7-14-2022

Heart Failure in Cardiac Rehabilitation: A REVIEW AND PRACTICAL CONSIDERATIONS

Steven J. Keteyian

Alexander T. Michaels

Heart Failure in Cardiac Rehabilitation

A REVIEW AND PRACTICAL CONSIDERATIONS

Steven J. Keteyian, PhD; Alexander Michaels, MD

Purpose: Exercise cardiac rehabilitation (CR) represents an evidence-based therapy for patients with heart failure with reduced ejection fraction (HFrEF) and this article provides a concise review of the relevant exercise testing and CR literature, including aspects unique to their care.

Clinical Considerations: A hallmark feature of HFrEF is exercise intolerance (eg, early-onset fatigue). Drug therapies for HFrEF target neurohormonal pathways to blunt negative remodeling of the cardiac architecture and restore favorable loading conditions. Guideline drug therapy includes β-adrenergic blocking agents; blockade of the renin-angiotensin system; aldosterone antagonism; sodium-glucose cotransport inhibition; and diuretics, as needed.

Exercise Testing and Training: Various assessments are used to quantify exercise capacity in patients with HFrEF, including peak oxygen uptake measured during an exercise test and 6-min walk distance. The mechanisms responsible for the exercise intolerance include abnormalities in (*a*) central transport (chronotropic response, stroke volume) and (*b*) the diffusion/utilization of oxygen in skeletal muscles. Cardiac rehabilitation improves exercise capacity, intermediate physiologic measures (eg, endothelial function and sympathetic nervous system activity), health-related quality of life (HRQoL), and likely clinical outcomes. The prescription of exercise in patients with HFrEF is generally similar to that for other patients with cardiovascular disease; however, patients having undergone an advanced surgical therapy do present with features that require attention.

Summary: Few patients with HFrEF enroll in CR and as such, many miss the derived benefits, including improved exercise capacity, a likely reduction in risk for subsequent clinical events (eg, rehospitalization), improved HRQoL, and adoption of disease management strategies.

Key Words: exercise prescription • exercise training • heart failure

Heart failure (HF) affects greater than 6.2 million Americans and as the population ages this number is increasing, with an estimated prevalence of 3% of the population by 2030.[1] The lifetime risk of HF is greater than one in five among patients aged 45-95 yr and risk is affected by race and sex, with African American women experiencing the highest risk.[1] Clinical risk factors for developing HF are similar to other cardiovascular diseases (CVDs) and include hypertension, obesity, diabetes, and smoking, and account for >50% of attributable risk.[2] Spending across the spectrum of the disease accounts for $30 billion annually.[3]

Author Affiliation: *Division of Cardiovascular Medicine, Henry Ford Hospital and Medical Group, Detroit, Michigan.*

The authors declare no conflicts of interest.

Correspondence: *Steven J. Keteyian, PhD, Division of Cardiovascular Medicine, 6525 Second Ave, Detroit, MI 48202 (sketeyi1@hfhs.org).*

DOI: 10.1097/HCR.0000000000000713

Exercise-based cardiac rehabilitation (CR) represents an evidence-based therapy for patients with HF with reduced ejection fraction (HFrEF).[4] This article provides a concise, minireview of the literature that focuses on important exercise testing and training/rehabilitation considerations for patients with HFrEF. It also addresses several contemporary issues unique to patients with HFrEF who participate in CR. This review does not address exercise training or CR in patients with HF with preserved ejection fraction, for such we refer readers to the review paper by Tucker et al.[5]

Heart failure is a complex clinical syndrome with symptoms and signs that result from any structural or functional impairment of ventricular filling or ejection of blood. In patients with HFrEF this occurs due to a loss of systolic function from any of a myriad of causes and is defined as an ejection fraction <40%. Clinically, patients are typically categorized across two different staging systems: American College of Cardiology/American Heart Association (ACC/AHA) stages A through D and New York Heart Association (NYHA) functional classes I through IV.[4] The ACC/AHA stages are progressive and help guide timing for implementation of guideline-directed medical therapy, with patients moving from being "at risk" of developing overt HF (stages A and B), to "symptomatic" HF (stages C and D), and finally to those with "end-stage" disease (stage D). This staging system contrasts with the NYHA classifications, which are dynamic and reflect the patient current symptom status (eg, dyspnea on exertion and early-onset fatigue). Class I represents no symptoms or limitation to ordinary activity; class II reflects mild symptoms and a slight limitation of ordinary daily activities; class III represents a marked limitation of activities due to symptoms, but no symptoms at rest; and class IV signifies symptoms even at rest. Objectively, NYHA classes broadly reflect the following resting metabolic equivalents of task (MET): class I >7 METs, class II 5-7 METs, class III ≥2-4.9 METs, and class IV <2 METs.[6]

Therapies for HFrEF primarily target neurohormonal pathways to blunt negative remodeling of the cardiac architecture and restore favorable cardiac loading conditions. Currently, the ACC has assigned a level 1 recommendation to several different classes of drugs for use in patients with chronic HFrEF, the data for each derived from large randomized clinical trials that demonstrated improvement in both morbidity and mortality.[7] The backbone of drug therapy lies with the use of (*a*) HFrEF-specific β-adrenergic blocking agents (so-called β-blockers); (*b*) blockade of the renin-angiotensin system, preferably with sacubitril-valsartan; (*c*) aldosterone antagonism; (*d*) most recently, sodium-glucose cotransport inhibition; and (*e*) a diuretic to reduce volume overload, as needed. After optimization of the aforementioned therapies, evidence also supports the use of hydralazine and nitrates in African American patients. Unfortunately, HFrEF is a progressive condition and as such, many patients develop symptoms or intolerance that is refractory to guideline-directed medical therapy, which signifies end-stage disease (stage D, class IV). Therapy

options for patients with ACC/AHA stage D HF is primarily limited to palliative measures for symptom relief; however, certain patients are candidates for advanced therapies including cardiac transplantation or surgical implant of a left ventricle assist device (LVAD).

REVIEW OF RELEVANT LITERATURE

EXERCISE TESTING

A graded exercise stress test or, preferably, a cardiopulmonary exercise test can be useful in patients with HFrEF for a variety of reasons, including collection of the needed information to optimize and guide intensity of effort during exercise training; quantifying change in cardiorespiratory fitness due to an exercise, device, or drug therapy; and measurement of exercise capacity to determine candidacy for an advanced therapy. Regarding the safety of exercise testing, Keteyian et al[8] observed in a cohort of younger patients with HFrEF (n = 2037, mean age: 59 yr) that safety is similar to that of other patients with a CVD; there were no deaths and <0.5 nonfatal, major cardiovascular events requiring hospitalization/1000 tests.

Dating back to the seminal article by Mancini et al,[9] the use of the cardiopulmonary exercise test in HFrEF is backed by >30 yr of data, much of which focused on using exercise duration, peak oxygen uptake ($\dot{V}O_{2peak}$), and percent predicted $\dot{V}O_{2peak}$ ($pp\dot{V}O_{2peak}$) to help stratify risk and determine eligibility for an advanced therapy. Concerning the latter, a cut-off for $\dot{V}O_{2peak}$ has been set at 14 $mL \cdot kg^{-1} \cdot min^{-1}$ in patients not on β-blockade therapy and 12 $mL \cdot kg^{-1} \cdot min^{-1}$ in those on a β-blocker.[10] These values, however, rely on patients achieving peak or maximal cardiometabolic stress during exercise testing, with submaximal stress associated with a respiratory exchange ratio (RER) <1.05, a value that reflects a potentially incomplete shift in skeletal muscle cellular energy production from predominately aerobic to anaerobic metabolism. Contemporary decision-making for disease severity and candidacy for advanced therapies now also include other exercise parameters,[11-13] such as (*a*) chronotropic response; (*b*) an assessment of ventilatory efficiency (slope of minute ventilation to carbon dioxide production, $\dot{V}_E/\dot{V}CO_2$ slope), which when elevated reflects alveolar ventilation-perfusion mismatch; and (*c*) the presence of an exercise oscillatory ventilation pattern, the etiology of which is not fully understood but may be associated with Cheyne-Stokes respirations seen during rest or sleep. These parameters are particularly helpful in providing for a more nuanced approach to risk stratification among patients classified as intermediate risk or those who achieve an RER <1.05.

The Figure represents a clinical decision tool used at Henry Ford Hospital, one that adapts prior work from Corrà et al[13] and Malhotra et al[14] and incorporates most of the above-identified variables. In this model a $\dot{V}_E/\dot{V}CO_2$ slope >35 and/or the presence of exercise oscillatory ventilation can shift a patient into a higher risk category, than is dictated by their $\dot{V}O_{2peak}$ or $pp\dot{V}O_{2peak}$ performance alone.[13-15]

The assessment of exercise capacity, measured as $\dot{V}O_{2peak}$ using indirect, open circuit spirometry, is important because it represents the ability of the body to transport (cardiac output) and utilize (arteriovenous O_2 difference [A-$\overline{V}O_2$Diff]) oxygen. In patients with HFrEF, $\dot{V}O_{2peak}$ is reduced by ~15-40% compared with age-matched healthy persons and typically ranges between 10-18 $mL \cdot kg^{-1} \cdot min^{-1}$.[16-18] This exercise intolerance is a hallmark feature of patients with HFrEF, often inducing a level of impairment that interferes with functional independence and activities of daily living.

Several pathophysiologic mechanisms are responsible for the reduced exercise capacity in patients with HFrEF (Table 1). These can be broadly categorized under central or local factors and pertinent information about each is briefly summarized next.

Central or Bulk Oxygen Transport

Impaired cardiac output reserve (up to 50% below normal) during exercise is due to attenuation of the increase in stroke volume,[17-19] elevated filling pressures, marked chronotropic incompetence, and reduced heart rate (HR) reserve.[19-21] Chronotropic incompetence is estimated to occur in up to ~50% of patients with HFrEF.

Exercise intolerance is also associated with abnormalities in the delivery of oxygen via the major conduit arteries (eg, femoral and brachial),[22] which includes an impaired ability of the vascular endothelium to sufficiently induce vasodilation and increase blood flow during exertion. Hambrecht et al[23] reported that both resting and the endothelial dependent increase in femoral blood flow during exercise were lower compared with age-matched controls, at −35% and −84%, respectively. Interestingly, the pulsatile sheer stress placed upon the endothelium of arterial walls, such as that which occurs during regular exercise-based CR, is likely responsible for the observed partial restoration of endothelial-dependent vasodilation.[23,24]

Local Diffusive Oxygen Transport and Oxygen Utilization

Although a reduced exercise cardiac output is typically cited as the primary reason for the exercise intolerance in HFrEF, an abnormality in microvascular (arteriole, metarteriole) diffusive function (movement of oxygen from hemoglobin in the microvascular and capillaries perfusing the skeletal muscles to the mitochondria inside the muscles) is involved as well, estimated to be up to 30% lower than healthy normals.[18,19] Additionally, the heightened or overactive neurohumoral axis that is common in patients with HFrEF is associated with elevated sympathetic activity[25]

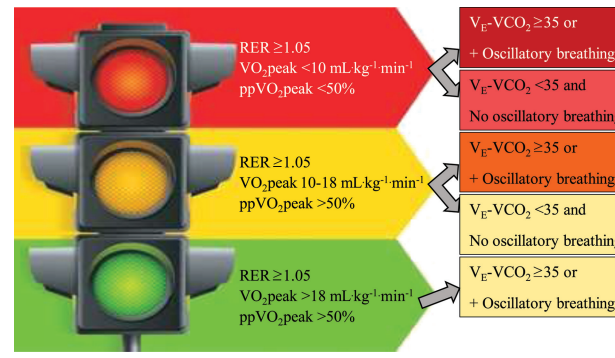

Figure. Decision algorithm used at Henry Ford Hospital for risk stratification using variables derived from a cardiopulmonary exercise test in patients with heart failure with reduced ejection fraction, adapted from Corrà et al,[13] Malhotra et al,[14] and Guazzi et al.[15] $ppVO_{2peak}$ indicates percent predicted peak oxygen uptake; RER, peak respiratory exchange ratio; V_E/VCO_2, slope line of minute ventilation to carbon dioxide production; VO_{2peak}, peak oxygen uptake. Green color associated with low risk (eg, >95% event-free survival at 1 yr) and yellow, orange, and red colors associated with intermediate and higher (eg, >10% 1-yr mortality) risk for a clinical event; the latter requiring more aggressive medical management or possible advanced surgical therapies. This figure is available in color online (www.jcrpjournal.com).

Table 1

Abnormalities in the Factors Responsible for the Transport and Utilization of Oxygen During Maximal Exercise in Patients With HFrEF (Compared With Normal)

	HFrEF	Normal
Central or bulk oxygen transport (heart and large conduit arteries)		
Cardiac output	↑/↑↑	↑↑↑
Stroke volume	↑	↑↑
Heart rate	↑↑/↑↑↑	↑↑↑↑
Peripheral artery dilation (eg, femoral artery)	↑/↑↑	↑↑↑
Local diffusive oxygen transport and oxygen utilization		
Local, metabolically mediated microvascular dilation	↑/↑↑	↑↑↑
Capillary density (capillaries per SM fiber)	↓	N
Percentage of type I aerobic or oxidative-type SM fibers	↓	N
Percentage of type II anaerobic or glycolytic-type SM fibers	↑	N
SM oxidative enzyme activity	↓↓	N
SM mitochondrial volume/density	↓↓	N

Abbreviations: HFrEF, heart failure with reduced ejection fraction; N, normal; SM, skeletal muscle; ↑, increase; ↓, decrease.

and increased plasma norepinephrine levels, both likely contributing to this microvascular dysfunction.

Another important factor is an impaired ability of the skeletal muscles to efficiently process the oxygen that it does receive during exercise. Specifically, a reduction in the percentage of type I (so-called oxidative) muscle fibers; reduced mitochondrial volume and function; a possible reduction in the ratio between capillaries and individual muscle fibers; and reductions in muscle size, strength, and endurance[20,26,27] all likely contribute to early-onset fatigue in patients with HFrEF. The mechanisms responsible for these skeletal muscle abnormalities are likely multifactorial, including (to some extent) the well-recognized increases in pro-inflammatory cytokines (eg, tissue necrosis factor-α, interleukin-6).[28]

Finally, in addition to the above central and local factors that contribute to the exercise intolerance observed in these patients, several common comorbidities are also known to be involved, including sedentary behavior, obesity,[29] and atrial fibrillation. Regarding atrial fibrillation, its prevalence varies between 10% and >40%, the extent of which is influenced greatly by the severity of the HF.[30] Among patients with HFrEF, Pardaens and colleagues[31] observed that exercise capacity (ie, $\dot{V}O_{2peak}$) was approximately 20% lower in those with atrial fibrillation (13.8 $mL \cdot kg^{-1} \cdot min^{-1}$) versus like patients in sinus rhythm (17.1 $mL \cdot kg^{-1}\ min^{-1}$).

EXERCISE-BASED CARDIAC REHABILITATION

Over the past 30 yr, literally dozens of single-site and multisite randomized trials and several meta-analyses have shown that exercise training alone and exercise-based CR improve various measures of exercise capacity, health-related quality of life (HRQoL), and clinical outcomes in patients with HFrEF. Because of such, in 2014 the Centers for Medicare & Medicaid Services expanded its coverage for CR to include Medicare beneficiaries with HFrEF.[32] The broad and systemic effects associated with exercise CR in patients with HFrEF are briefly summarized next (see also Table 2).

Exercise Capacity

Prior to 2009, numerous small, single-site trials involving patients with HFrEF showed that regular exercise training improves $\dot{V}O_{2peak}$, 6-min walk test (6MWT) distance, and exercise duration between 10% and 30%.[33,34] In 2009, the 82-site HF-ACTION trial reported that among 2331 patients with HFrEF (ejection fraction <35%) randomized to 36 sessions of supervised exercise training plus up to 1-yr of home-based exercise versus usual care, after 3 mo of exercise training, exercise duration, 6MWT distance, and $\dot{V}O_{2peak}$ were significantly (all $P < .001$) increased 1.5 min, 20 m, and 0.6 $mL \cdot kg^{-1} \cdot min^{-1}$, respectively.[35] The magnitude of the increase in $\dot{V}O_{2peak}$ was less than what is typically reported from single-site trials, likely partly due to suboptimal adherence among patients in the exercise group. Using patient-level data from eight trials, in 2019 the ExTraMATCH II Collaborative reported significant improvement in 6MWT distance (mean difference: +24.0 m; 95% CI: 5.3-42.7) at 1 yr among exercise trained patients versus controls.[36] Several studies have evaluated higher-intensity interval training in HFrEF, with the magnitude of the increase in $\dot{V}O_{2peak}$ appearing to be larger (≥2 $mL \cdot kg^{-1} \cdot min^{-1}$) in shorter-duration single-site trials[24] versus longer-duration (1 yr) multi-site trials.[37]

Improvements in exercise tolerance (ie, 6MWT distance and $\dot{V}O_{2peak}$) are likely due to a variety of mechanisms including (*a*) improved delivery of oxygen to the metabolically more active skeletal muscles (secondary to improved chronotropic responsiveness and enhanced endothelial function of the conduit arteries)[23,24,38] and (*b*) partial restoration in the ability of the metabolically active skeletal muscles to utilize oxygen—the latter due to improvement in cellular histochemistry and increased muscle strength and endurance.[39] These changes are summarized in Table 2.

Clinical Outcomes

Per the HF-ACTION trial, the combined primary endpoint of all-cause mortality or hospitalization was nonsignificantly reduced in the exercise group versus usual care (HR = 0.93: 95% CI, 0.84-1.02; $P = .13$).[35] However, following adjustment for highly prognostic, prespecified baseline characteristics, exercise training was associated with a significant 11% reduction in this same endpoint (HR = 0.89: 95% CI, 0.81-0.99; $P = .03$). A subsequent meta-analysis using individual data from patients with HFrEF (n = 3912) found no significant difference in pooled time-to-event estimates for exercise training versus controls for all-cause mortality (HR = 0.83: 95% CI, 0.67-1.04) or all-cause hospitalization (HR = 0.90: 95% CI, 0.76-1.06).[40]

Two secondary analyses from HF-ACTION are worth mentioning. First, Keteyian et al[41] showed that, among patients randomized to the exercise training arm of that trial, exercise volume (ie, MET-hr/wk) completed was a significant, independent predictor of all-cause mortality or hospitalization and cardiovascular mortality or HF hospitalization. Specifically, among patients who exercised as prescribed and completed between 3 and 7 MET-hr/wk, subsequent risk for clinical events was reduced ≥30%; 5 MET-hr/wk is equivalent to ~30 min of walking at 2 mph, 4 times/wk. Second, Swank et al[42] looked at the influence of change in cardiorespiratory fitness on risk for clinical events and reported that every 6% increase in $\dot{V}O_{2peak}$ was associated with a 5% lower risk for all-cause mortality and hospitalization (adjusted HR = 0.95: 95% CI, 0.93-0.98; $P < .001$) and an 8% lower risk of CVD mortality or HF hospitalization (adjusted HR = 0.92: 95% CI, 0.88-0.96;

Table 2

Summary of Common Physiologic and Clinical Outcomes Due to Exercise Cardiac Rehabilitation in Patients With HFrEF

Outcome	Response or Adaptation	Comment
Exercise capacity ($\dot{V}O_{2peak}$, 6MWT distance, power output or W, exercise duration)	Modest improvement typically observed across all measures of cardiorespiratory fitness	$\dot{V}O_{2peak}$ typically increased 10-20% 25- to 30-m increase in 6MWT distance
Cardiac function	Increase in peak cardiac output, with generally no change or a mild increase in peak stroke volume No change or mild increase in peak HR (up to 4-10 bpm) No change or slight increase in resting ejection fraction (3-5 percentage points)	Increase in peak HR observed most often in patients not taking β-adrenergic blockade therapy
Peripheral conduit artery (eg, brachial) function	Partial restoration or normalization of endothelial-dependent vasodilatory function	Improvements in blood flow and vascular diameter
Skeletal muscle function	Partial restoration or normalization of muscle function	Improvements in mass, strength, and endurance Improvement in mitochondrial oxidative enzyme activity
Sympathetic nervous system activity	Reduced at both rest and during exercise, as measured by muscle sympathetic nervous system activity (bursts/min)	Near normalization of resting sympathetic nerve activity Reductions in plasma norepinephrine levels at rest and during exercise
Health status and quality of life	For both the Kansas City Cardiomyopathy Questionnaire and the Minnesota Living with Heart Failure Questionnaire, consistent improvements in overall score and in most submeasures	Modest reduction in depressive symptoms
Clinical outcomes	Modest reduction in risk for all-cause and HF-specific hospitalization is likely Likely no significant effect on risk for mortality	Volume of exercise completed is associated with the magnitude of reduction in observed risk

Abbreviations: 6MWT, 6-min walk test; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; HR, heart rate; $\dot{V}O_{2peak}$, peak oxygen uptake.

$P < .001$). These two studies further strengthened the importance of engaging patients with HFrEF in a regular exercise-based CR regimen.

The saltatory effects of exercise training and CR in patients with HFrEF also extend to HRQoL and depression. Specifically, ExTraMATCH II showed that exercise training improved HRQoL, as assessed by the Minnesota Living with Heart Failure Questionnaire, versus controls (12-mo follow-up: mean improvement 5.9 points; 95% CI, 1.0-10.9; $P = .018$).[36] Additionally, depression is a common comorbidity in patients with HFrEF, and Blumenthal and coworkers[43] noted that, among patients who report clinically significant depressive symptoms, depression scores following both 3 mo and 12 mo of exercise training were significantly reduced (both $P < .05$).

PRESCRIBING EXERCISE IN PATIENTS WITH HFrEF

Overall, there are only a few differences or concerns between the exercise prescription/programming methods for patients with HFrEF and those for patients with other types of CVD. The specifics associated with these concerns are identified in Table 3 and mostly target the earlier-onset fatigue that is common in patients with HFrEF and the greater comorbid burden that these patients often experience.

The above-notwithstanding, within the context of patients with HFrEF, it is appropriate to review the general tenets associated with prescribing exercise. Specifically, since a primary reason for undertaking exercise training in patients with HFrEF is to reverse exercise intolerance, the principle of *specificity of training* dictates that large-muscle, whole-body (eg, walking and cycling) activities that stimulate the cardiorespiratory system should be employed. Additionally, three other factors (ie, intensity, duration, and frequency of effort) must be considered to impose the necessary training stimulus or overload[44,45] (Table 3). As tolerated, the clinical exercise physiologist or other exercise professional responsible for writing the exercise prescription and overseeing the patient progression needs to ensure that the volume of exercise performed each week is slowly but consistently adjusted over time.[45] For most patients with HFrEF, progressing up to the initially targeted volume of exercise (eg, 5 MET-hr/wk) will require between 1-3 wk. Duration and frequency of effort should both be progressively uptitrated before intensity.

With respect to exercise training intensity, the preferred approach for prescribing such involves the HR reserve method, which requires measured peak HR from a maximal graded exercise stress test. However, such testing is not routinely completed by most patients enrolled in CR today.[46] Should an exercise test be performed for CR or the risk stratification purposes discussed previously, the HR-based method outlined in Table 3 is applicable. In the absence of an exercise stress test, the American College of Sports Medicine recommends guiding exercise intensity at 11-14 on the Borg 6-20 rating of perceived exertion scale.[44,45]

Finally, since disorders of skeletal muscle strength, function, and endurance are common in patients with HFrEF, the incorporation of resistance training into the overall exercise regimen for selected patients is justified. Regarding such, it is prudent to consider the methods advanced for healthy individuals and patients with other CVD (Table 3).[47]

DISCUSSION AND SPECIAL CONSIDERATION

Even though CR is an evidence-based guideline recommendation for patents with HFrEF,[4] literally hundreds of

Table 3

Summary of Exercise Prescription for Patients With Heart Failure Using the FITT Principle

Training Method	*F*requency	*I*ntensity	*T*ime (Duration)	*T*ype (Modality)
Cardiorespiratory	Progress from 3 to 5 d/wk	If data from an exercise stress test is available, use HR-reserve method set at 60-80% If data from a stress test is not available, set intensity at an RPE of 11-14 (using 6-20 Borg scale)	Progressively increase to ≥30 min/session In selected patients, consider higher-intensity interval	Treadmill, free walking, cycle ergometer, dual-action seated stepper, and arm ergometer
Resistance	1-2 nonconsecutive d/wk	Begin with 40% of 1 RM for upper body lifts and 50% of 1 RM for lower body lifts; progress both to 70% of 1 RM over time Alternately, guide lift intensity by RPE, between 11 and 13 on a 6- to 20-point scale	One to two sets for each of the involved muscle groups Higher repetition and lower weight model; 10-15 repetitions/set	Use fixed weight machines, hand weights, bands/tubing, or body weight exercises Six to eight primary regional exercises

Special considerations:

- It is common for patients with HFrEF to experience early-onset fatigue during the first 1-3 wk of CR; consider starting with 10-min bouts of exercise, progressing up to the planned amount of 30-40 min/session as tolerated; progress duration before exercise intensity.
- Multiple comorbidities (atrial fibrillation, obesity, renal disease, and diabetes) are common in patients with HFrEF and as a result, attendance to CR is often interrupted because of such; reinforce with patients the importance of attending CR when they are well enough to do so.
- Frailty and marked impairments of balance, mobility, and strength are very common in patients with HFrEF; adopt a multidisciplinary approach (nursing, exercise physiology, and physical therapy) to ensure physical rehabilitation extends beyond improving cardiorespiratory fitness alone; strive to improve daily physical function, improve cognition, and reduce injuries and falls.
- For patients able to engage in higher-intensity interval training, set work intervals at 80-90% of HR-reserve or RPE of 14-15 and recovery intervals at 60-70% of HR reserve or RPE of 11-12; set ratio of work-recovery intervals at 1 min:1 min or 4 min:3 min.
- In patients with a left ventricular assist device, resistance training should be limited to bands/tubing only, avoid activities that involve trunk flexion (eg, sit-ups), and focus should be on improving leg strength with body resistance activities (eg, wall sits and toe raises). If the patient is pacemaker independent and results of recent exercise stress test are available, then an HR-based approach is appropriate to guide exercise intensity; use RPE if exercise stress test data are not available or the patient is pacemaker dependent.
- In patients with atrial fibrillation or those having undergone cardiac transplant, guide exercise intensity using RPE of 11-14 only.

Abbreviations: CR, cardiac rehabilitation; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; HR, heart rate; RM, repetition maximum; RPE, rating of perceived exertion.

thousands of patients each year do not initiate and benefit from such a therapy. For example, among the more than 397 000 Medicare beneficiaries with HF who were eligible for CR in 2017, only 2.6% completed ≥1 CR session sometime during the subsequent 12 mo; in these CR patients the average number of sessions completed was 22 and 20% completed all 36 allowable sessions.[48] This data are especially troublesome because patients with HF are often older, representing a cohort at increased risk for mortality and presenting with multiple morbidities (eg, frequent hospitalizations and frailty). As such, they are well positioned to benefit from a CR program that provides age-appropriate programming (eg, strength/balance/multi-component training, and tai chi).[49,50] We concur with the recent call-to-action that "clinicians, health care leaders, and payers should prioritize incorporating CR as part of the standard of care for patients with HF."[20]

Much of the above material has focused on the delivery of traditional CR-related care to patients with HFrEF. There are, however, other important issues that need to be considered relative to providing high-quality and contemporary patient care to patients with HFrEF in CR. These issues are addressed next.

STARTING CARDIAC REHABILITATION AND SELF-CARE DISEASE MANAGEMENT

Cardiac rehabilitation, by its very nature, delivers much of the self-care education and CVD management (eg, medication compliance) care that is known to benefit patients with HF (Table 4).[51,52] That said, the timing of enrolling patients with HFrEF into CR is hampered by Medicare policy, in that it will only pay for exercise CR sessions that are completed after the patient has waited 6 wk after an HF-related hospitalization. Although some patients may require the full 6-wk period (or more) to become clinically stable to engage in supervised exercise, many others are clinically stable, behaviorally engaged, and internally motivated and ready to start exercise CR before the 6-wk waiting period has passed. Thus, CR programs should strive to begin engaging all eligible patients with HFrEF either during their hospitalization[53] or within 2-3 wk after hospital discharge, with the plan to complete any preprogram orientation requirements and begin program-offered patient education and self-management activities so that when 6 wk after hospital discharge has elapsed, the patient can attend their first billable CR exercise session. Additionally, Davidson et al[54] incorporated a structured HF-specific disease management component into CR and at 12-mo follow-up, patients in the intervention group experienced significant reductions in all-cause hospital readmissions (44 vs 69%, $P = .01$), cardiac readmissions (24 vs 55%, $P = .001$), and all-cause mortality (7 vs 21%, $P = .03$).

ADVANCED THERAPIES

Most CR programs today enroll patients who received an advanced HF therapy, such as mechanical support (ie, LVAD) or cardiac transplant. Although the exercise training practices for these patients in CR are quite similar to those for other patients with a CVD, there are differences worth mentioning. For patients with an LVAD: (*a*) withhold exercise if seated Doppler blood pressure prior to exercise, which approximates mean arterial pressure, is <60 or > 110 mm Hg;

Table 4

Common Self-care Disease Management Behaviors for Patients With Heart Failure[a]

- Maintain compliance with any provider requested sodium restriction (eg, <2 g $\cdot$ d^{-1})
- Maintain compliance with any provider requested fluid restriction (eg, <2 L $\cdot$ d^{-1})
- Establish and reinforce a system or process for medication compliance
- Inform provider of any self-prescribed dietary supplements, including nutraceuticals
- Acquire an accurate scale for daily measurement of body weight; monitor for excessive weight change (eg, $\geq$2 lb in 1 d or 5 lb in 7 d)
- Monitor breathing for having to prop oneself up with more pillows to sleep or worsening shortness of breath while eating, talking, walking, or getting dressed
- Monitor for other signs/symptoms of worsening heart failure (eg, swelling in abdomen, less alert, and having to sleep sitting up)
- Abstain from tobacco products and recreational drugs; avoid secondhand tobacco smoke
- Establish treatment for sleep disturbance and heavy snoring, if needed
- Establish treatment for depression and anxiety, if needed
- Maintain vaccinations/immunizations (COVID-19, influenza, and pneumococcal pneumonia)
- Maintain a schedule of planned physical activity/exercise (eg, 150 min/wk of moderate-intensity exertion)
- Attend/keep all scheduled in-person or telehealth appointments with providers

[a]Adapted from Heindenreich et al,[4] Ades et al[51] and Riegel et al.[52]

(*b*) limit resistance training to resistance bands or light hand weights (10-15 repetitions/set); (*c*) avoid extensive trunk flexion (sit-ups, leg lifts) to both avoid a potentially harmful increase in intra-abdominal pressure and avoid infection/maintain integrity at the site where the driveline exits the skin; (*d*) limit lower body resistance exercises that target increasing leg strength to sit-to-stand activities or partial wall squats; and (*e*) extend cooldown periods and consider hydration during recovery to avoid provocation of hypotension, dizziness/orthostasis, or device low flow alarms related to blood pressure dysregulation or dehydration.[55]

Regarding patients who have undergone cardiac transplant and are clinically stable, there is no policy that they too must wait 6 wk before starting CR, but there are some unique issues pertinent to their participation. These are: (*a*) because the transplanted heart is decentralized from the autonomic nervous system, use of an HR-based approach to guide exercise intensity is not valid and should be replaced with rating of perceived exertion set at 11-14 (on a 6- to 20-point scale)[56]; (*b*) resistance training can play an important role in attenuating/reversing the losses in bone mineral content and muscle strength/endurance that often occurs among patients taking long-term corticosteroids to suppress immune function; and (*c*) like other patients with a median sternotomy, emphasize range of motion and withhold ballistic-type, upper extremity exercises until sternal healing is completed at 6-8 wk after surgery.

HYBRID CARDIAC REHABILITATION

The use of hybrid CR, which is a patient-individualized approach that utilizes a combination of both in-facility CR and the synchronized audiovisual (eg, telehealth) supervised exercise conducted at home or in the community, is gaining increased acceptance,[57-59] including among patients with stable HFrEF.[60,61] That said, because these patients can represent a cohort considered to be at some level of increased risk for experiencing a complication during exercise, clinical discretion is advised relative to ensuring the safety of exercising at home. The HF-ACTION trial demonstrated no safety concerns among patients with HFrEF[36] relative to risk for an adverse event during or within 3 hr of exercise, including among patients with an implantable cardioverter defibrillator.[62] Although prior research involving telehealth-based CR in patients with HFrEF demonstrates improvements in exercise capacity and quality of life,[60,61] additional information is needed to further address safety; its effect on clinical outcomes; best methods of delivery and role for adjunctive technology; financial viability; scalability and customizability; burden on patients and staff; and data security.[57,63]

SUMMARY

Heart failure with reduced ejection fraction is a disorder that is easily diagnosed and associated with well-defined treatment guidelines. Unfortunately, however, few patients with HFrEF enroll in CR and as such, many partially or fully miss the benefits garnered from an evidence-based guideline therapy. Such benefits include improved exercise capacity, a likely reduction in risk for subsequent clinical events (eg, rehospitalization), improved HRQoL, and adoption of disease management strategies.

REFERENCES

1. Benjamin EJ, Muntner P, Alonso A, et al. Heart disease and stroke statistics—2019 update: a report from the American Heart Association. *Circulation*. 2019;139(10):e56-e528.
2. Dunlay SM, Weston SA, Jacobsen SJ, Roger VL. Risk factors for heart failure: a population-based case-control study. *Am J Med*. 2009;122(11):1023-1028.
3. Cook C, Cole G, Asaria P, Jabbour R, Francis DP. The annual global economic burden of heart failure. *Int J Cardiol*. 2014;171(3):368-376.
4. Heidenreich PA, Bozkurt B, Aguilar D, et al. AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;145:e895-e1032.
5. Tucker WJ, Angadi SS, Haykowsky MJ, Nelson MD, Sarma S, Tomczak CR. Pathophysiology of exercise intolerance and its treatment with exercise-based cardiac rehabilitation in heart failure with preserved ejection fraction. *J Cardiopulm Rehabil Prev*. 2020;40(1):9-16.
6. Russell SD, Saval MA, Robbins JL, et al. New York Heart Association functional class predicts exercise parameters in the current era. *Am Heart J*. 2009;158(4 suppl):S24-S30.
7. Writing C, Maddox TM, Januzzi JL, et al. 2021 update to the 2017 ACC Expert Consensus Decision Pathway for optimization of heart failure treatment: answers to 10 pivotal issues about heart failure with reduced ejection fraction: a report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol*. 2021;77(6):772-810.
8. Keteyian SJ, Isaac D, Thadani U, et al. Safety of symptom-limited cardiopulmonary exercise testing in patients with chronic heart failure due to severe left ventricular systolic dysfunction. *Am Heart J*. 2009;158(4 suppl):S72-S77.
9. Mancini DM, Eisen H, Kussmaul W, Mull R, Edmunds LH Jr, Wilson JR. Value of peak exercise oxygen consumption for optimal timing of cardiac transplantation in ambulatory patients with heart failure. *Circulation*. 1991;83(3):778-786.
10. Mehra MR, Canter CE, Hannan MM, et al. The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: a 10-year update. *J Heart Lung Transplant*. 2016;35(1):1-23.
11. Mezzani A. Cardiopulmonary exercise testing: basics of methodology and measurements. *Ann Am Thorac Soc*. 2017;14(suppl 1):S3-S11.

12. Keteyian SJ, Patel M, Kraus WE, et al. Variables measured during cardiopulmonary exercise testing as predictors of mortality in chronic systolic heart failure. *J Am Coll Cardiol*. 2016;67(7):780-789.
13. Corrà U, Agostoni PG, Anker SD, et al. Role of cardiopulmonary exercise testing in clinical stratification in heart failure. A position paper from the Committee on Exercise Physiology and Training of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2018;20(1):3-15.
14. Malhotra R, Bakken K, D'Elia E, Lewis GD. Cardiopulmonary exercise testing in heart failure. *JACC Heart Fail*. 2016;4(8):607-616
15. Guazzi M, Arena R, Ascione A, Piepoli M, Guazzi MD, Gruppo di Studio Fisiologia dell'Esercizio, Cardiologia dello Sport e Riabilitazione Cardiovascolare of the Italian Society of Cardiology. Exercise oscillatory breathing and increased ventilation to carbon dioxide production slope in heart failure: an unfavorable combination with high prognostic value. *Am Heart J*. 2007;153(5):859-867.
16. Kitzman DW, Little WC, Brubaker PH, et al. Pathophysiological characterization of isolated diastolic heart failure in comparison to systolic heart failure. *JAMA*. 2002;288(17):2144-2150.
17. Peterman JE, Arena R, Myers J, et al. Reference standards for cardiorespiratory fitness by cardiovascular disease category and testing modality: data from FRIEND. *J Am Heart Assoc*. 2021;10(22):e022336. doi:10.1161/JAHA.121.022336.
18. Esposito F, Mathieu-Costello O, Shabetai R, Wagner PD, Richardson RS. Limited maximal exercise capacity in patients with chronic heart failure: partitioning the contributors. *J Am Coll Cardiol*. 2010;55(18):1945-1954.
19. Haykowsky MJ, Tomczak CR, Scott JM, Paterson DI, Kitzman DW. Determinants of exercise intolerance in patients with heart failure and reduced or preserved ejection fraction. *J Appl Physiol (1985)*. 2015;119(6):739-744.
20. Bozkurt B, Fonarow GC, Goldberg LR, et al. Cardiac rehabilitation for patients with heart failure: JACC expert panel. *J Am Coll Cardiol*. 2021;77(11):1454-1469.
21. Brubaker PH, Kitzman DW. Chronotropic incompetence: causes, consequences, and management. *Circulation*. 2011;123(9):1010-1020.
22. Sullivan MJ, Knight JD, Higginbotham MB, Cobb FR Relation between central and peripheral hemodynamics during exercise in patients with chronic heart failure. Muscle blood flow is reduced with maintenance of arterial perfusion pressure. *Circulation*. 1989;80(4):769-781.
23. Hambrecht R, Fiehn E, Weigl C, et al. Regular physical exercise corrects endothelial dysfunction and improves exercise capacity in patients with chronic heart failure. *Circulation*. 1998;98(24):2709-2715.
24. Wisløff U, Støylen A, Loennechen JP, et al. Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: a randomized study. *Circulation*. 2007;115(24):3086-3094.
25. Roveda F, Middlekauff HR, Rondon MU, et al. The effects of exercise training on sympathetic neural activation in advanced heart failure: a randomized controlled trial. *J Am Coll Cardiol*. 2003;42(5):854-860.
26. Minotti JR, Christoph I, Oka R, Weiner MW, Wells L, Massie BM. Impaired skeletal muscle function in patients with congestive heart failure. Relationship to systemic exercise performance. *J Clin Invest*. 1991;88(6):2077-2082.
27. Volterrani M, Clark AL, Ludman PF, et al. Predictors of exercise capacity in chronic heart failure. *Eur Heart J*. 1994;15(6):801-809.
28. Niebauer J. Effects of exercise training on inflammatory markers in patients with heart failure. *Heart Fail Rev*. 2008;13(1):39-49.
29. Horwich TB, Leifer ES, Brawner CA, Fitz-Gerald MB, Fonarow GC; HF-ACTION Investigators. The relationship between body mass index and cardiopulmonary exercise testing in chronic systolic heart failure. *Am Heart J*. 2009;158(4 suppl):S31-S36.
30. Anter E, Jessup M, Callans DJ. Atrial fibrillation and heart failure: treatment considerations for a dual epidemic. *Circulation*. 2009;119(18):2516-2525.
31. Pardaens K, Van Cleemput J, Vanhaecke J, Fagard RH. Atrial fibrillation is associated with a lower exercise capacity in male chronic heart failure patients. *Heart*. 1997;78(6):564-568.
32. Centers for Medicare and Medicaid Services. Decision Memo for Cardiac Rehabilitation (CR) Programs—Chronic Heart Failure (CAG-00437N). https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=270. Published 2014.
33. Keteyian SJ, Fleg JL, Brawner CA, Pina IL. Role and benefits of exercise in the management of patients with heart failure. *Heart Failure Rev*. 2010;15(6):523-530.
34. Gudjonsdottir M, Thoroddsen E, Karlsdottir AE, et al. Evaluating the benefits of exercise training in HFrEF or COPD patients: ISO-level comparison can add valuable information to VO_2peak. *J Cardiopulm Rehabil Prev*. 2020;40(6):421-426.
35. O'Connor CM, Whellan DJ, Lee KL, et al. The efficacy and safety of exercise training in patients with chronic heart failure: the HF-ACTION randomized controlled trial. *JAMA*. 2009;301(14):1439-1450.
36. Taylor RS, Walker S, Smart NA, et al. Impact of exercise rehabilitation on exercise capacity and quality-of-life in heart failure: individual participant meta-analysis. *J Am Coll Cardiol*. 2019;73(12):1430-1443.
37. Ellingsen Ø, Halle M, Conraads V, et al. High-intensity interval training in patients with heart failure with reduced ejection fraction. *Circulation*. 2017;135(9):839-849.
38. Keteyian SJ, Levine AB, Brawner CA, et al. Exercise training in patients with heart failure: a randomized controlled trial. *Ann Internal Med*, 1996;124(12):1051-1057.
39. Duscha BD, Schulze PC, Robbins JL, Forman DE. Implications of chronic heart failure on peripheral vasculature and skeletal muscle before and after exercise training. *Heart Fail Rev*. 2008;13(1):21-37.
40. Taylor RS, Walker S, Smart NA, et al. Impact of exercise-based cardiac rehabilitation in patients with heart failure (ExTraMATCH II) on mortality and hospitalisation: an individual patient data meta-analysis of randomised trials. *Eur J Heart Fail*. 2018;20(12):1735-1743.
41. Keteyian SJ, Leifer ES, Houston-Miller N, et al. Relation between volume of exercise and clinical outcomes in patients with heart failure. *J Am Coll Cardiol*. 2012;60(19):1899-1905.
42. Swank AM, Horton J, Fleg JL, et al. Modest increase in peak VO_2 is related to better clinical outcomes in chronic heart failure patients: results from heart failure and a controlled trial to investigate outcomes of exercise training. *Circ Heart Fail*. 2012;5(5):579-585.
43. Blumenthal JA, Babyak MA, O'Connor C, et al. Effects of exercise training on depressive symptoms in patients with chronic heart failure: the HF-ACTION randomized trial. *JAMA*. 2012;308(5):465-474.
44. American College of Sports Medicine. *ACSM's Guidelines for Exercise Testing and Prescription*. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2018:145-152, 239.
45. Squires RW, Kaminsky LA, Porcari JP, Ruff JE, Savage PD, Williams MA. Progression of exercise training in early outpatient cardiac rehabilitation: an official Statement from the American Association of Cardiovascular and Pulmonary Rehabilitation. *J Cardiopulm Rehabil Prev*. 2018;38(3):139-146.
46. Pack QR, Shea M, Brawner CA, et al. Exercise prescription methods and attitudes in cardiac rehabilitation: a national survey [published online ahead of print February 18, 2022]. *J Cardiopulm Rehabil Prev*. doi:10.1097/HCR.0000000000000680.
47. Williams MA, Haskell WL, Ades PA, et al. Resistance exercise in individuals with and without cardiovascular disease: 2007 update. *Circulation*. 2007;116(5):572-584.
48. Keteyian SJ, Jackson SL, Chang A, et al. Tracking cardiac rehabilitation utilization in Medicare beneficiaries—2017 update [published online ahead of print February 8, 2022]. *J Cardiopulm Rehabil Prev*. doi:10.1097/HCR.0000000000000675.
49. O'Neill D, Forman DE. Never too old for cardiac rehabilitation. *Clin Geriatr Med*. 2019;35(4):407-421.
50. Baldasseroni S, Pratesi A, Francini S, et al. Cardiac rehabilitation in very old adults: effects of baseline functional capacity on treatment effectiveness. *J Am Geriatr Soc*. 2016;64(8):1640-1645.
51. Ades PA, Keteyian SJ, Balady GJ, et al. Cardiac rehabilitation exercise and self-care for chronic heart failure. *JACC Heart Fail*. 2013;1(6):540-547.
52. Riegel B, Moser DK, Anker SD, et. al. State of the science: promoting self-care in persons with heart failure: a scientific statement

from the American Heart Association. *Circulation*. 2009;120(12):1141-1163.
53. Kitzman DW, Whellan DJ, Duncan P, et al. Physical rehabilitation for older patients hospitalized for heart failure. *N Engl J Med*. 2021;385(3):203-216.
54. Davidson PM, Cockburn J, Newton PJ, et al. Can a heart-failure specific cardiac rehabilitation program decrease hospitalizations and improve outcomes in high-risk patients? *Eur J Cardiovasc Prev Rehabil*. 2010;17(4):393-402.
55. Kerrigan DJ, Cowger JA, Keteyian SJ. Exercise in patients with left ventricular devices: the interaction between the device and patient and acute and chronic exercise training responses. *Prog Cardiovasc Dis*. 2022;70:33-39.
56. Keteyian S, Ehrman J, Fedel F, Rhoads K. Heart rate-perceived exertion relationship during exercise in orthotopic heart transplant patients. *J Cardiopulm Rehabil*. 1990;10:287-295
57. Keteyian SJ, Ades PA, Beatty AL, et al. A review of the design and implementation of a hybrid cardiac rehabilitation program: an expanding opportunity for optimizing cardiovascular care. *J Cardiopulm Rehabil Prev*. 2022;42(1):1-9.
58. Beatty AL, Brown TM, Corbett M, et al. The Million Hearts Cardiac Rehabilitation Think Tank: accelerating new care models. *Circ Cardiovasc Qual Outcomes*. 2021;14(10):e008215.
59. Thomas RJ, Beatty AL, Beckie TM, et al. Home-based cardiac rehabilitation: a scientific statement from the American Association of Cardiovascular and Pulmonary Rehabilitation, the American Heart Association, and the American College of Cardiology. *J Cardiopulm Rehabil Prev*. 2019;39(4):208-225.
60. Piotrowicz E, Pencina MJ, Opolski G, et al. Effects of a 9-week hybrid comprehensive telerehabilitation program on long-term outcomes in patients with heart failure: the Telerehabilitation in Heart Failure Patients (TELEREH-HF) randomized clinical trial. *JAMA Cardiol*. 2020;5(3):300-308.
61. Hwang R, Bruning J, Morris NR, Mandrusiak A, Russell T. Home-based telerehabilitation is not inferior to a centre-based program in patients with chronic heart failure: a randomised trial. *J Physiother*. 2017;63(2):101-107.
62. Piccini JP, Hellkamp AS, Whellan DJ, et al. Exercise training and implantable cardioverter-defibrillator shocks in patients with heart failure: results from HF-ACTION (Heart Failure and A Controlled Trial Investigating Outcomes of Exercise TraiNing). *JACC Heart Fail*. 2013;1(2):142-148.
63. Thomas RJ, Petersen CE, Olson TP, Beatty AL, Ding R, Supervia M. Asynchronous and synchronous delivery models for home-based cardiac rehabilitation: a scientific review. *J Cardiopulm Rehabil Prev*. 2021;41(6):407-412.