, and post-cardiac surgery patients.<sup>64)</sup> These low participation rates have been attributed to several barriers, including patient factors, professional factors, and service factors (**Figure 3**).<sup>65)</sup> The most effective method for increasing the CR participation rates is automatic referral of patients with HF to a CR program before discharge. Moreover, a nurse-led follow-up CR program should be linked with the self-care HF program. Another means to increase the CR participation rates in patients with HF is a smartphone-based CR program. Limited data related to CR in patients



**Figure 3.** Barriers to CR. CR = cardiac rehabilitation. with HF are available in Korea, and both physicians and patients have a low-level awareness about the importance and necessity of CR. The medical fees for CR are usually covered by the national health system, and this poses a realistic barrier in that the demand and profit may not be high enough to operate CR centers. Contrary to this reality, patients with HF in South Korea show high usage of internet and interest in mobile health technology,<sup>66</sup> and smartphone-based cardiac telerehabilitation programs are expected to develop in high-demand areas. As the telemonitoring method using wearable devices has been recently approved for insurance coverage in Korea, it is expected that telerehabilitation programs using such medical devices will also be widely performed in the near future.

# CURRENT STATUS OF CR IN SOUTH KOREA AND PERSPECTIVES

CR has become recognized as a significant component in the continuum of care for cardiovascular patients because its effectiveness, safety, and recommendation level are established worldwide; however, the actual rate of participation in CR is very low owing to various interfering causes. The motivation for participating in CR and for overcoming the patients' barriers to CR before discharge should be provided to each patient during hospitalization. Further, for patients who have difficulty in accessing center-based CR, home-based or community-based CR programs should be provided. Currently, the number of patients with HF and the demand for CR in cardiovascular centers in Korea is increasing, particularly in the setting of HF-specific management including intracardiac device therapy, heart transplantation, and VAD therapy. As the demand increases, the interest of physicians treating patients with HF should be intensified, and efforts should be made to demonstrate the characteristics and efficacy of CR using current data. On the basis of these efforts, we hope that an appropriately developed CR system in each center will ultimately contribute to improving the health of patients with HF. As mentioned above, telerehabilitation is one of the options for this development. In conclusion, the current guidelines strongly recommend applying a CR program in all eligible patients with HF. With the domestic CR insurance that has been effective in South Korea since 2017, it is expected that the long-term prognosis of patients with HF in South Korea will be greatly improved.

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