Exercise and Heart Failure: A Statement From the American Heart Association Committee on Exercise, Rehabilitation, and Prevention

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AHA Scientific Statement

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I. Introduction

Heart failure (HF) may be defined as the inability of the heart to meet the demands of the tissues, which results in symptoms of fatigue or dyspnea on exertion progressing to dyspnea at rest. The inability to perform exercise without discomfort may be one of the first symptoms experienced by patients with HF and is often the principal reason for seeking medical care. Therefore, exercise intolerance is inextricably linked to the diagnosis of HF. It might be expected that a tight relationship would exist between indices of resting ventricular function and exercise capacity. Data indicate, however, that indices of resting ventricular function (such as ejection fraction [EF]) are only weakly correlated to exercise tolerance.[1]

Exercise intolerance is defined as the reduced ability to perform activities that involve dynamic movement of large skeletal muscles because of symptoms of dyspnea or fatigue. Many investigators have sought mechanisms to explain the source of exercise intolerance. The aims of this position statement are to review (1) factors that affect exercise tolerance, with specific emphasis on chronic HF due to systolic dysfunction; (2) data that support the role of exercise training in chronic systolic HF, including the risks and benefits; (3) data on exercise training in patients with HF due to diastolic dysfunction; and finally (4) the subgroups of patients with HF for which data are lacking, and (5) the subgroups of patients who should not be included in exercise training programs. We anticipate this report will stimulate appropriate use of exercise training in patients with HF when indicated and encourage further studies in those areas in which data are lacking.

II. Factors Affecting Exercise Tolerance

Cardiovascular

The capacity for performing aerobic exercise depends on the ability of the heart to augment its output to the exercising muscles and the ability of these muscles to utilize oxygen from the delivered blood. Thus, maximal oxygen uptake ($\dot{V}O_2max$) = cardiac output × arteriovenous oxygen difference. The increase in cardiac output during maximal upright exercise is typically 4 to 6 fold in healthy subjects. This is accomplished by a 2- to 4-fold increase in heart rate and a 20% to 50% augmentation of stroke volume. The stroke volume increase is accomplished both by use of the Frank-Starling mechanism to maintain left ventricular (LV) end-diastolic volume and by more complete LV emptying to reduce end-systolic volume. Both enhanced LV contractility and peripheral vasodilation contribute to the more complete LV emptying observed during exercise (see Figure, A).

Cardiovascular disease has obvious limiting effects on the ability of cardiac output to increase during exercise, but age, sex, and conditioning status also modify this response. With advancing age, maximum heart rate declines by ≈1 bpm/y. In contrast, age seems to have a relatively small effect on maximal exercise stroke volume. In the Baltimore Longitudinal Study of Aging,[2] volunteers were screened carefully by exercise ECG and thallium scans to exclude silent coronary heart disease. Stroke volume during exhaustive upright cycle ergometry was unaffected by age, even into the ninth decade of life.[2] With aging, however, the heart is less able to reduce LV end-systolic volume and relies instead on greater enhancement of preload.

At any given age, women have a lower aerobic capacity than men. Although this difference between the sexes is explained largely by the lower blood hemoglobin level and reduced peripheral oxygen extraction[3] in women, maximal stroke volume is also somewhat lower in women than men, even after normalization for body size in some studies.

Endurance-trained individuals typically demonstrate 10% to 50% higher aerobic capacity than their sedentary peers matched for age and sex. This enhanced aerobic capacity is accomplished to a similar extent by a larger stroke volume

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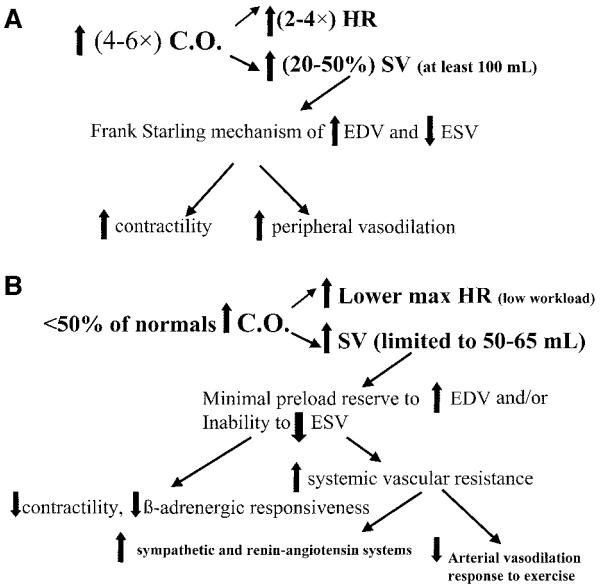

Mechanisms to augment cardiac output (C.O.) in (A) healthy persons without HF and (B) patients with HF. $\dot{V}O_2max = C.O. (HR \times SV) \times \Delta A-V)O_2$. C.O. indicates cardiac output; HR, heart rate; SV, stroke volume; $\Delta A-V)O_2$, arteriovenous oxygen difference; EDV, end-diastolic volume; and ESV, end-systolic volume. See text.

and increased arteriovenous oxygen difference.[4,5] The augmentation of stroke volume in trained subjects is attributable primarily to a larger end-diastolic volume, although enhanced systolic emptying may also contribute to this finding.[5,6] Maximal heart rate, however, is not significantly affected by training status.

A hallmark of HF is a reduced ability to perform aerobic exercise. This reduction in aerobic capacity seems to be largely mediated by inadequate blood flow to active skeletal muscle secondary to impaired cardiac output.[7,8] Patients with HF may achieve <50% of the maximal cardiac output attained by healthy individuals at peak exercise. Stroke volume, which is already decreased at rest, rises only modestly up to a peak of 50 to 65 mL, compared with ≥100 mL in healthy subjects (see Figure, B). The inability to increase cardiac output is related primarily to the minimal increase in stroke volume coupled with a lower maximal heart rate achieved at a lower workload.[8] In the dilated LV and with reduced resting LV systolic function, stroke volume typically increases only modestly during exercise because of a blunted ability to increase both LV preload and EF.[8,9] The reduced ability to augment LV end-diastolic volume is explained by the fact that the already dilated LV is operating near its maximal volume and has thus exhausted most of its preload reserve. Some studies, however, have shown acute exercise-induced increases in LV preload in patients with HF, particularly those with coronary artery disease.[10] The failure to increase LV systolic emptying and thus augment LVEF derives from a combination of impaired intrinsic contractility, reduced β-adrenergic responsiveness, elevated systemic vascular resistance due to increased activity of the sympathetic and renin-angiotensin systems, and a blunted peripheral arterial vasodilator response to exercise. In patients with coronary artery disease, stroke volume may fall during exercise if myocardial ischemia develops as a result of excessive myocardial oxygen demand. Mitral regurgitation is often present during exercise in patients with HF and systolic dysfunction because of dilation of the mitral annulus. This exercise-related mitral regurgitation reduces forward stroke volume but can be attenuated with vasodilators and diuretics.[11]

Thus, the primary means to augment cardiac output in patients with HF is by cardioacceleration. Whereas maximal heart rate is usually only mildly reduced in patients with HF, heart rate reserve (ie, the degree of heart rate augmentation above resting values) is blunted more substantially because of the elevated resting heart rate. Nonetheless, patients with HF achieve a lower heart rate at maximal exercise although the slope of increase in heart rate is nearly identical to that of people without HF.[8] A strong correlation exists between the degree of impairment in aerobic capacity and the reduction in maximal cardiac output.[7,8] These alterations in hemodynamics parallel a low peak $\dot{V}O_2$ when compared with healthy persons, eg, 10 to 20 mL · kg^{-1} · min^{-1} in HF compared with 30 to 40 mL · kg^{-1} · min^{-1} in healthy middle-aged individuals. Although optimal treatment with digitalis, diuretics, and vasodilators may enhance exercise stroke volume and cardiac output, such improvement is usually modest and may be short-lived.[12] Whereas β-blocker therapy is considered today as optimal adjunctive therapy for patients with HF, most studies noted were performed before the extensive use of these agents.

Peripheral

An appreciation for the role of peripheral factors in explaining exercise intolerance in HF, including abnormalities of endothelial function, ergoreflex activation, vasodilatory capacity, and distribution of cardiac output, has now emerged. Interest in these mechanisms has evolved because abnormalities in central hemodynamic function are not sufficient in themselves to explain exercise intolerance in HF. Commonly postulated mechanisms in support of the periphery participating in exercise intolerance in HF include: (1) Exercise capacity and measures of LV systolic function are poorly correlated[1,13,14]; and (2) central hemodynamic improvements with pharmacological therapy are rapid, but corresponding improvements in exercise capacity are delayed for weeks or months.[15,16]

Abnormalities in Blood Flow

The failure of muscle blood flow to increase normally during exercise in patients with HF is due not just to a reduction in cardiac output but also to an abnormality in peripheral vasodilation. The demonstration that peripheral vasodilatory capacity is impaired in response to an ischemic challenge (postocclusion hyperemia) was made more than 30 years ago.[17] Studies by Zelis and colleagues[17–19] demonstrated that forearm blood flow during rest and exercise was reduced in patients with HF, and this abnormality was present in response to a variety of stimuli, including isotonic and isometric exercise, adrenergic blockade, ischemia, and direct arterial vasodilation. Studies have demonstrated a failure of leg

vascular resistance to decrease normally during exercise.[20,21] This impairment in vasodilatory capacity has been attributed to excessive sympathetic stimulation causing vasoconstriction, activation of the plasma renin-angiotensin system, and higher-than-normal levels of endothelin.[22,23] An additional mechanism may involve vascular stiffness secondary to increased vascular sodium content. This is supported by the observations that the capillary basement membranes may be thickened in HF[24] and that vascular responsiveness is partially improved by diuretic therapy.[25] Angiotensin-converting enzyme (ACE) inhibition has been demonstrated to partially normalize impaired vasodilation after long-term but not short-term administration.[16,26] Improvements in leg blood flow after ACE inhibition parallel increases in exercise capacity.[26] In addition, a "vascular deconditioning" hypothesis suggests that abnormal vasodilatory capacity is related to disuse and that localized training of a specific limb may improve the vasodilatory response in HF.[27,28]

Endothelial Function

The vascular endothelium releases vasoactive substances that play an important regulatory role in peripheral vasomotor tone. Vasodilating and vasoconstricting factors, including nitric oxide, endothelins, and prostaglandins derived from the endothelium, are released in response to various chemical, pharmacological, mechanical, and exercise stimuli. A pivotal role of the endothelium in coordinating tissue perfusion has now been recognized in HF. Studies demonstrate that endothelium-dependent dilation of the forearm vasculature is impaired in HF, demonstrated by a reduction in the release of nitric oxide in response to acetylcholine.[29–31] The release of nitric oxide, an important mediator of flow-dependent vasodilation, is stimulated by exercise in healthy individuals but seems to be attenuated in patients with HF. This may contribute to a reduction in peripheral vasodilation and thus tissue perfusion. Blood flow during reactive hyperemia or exercise is reduced in response to blockade of nitric oxide synthesis.[32–34] Supplementation with L-arginine (a nitric oxide precursor) improves abnormal vasodilation in response to acetylcholine or an ischemic stimulus in HF. These observations are consistent with the concept that impaired endothelial function contributes to reduced vasodilatory capacity in HF.[35] The impairment in endothelial-dependent vasodilation is correlated with the degree of exercise intolerance and severity of New York Heart Association class.[36] Exercise training has been shown to improve endothelial nitric oxide formation and endothelial-dependent vasodilation of the skeletal muscle vasculature.[37]

Muscle

Anaerobic metabolism occurs early during exercise in HF and is likely an important cause of exercise intolerance. Previous studies that used ^{31}P-MRI have demonstrated that early anaerobic metabolism occurs independently of reduced muscle blood flow.[38,39] Abnormalities in skeletal muscle metabolism occur in patients with HF when compared with healthy individuals during exercise under ischemic conditions.[40] Skeletal muscle characteristics have important ramifications on substrate and oxygen utilization during exercise. Patients with HF have shown decreases in oxidative type I fibers and increases in glycolytic type IIb fibers compared with healthy individuals.[41–43] Myosin heavy-chain type I isoforms have also been shown to be decreased in proportion to peak oxygen consumption in HF.[44] Although levels of glycolytic enzymes seem to be unchanged, levels of oxidative enzymes are decreased in HF.[42] Specifically, mitochondrial enzymes (citrate synthase and succinic dehydrogenase) and enzymes involved in β-oxidation of fatty acids (3-hydroxyl CoA dehydrogenase) have been shown to be decreased. Sullivan et al[45] found an inverse relationship between oxidative enzyme activity and blood lactate accumulation during submaximal exercise. Drexler et al[43] demonstrated a close relationship between cytochrome *c* oxidase, mitochondrial volume density or cristae surface density, and peak $\dot{V}O_2$. Although some studies report capillary rarefaction as a contributing mechanism to exercise intolerance, these findings are inconsistent and suggest only that subpopulations of patients with HF have abnormal skeletal muscle capillary density.[41,43,46] It is possible that patients with HF who have severely compromised aerobic capacities may have a maladaptive angiogenic response to exercise, thereby increasing capillary density before other skeletal muscle changes, as suggested by Duscha et al.[47] Together, these findings suggest that alterations in skeletal muscle may contribute to abnormal oxygen extraction or substrate delivery/utilization and may further limit exercise tolerance in HF.

Distribution of Cardiac Output

Exercise tolerance depends not only on the capacity of the cardiopulmonary system to deliver oxygen to the working muscle, but also on regional flow, ie, the capacity of the vasculature to redistribute cardiac output to the muscle during exercise. In healthy subjects, as much as 85% of the cardiac output is redistributed to the muscle at high levels of exercise. Although some evidence suggests that muscle blood flow is reduced in parallel to the reduction in cardiac output in HF,[48] several studies have demonstrated the reduction in flow to the muscle during exercise occurs to a degree out of proportion to the reduction in cardiac output. Sullivan and Cobb[8] reported that the percentage of cardiac output distributed to both lower extremities during maximal exercise was attenuated in patients with HF when compared with a group of healthy subjects, ie, 51% versus 76%. Vascular resistance in the muscle fails to decrease normally during exercise in patients with HF, and flow to the nonexercising tissues may be preferentially maintained at the expense of hypoperfusion in the exercising muscle.[20,49]

Ergoreflex Activation

A new paradigm suggests the presence of a specific signal arising from the exercising muscle (possibly including respiratory muscle) that is abnormally enhanced in HF.[50,51] These signals contribute to the abnormal hemodynamic, autonomic, and ventilatory responses to exercise that characterize HF. Afferent fibers present in the skeletal muscle are sensitive to metabolic changes related to muscular work (ergoreceptors). These receptors, which mediate circulatory adaptations occurring in the early stages of exercise, are stimulated by metabolic acidosis and are partially responsible for sympathetic vasoconstriction and an increase in heart rate.[52–55] The

TABLE 1. Controlled Trials of Exercise Training in HF That Have Shown Improvements in Peak $\dot{V}o_2$

Authors (Year of Publication)	No. of Patients	Exercise Program: Duration, wk	Exercise Program: Activity, Intensity, and Frequency	$\dot{V}o_2$ Increase, % (Outcome vs Controls)
Jette et al (1991)[56]	18	4	Mon–Fri. AM: Jog at 70% to 80% max HR for 5 min 3×/wk; calisthenics 30 min; cycle 15 min at 70% to 80% max HR. PM: Walk 30 to 60 min.	22 in group with EF <30%
Belardinelli et al (1992)[63]	20	8	Cycle at 40% peak $\dot{V}o_2$ 3×/wk.	20
Coats et al (1992)[57]	17	8	Cycle 20 min at 60% to 80% max HR 3×/wk.	18
Belardinelli et al (1995)[58]	55	8	Cycle 40 min at 60% $\dot{V}o_2$max 3×/wk.	12
Hambrecht et al (1995)[59]	22	3	Walk 10 min 6×/d at 70% $\dot{V}o_2$max 2×/wk.	31
Keteyian et al (1996)[60]	29	24	Rating of perceived exertion, 12–14. Treadmill, cycle, rowing, and arm ergometer at 60% exercise capacity for 33 min 3×/wk.	16.3
Radaelli et al (1996)[64]	6	5	Cycle 20 min 5 d/wk.	15
Dubach et al (1997)[87]	25	4	Walk 60 min 2×/d; cycle 40 min 4×/wk at 80% $\dot{V}o_2$max.	26
Tyni-Lenne et al (1997)[65]	16	8	Knee extensor: 60 repeats/min for 15 min for 8 wk (at 65% peak work rate for 4 wk and then 75% peak work rate for 4 wk).	14
Callaerts-Vegh et al (1998)[66]	17	8	Walk 1 h, 2×/d; cycle 45 min at 70% to 80% HR reserve 4×/wk.	30.9
Reinhart et al (1998)[67]	25	8	Cycle 40 min at 70% to 80% max capacity 4×/wk; walk 1 hour 2×/d.	29
Belardinelli et al (1999)[62]	99	8 (plus maintenance)	Cycle at 60% peak $\dot{V}o_2$ 3×/wk for 8 wk. Maintenance: 2×/wk for 12 mo.	18 at 2 mo; 23 at 14 mo
Taylor (1999)[68]	8	8	Train 30 min at 45% to 70% peak $\dot{V}o_2$ 3×/wk.	17.6
Sturm et al (1999)[69]	26	12 (plus maintenance)	Step aerobics and cycle at 50% capacity for 12 wk; then step aerobics 100 min/wk and cycle 50 min/wk.	23.3
Keteyian et al (1999)[70]	43	24	Treadmill, cycle, and arm ergometer at 60% to 80% max HR for 33 min 3×/wk.	14.3

HR indicates heart rate (bpm); max, maximum.

result of this enhanced ergoreflex response is hyperventilation and heightened sympathetic outflow, causing an increase in peripheral resistance and thus a decrease in muscle perfusion. Activation of these reflexes seems to be attenuated by exercise training.[50]

III. Role of Exercise Training in HF

Benefits

Exercise Capacity

The benefits of exercise training in patients with HF include an improvement in exercise tolerance as assessed not only by exercise duration but more importantly by peak $\dot{V}O_2$.[56–71] Table 1 lists randomized, parallel, or crossover training studies with definitive improvements in peak $\dot{V}O_2$. The exercise training program has varied by such factors as setting (supervised or home training), type of activity (treadmill or bicycle), duration (from 8 weeks to 3 months), and intensity (from low to moderate). One study that used primarily circuit weight training for 8 weeks elicited a modest but significant increase in peak $\dot{V}O_2$.[71] Changes in peak $\dot{V}O_2$ have ranged from 12% to 31%. Most of the improvement occurs by week 3 but can continue up to 6 months if compliance with the training program continues.[72,73] Not only is maximal exercise performance improved but also indices of submaximal exercise as measured by the 6-minute walk or the ventilatory threshold.[59] Changes in peak $\dot{V}O_2$ have been reported to be greater in patients with nonischemic than with ischemic cardiomyopathy.[60] The increases in peak $\dot{V}O_2$ have correlated with other improvements, such as an increase in muscle mitochondria[59] and decreased ventilation.[57]

A review from the European Heart Failure Training Group included randomized, controlled trials of exercise in 134 patients with chronic HF using a preset protocol designed by this group of exercise specialists.[74] The mean age was 60 years (94% male), and the mean EF was 25%. One half of the patients were classified as New York Heart Association Class II, and 48% were Class III. Cycle ergometry was used as the modality for 20 minutes 4 to 5 times per week. The intensity was set at 70% to 80% of the peak heart rate as determined by a previous exercise test. Calisthenics were added to 40% of the patients. Training lasted 6 to 16 weeks. More than one half of the patients trained at home. The benefits in terms of peak $\dot{V}O_2$ and exercise time were independent of age and sex. Those patients who underwent a combination of cycle ergometry and calisthenics derived a greater benefit in terms of $\dot{V}O_2$ improvement. The training effect also correlated with the duration of the program. No significant complications occurred in the study.

Not all trials have been favorable, however. Although not an HF trial per se, the study by Jugdutt and colleagues[75] reported in 1988 is worth mentioning. This was a nonrandomized, controlled study of patients who had suffered a Q-wave anterior wall infarction and showed significant worsening of asynergy in the exercising group when compared

with the nonexercising control group.[75] The EF dropped from 43% to 30% after 12 weeks of training. In contrast, Cannistra et al[76] reported variability in subsequent ventricular dilatation in patients who had had a myocardial infarction and were randomized to a training or a control group. Some patients dilated further, others did not change, and others demonstrated a reduction in dilatation. There was no significant difference between the trained and the nontraining group in predicting ventricular changes. Hedback and Perk[77] compared high-risk and low-risk patients after myocardial infarction and found no exercise-related complications and similar improvements in exercise tolerance for both groups.

Catecholamines

Because increased plasma catecholamines have been associated with a poor prognosis in patients with HF, investigators have measured changes in catecholamines in response to exercise training with the hopes that they would decrease. The results of these studies, however, have been variable. Kiilavuori et al[78] found a 19% drop in resting epinephrine after a 3-month training program, whereas Keteyian and colleagues[70] found no changes in resting norepinephrine after 24 weeks of training. Hambrecht et al,[79] on the other hand, described a significant drop in epinephrine levels not only at rest but also during submaximal exercise. Enhanced vagal control of heart rate variability, with a shift away from sympathetic dominance, has been documented in a small but well-designed crossover trial of 8 weeks of home training.[57] Tyni-Lenne and colleagues[80] have found that local muscle training could not only improve aerobic activity but also lower catecholamine levels. The variability in these findings may be related to the severity of disease, etiology and duration of the HF syndrome, intensity and duration of exercise training, and the presence of sympathetic activity–modulating drugs, eg, ACE inhibitors or β-adrenergic blockers.

Ventilatory Responses

Symptoms in patients with HF are related to an excessive increase in blood lactate during low exercise levels, reduction in $\dot{V}O_2$ at peak exercise, and disproportionate increases in ventilation at submaximal and peak workloads. The increased ventilatory requirement assessed by the hyperventilatory response to exercise and increase in pulmonary dead space leads to rapid and shallow breathing during exercise. Because skeletal muscles become deconditioned, one would expect the same state of deconditioning in the respiratory muscles. Exercise training has the potential to improve these abnormalities. The changes are achieved primarily through peripheral mechanisms, with little or no effect on resting LV function.

Several studies have detailed the favorable effects of exercise training on ventilatory abnormalities in HF.[57,81,82] The mechanism for the reduced ventilatory response to training is largely a delay in blood lactate accumulation, although better ventilation/perfusion matching in the lung and an attenuation of ergoreflex activation likely contribute.[50,51,81] The effect of respiratory muscle training in patients with chronic HF was examined by Mancini et al.[81] In this relatively small series of 14 subjects with chronic HF (average LVEF 22%), 8 patients completed the 3-month training program. Results were compared before and after training and compared with the 6 patients who did not complete the program. Maximal sustainable ventilatory capacity increased from 48.6 to 76.9 L/min, and maximum voluntary ventilation increased from 100 to 115 L/min. Inspiratory and expiratory respiratory muscle strength was significantly increased, as was submaximal and maximal exercise capacity. Peak exercise $\dot{V}O_2$ increased from 11.4 to 13.3 mL $\cdot$ kg^{-1} $\cdot$ min^{-1}. No change in peak $\dot{V}O_2$ occurred in the control group. The data suggest that selective respiratory muscle training improves ventilatory muscle endurance, decreases perceived dyspnea during volitional isocapnic hyperpnea, and increases maximal exercise capacity.

Endothelial Function

Both invasive and noninvasive studies have shown a significant correlation between the endothelial function of the coronary and forearm arteries in patients with coronary artery disease.[82] Thus, the response of brachial artery diameter to reactive hyperemia or acetylcholine can reflect the endothelium-dependent relaxation of arteries of similar size in other locations. On the basis of these premises, it can be hypothesized that exercise training might improve flow-dependent relaxation of peripheral arteries and that this beneficial effect can translate into an increased blood flow to skeletal muscles. Hornig et al,[83] who studied 12 patients with stable chronic HF and 7 age-matched healthy subjects, have tested this hypothesis. They measured both the diameter and blood flow velocity of the radial artery of the dominant forearm at rest, during reactive hyperemia (endothelium-dependent dilation), and during sodium nitroprusside (endothelium-independent dilation) before and after 4 weeks of daily handgrip exercise. They found that physical training involving upper-extremity skeletal muscles significantly improved the endothelium-dependent relaxation in blood vessels of the exercising arm in patients with HF. Hambrecht and colleagues[37] investigated the effects of regular aerobic exercise training in 20 male patients with EF $<$40% and found that leg blood flow during acetylcholine was enhanced compared with a nontraining control group. The improvement was attributed to an increase in endothelium-dependent vasodilation with an increase in basal NO formation.

Another study by Hambrecht and colleagues[84] demonstrated improvement in endothelium-dependent vasodilation in epicardial vessels as well as in resistance vessels in patients with known coronary artery disease. After 4 weeks of cycle training, the exercise group had a 29% increase in coronary artery flow reserve in comparison with the nonexercise control group. More trials are needed to confirm this important finding.

Myocardial Adaptations

Although an improvement in exercise capacity after exercise training seems to be mainly related to peripheral adaptations, studies have suggested a favorable effect on myocardial adaptations as well as on the outcome of exercise-induced coronary vessel adaptations. The majority of studies, however, have shown minimal or no changes in EF.[58,85,86] The seminal work of Sullivan and colleagues[86] has demonstrated

that exercise training can elicit modest improvements in stroke volume, which translates into increases in maximal cardiac output achieved at higher workloads. These changes were not paralleled by alterations in resting LVEF or resting end-diastolic or end-systolic volumes. After training, heart rate at rest and at peak exercise was reduced. MRI assessments of ventricular volumes and wall thickness by Dubach et al[87] demonstrated that a high-intensity training program failed to show any deleterious effects on LV wall thickness or ventricular volumes in a group of post–myocardial infarction patients with a mean EF of 32%.

Improvements in peak $\dot{V}O_2$ and cardiac output may also be related to increases in peak ventricular filling rate. In a group of patients with ischemic cardiomyopathy and EF of <30%, Belardinelli et al[58] demonstrated that an 8-week training program at an intensity of 60% of peak $\dot{V}O_2$ intensity improved resting peak diastolic filling rate, which correlated with increases in cardiac index during exercise. The changes noted in resting and exercise stroke volume in various studies may be related to improvements in peripheral resistance, which also lead to reductions in cardiomegaly.[79]

In patients with ischemic cardiomyopathy, a common finding is the coexistence of epicardial coronary artery stenoses with different amounts of fibrotic, ischemic, hibernating, and normal myocardial cells. This scenario seems not to represent a contraindication to exercise training, given a stable clinical picture. Evidence exists that (1) the presence of significant coronary stenoses in one or more epicardial vessels does not prevent an increase in exercise capacity with training programs; and (2) the identification of hibernating dysfunctional myocardium is associated with an increase in peak $\dot{V}O_2$ after a 10-week exercise-training program at 60% of peak $\dot{V}O_2$.[85] In this latter study, stepwise logistic regression analysis with cardiovascular events as the outcome showed that pre- to post-training change in LVEF at peak dobutamine infusion and the presence of viable myocardial segments at baseline were the variables most predictive of an increase in functional capacity with training.[85] Trained patients also experienced a higher event-free survival rate than untrained controls over a 2-year follow-up. This trend was also evident in a previous study that demonstrated that an increase in peak early filling rate assessed by Doppler echocardiography could identify patients who would benefit the most from exercise training.[58]

Survival

To date, no large-scale, randomized trials that evaluate the long-term clinical efficacy or patient survival rates of exercise training in HF have been reported. Currently published trials are single-center experiences of a small number of patients followed up for a short duration. Furthermore, published trials have predated the increasing and current use of β-blockers in HF.

An exercise regimen of short duration may fail to show any improvement in 1-year survival. Belardinelli and colleagues[62] studied the effects of a long-term (14-month) exercise-training program of moderate intensity in 99 patients with stable chronic HF of various New York Heart Association functional classes. Eighty-five percent of the patients had an ischemic etiology. One group underwent supervised exercise training at 60% of peak $\dot{V}O_2$ initially 3 times a week for 2 months, then twice a week for 12 more months. At 2 months, the percentage of both myocardial perfusion defects with improved thallium activity and reversible defects were significantly higher in trained than control patients. An improved thallium uptake was evident in 75% of trained and only 2% of untrained patients at 2 months. This trend was maintained at 14 months. In addition, cardiac events were more frequent in the control group (37 versus 17 events, $P=0.006$) and comprised 25 nonfatal events and 29 cardiac deaths. Furthermore, both the rate of hospital readmission for HF and rate of cardiac mortality were significantly lower in trained than control patients ($P=0.02$). A significant separation of survival curves was observed beyond the first year of follow-up, which confirms the results of previous studies.[74]

These promising preliminary results should stimulate a wider clinical application of exercise training in patients with stable HF. The results of this trial, however, cannot be considered proof of a mortality reduction because it was not powered to show survival differences. Nonetheless, this positive trend should provide encouragement for investigators to design a large, randomized, prospective mortality trial.

Quality of Life

Studies that address quality of life (QOL) in patients with HF participating in an exercise program are limited. In addition, the QOL measurement tools vary, and results are inconsistent. Tools that focus on symptoms such as dyspnea and fatigue as well as psychosocial status (eg, emotional function and mastery or perceived control over symptoms) are more likely to detect favorable responses to an intervention.

The commonly used "Minnesota Living With Heart Failure Questionnaire"[88] assesses disease-specific health-related QOL by including the patient's perceptions of the effects of HF and its treatment on his or her daily life; however, two randomized prospective exercise-training studies and one observational study failed to show significant improvement in QOL when utilizing this tool.[70,73,89] One did show a relation between change in total score and change in peak $\dot{V}O_2$.[70] Two of these studies demonstrated significant improvement in exercise capacity,[70,73] and the third showed a trend toward improvement.[89]

Seven other randomized, controlled studies that measured QOL in HF ranged in sample size from 25 to 99 and consisted of men aged 30 to 76 years undergoing 3 to 12 months of exercise training. Several different assessment tools were used.[62,90–95] All seven studies showed improvement in exercise capacity and in most measures of QOL in the patients randomized to exercise training. An 8-week crossover trial addressing only women used the "Sickness Impact Profile" which measures health-related QOL. These researchers showed an improvement in both QOL and exercise capacity during the exercise training phase. There was no change in the "Sense of Coherence Scale," which measures coping.[65] A nonrandomized, controlled trial of 30 men and women showed a trend toward improved QOL but significant improvement in exercise parameters.[96] In summary, there is limited research examining QOL in patients with HF who

TABLE 2. Trials of Exercise Training That Have Shown Improvements in Clinical and Biological Parameters Other Than $\dot{V}O_2$

Authors (Year of Publication)	Exercise Program	Improvement
Kiilavuori et al (1999)[78]	Cycle 30 min 3×/wk at 50% to 60% $\dot{V}O_2$max for 3 mo.	Plasma norepinephrine decreased at rest; no adverse effects on catabolic hormones
Coats et al (1992)[57]	Cycle 20 min 3×/wk at 60% to 80% max HR for 8 wk.	Improved HR variability; decreased ventilation
Belardinelli et al (1995)[58]	Cycle 40 min 3×/wk at 60% $\dot{V}O_2$max for 8 wk.	Improved indices of diastolic function
Hambrecht et al (1995)[59]	Walk 10 min 6×/d at 70% $\dot{V}O_2$max for 3 wk.	Increased muscle mitochondria volume density
Radaelli et al (1996)[64]	Cycle 20 min 5 d/wk for 5 wk.	Improved autonomic control of HR
Tyni-Lenne et al (1997)[65]	Knee extensor for 8 wk.	Increased citrate synthetase, lactate dehydrogenase; improved QOL
Belardinelli et al (1999)[62]	Cycle 3×/wk at 60% peak $\dot{V}O_2$ for 8 wk. Maintenance: 2×/wk for 12 mo.	Fewer hospital readmissions for HF and reduced mortality
Taylor (1999)[68]	Train 3×/wk for 8 wk.	Peak cardiac index increased by 10%
Keteyian et al (1999)[70]	Treadmill, cycle, and arm ergometer 33 min at 60% to 80% max HR 3×/wk for 24 wk.	Improved chronotropic response to exercise
Maiorana et al (2000)[71]	Circuit weight training for 8 wk; 1 h, 3×/wk; 55% MVC for 4 wk; 65% MVC after 4 wk.	Isotonic voluntary contractile skeletal muscle strength increased by 17.9%

HR indicates heart rate (bpm); max, maximum; and MVC, maximal voluntary contractile strength.

have participated in exercise training; however, the majority of the existing data support an improvement in QOL after training in this population. Table 2 summarizes trials that have shown improvements in clinical and biological outcomes beyond exercise function alone.

Diastolic Dysfunction and Exercise Training

Isolated diastolic dysfunction (ie, HF with normal systolic function) is now recognized as a common cause of HF and dyspnea on exertion. However, there are no adequate clinical trials with appropriate outcome end points, such as increased longevity, decreased symptoms, or improved QOL, to definitively prove the benefits of exercise training in patients with isolated diastolic dysfunction and normal systolic function. Several clinical and experimental studies, however, suggest that exercise training would be beneficial for such patients. Diastolic dysfunction is usually the consequence of aging, hypertrophy, ischemia, or some combination of these factors. Exercise training has been shown to favorably influence all of these effects.

Aging

Even in the absence of overt cardiovascular disease, indices of early diastolic function decrease with age; this decline may contribute to the increase in clinical, symptomatic diastolic dysfunction as a cause of HF in the elderly. Aging is characterized by impaired early diastolic relaxation, a decreased peak early filling rate, an increased peak atrial filling rate, and a decreased E/A ratio.[97–105] Whether exercise training improves diastolic function in older, healthy subjects is controversial, however. Fleg et al[106] found no improvement of diastolic filling in older men in response to exercise training; they reported that older men (52 to 76 years of age) with a long history of intensive endurance training had impaired early diastolic filling similar to that of their sedentary peers, and they concluded that impairment of early diastolic filling seems to be intrinsic to normative aging. Levy et al,[107] however, reported that endurance training in healthy older men (60 to 82 years of age) resulted in increased early diastolic filling and reduced atrial filling rates and suggested that this may be an important adaptation to increase stroke volume and cardiac output during exercise. Similarly, Takemoto et al[108] compared healthy, older (60±5 years of age) long-distance runners who ran an average of 45 miles per week for 15 years to age-matched sedentary individuals; the exercise group had higher indices of early diastolic filling and lower rates of late diastolic filling than the sedentary group. They concluded that the LV diastolic dysfunction associated with "normal" aging is less pronounced in those persons who are exercise trained. Because maximal oxygen consumption correlated closely with both resting and exercise measurements of early diastolic filling,[107] and both early diastolic filling and exercise capacity deteriorate with age,[101,107,108] exercise training may have some potential to counteract the functional aerobic impairment frequently observed in the elderly. None of these studies, however, addressed the issue of exercise training as therapy for symptomatic diastolic dysfunction; in all of these studies, the elderly or older subjects undergoing exercise training were considered to be healthy and/or normal.

Dynamic Versus Static Exercise: Consequences for Diastole

Exercise training alters LV geometry, and such geometric changes have the potential to affect diastolic function. The type and extent of geometric alteration depends on the specific sport[109–113] and whether the associated training requires isotonic, dynamic, or endurance training, eg, distance running or cycling, as opposed to static-type exercise, eg, weight lifting. In general, dynamic endurance training causes parallel increases in LV end-diastolic radius and wall thickness such that wall stress, as calculated by the Laplace relation, remains normal. Dynamic training also induces a relative sinus bradycardia, secondary to increased vagal tone[114] or volume-induced baroreceptor activation, which prolongs the time for diastolic filling; although unproved, this might benefit the patient with diastolic dysfunction. In contrast, static exercise training results in an increase in LV

wall thickness relative to radius, similar to the geometric changes that occur with pressure-overload hypertrophy. Several small studies have evaluated diastolic function in endurance-trained and power-trained (static exercise) athletes.[115–118] None have demonstrated abnormal diastolic function with exercise training despite increases in LV mass. Alternatively, some of these studies suggest that diastolic function may be enhanced with exercise training.[115,116]

Reversal of Pathological Hypertrophy by Exercise Training

Exercise conditioning of rats (8- to 10-week swimming program) reversed several abnormalities associated with pathological, pressure-overload hypertrophy due to renovascular hypertension, such as the LV hypertrophy (LVH)–associated decrease in myocardial actomyosin, Ca^{2+} myosin, and actin-activated Mg^{++}-myosin ATPase activities and the increase in myosin isoform V_3 content.[119] The swimming program also partially or completely reversed the LVH-associated abnormalities of cardiac function, coronary flow, and oxygen consumption.[120] A similar improvement in cardiac function was observed when swim conditioning was superimposed on the concentric LVH caused by aortic stenosis.[121]

Long-Term Exercise Training and Protection Against Hypoxic and Ischemic Injury

Myocardial ischemia may be a significant component of the clinical diastolic dysfunction syndrome. Because exercise training may increase myocardial tolerance to hypoxia and ischemia,[122] it may reduce the ischemic contribution to diastolic dysfunction. Both swimming[123] and treadmill running[124,125] seem to protect the rat heart from the contractile dysfunction associated with hypoxia and reoxygenation. Hearts from trained rats generated greater cardiac outputs and performed more work than untrained controls during hypoxia; oxygen delivery and energy production were similar between trained and untrained animals, which suggests that training resulted in more efficient myocardial energy utilization.[123,124] Similarly, exercise training seems to reduce the contractile dysfunction caused by ischemia and reperfusion, and the degree of antiischemic protection is related to the intensity of the exercise-training regimen.[126–128] Studies that use less intense training programs have not consistently observed protection from ischemia and reperfusion.[124,127,129,130]

In summary, in the majority of clinical and experimental studies, endurance-type exercise training has improved indices of diastolic function in elderly and younger humans and in rats with LVH. Thus, exercise training may have beneficial potential in clinically significant, symptomatic diastolic dysfunction. Such clinical benefit remains unproved, however. This issue is confounded by the fact that many patients with diastolic dysfunction have mildly to severely limited exercise tolerance that may impair their ability to achieve conditioning. Until definitive clinical trials are performed, a reasonable policy is to recommend endurance-type exercise training, initially with careful supervision, and with the caveat that training intensity is monitored to avoid excessive dyspnea or pulmonary congestion. The safety of resistance training in such patients has not been studied. Patients with diastolic dysfunction secondary to hemodynamically significant aortic stenosis should not undergo exercise training until the stenosis is corrected.

Valvular Disease

Exercise training has no therapeutic role in patients with HF in the setting of severe stenotic or regurgitant valvular heart disease. Such patients should be evaluated and treated according to the recommendations of the American College of Cardiology (ACC)/American Heart Association (AHA).[131]

At present, no data support the safety and efficacy of exercise training in those patients with HF and mild to moderate stenotic or regurgitant valvular disease. If HF is determined to be secondary to valvular disease, exercise training should be postponed, and these patients should be treated according to the ACC/AHA Guidelines for the Management of Patients with Valvular Heart Disease.[131]

Patients with dilated cardiomyopathy often have secondary mitral regurgitation. No data specifically evaluate the clinical outcome and LV responses to exercise training in such patients. Of the 20 studies on exercise training in patients with chronic HF listed in Table 3,[37,56–62,74,86,89,90,96,132–138] most do not mention the presence of mitral regurgitation in their patient populations.[56,57,59,60,74,75,89,90,96,132–138] Other studies specifically exclude patients with significant mitral regurgitation.[37,86] In 2 studies that included patients with mild to moderate mitral regurgitation,[54,61] no separate analysis of their outcome is provided.

Data on the effects of acute exercise on LV geometry, volume, and ejection performance in patients with mitral regurgitation are also limited. Furthermore, the few studies that examined effects of acute exercise on mitral regurgitation have yielded variable results.[139–146] Although some studies report a decrease in regurgitant volume with acute isotonic exercise,[139,142,144] others show either an increase[143] or no change in the regurgitant volume and fraction.[147,140,141] Thus, there seems to be a wide spectrum of responses to acute bouts of exercise in patients with mitral regurgitation. The considerable variability of the reported changes may be due, at least in part, to the differences in patient populations. For example, in one study of asymptomatic patients with mitral regurgitation, mild LV dilation, and normal EF,[146] the changes in EF and ventricular volumes during acute exercise were similar to those of healthy controls. In contrast, symptomatic patients[141] and those with ventricular dilation[146] failed to increase LVEF during exercise. On the basis of the available information, it remains uncertain if exposure to chronic exercise during training can lead to a worsening of mild to moderate mitral regurgitation. It is prudent to evaluate each patient and proceed with caution if the expected benefits of exercise training seem to outweigh the risks. Such patients should be monitored closely for worsening of symptoms and severity of mitral regurgitation.

Patients may have chronic HF after heart valve surgery because of LV dysfunction that was present preoperatively. Although specific data on exercise training outcomes in such patients do not exist, exercise training may be beneficial.[146] For patients with controlled HF attributable to inoperable valvular disease, the safety of exercise for conditioning

TABLE 3. Studies on Exercise Training in Chronic HF Due to Systolic Dysfunction: Adverse Events

Authors (Year of Publication)	No. of Patients	EF, %	Exercise Program: Duration, wk	Exercise Program: Intensity (% Peak HR or $\dot{V}O_2$)	Adverse Events
(1) Conn et al (1982)[132]	10	29	5 to 8	70% to 80% HR	None during training
(2) Sullivan et al (1988)[86]	12	24	16 to 24	75% $\dot{V}O_2$	Worsened HF (n=1); exhaustion (n=1)
(3) Jette et al (1991)[56]	7	24	4	70% to 80% HR	Worsened HF (n=3); ventricular tachycardia (n=1)
(4) Meyer et al (1991)[133]	12	23	6	70% to 80% HR	Worsened congestive HF (n=1)
(5) Coats et al (1992)[57]	17	19	8	70% to 80% HR	None during training
(6) Koch et al (1992)[90]	12	26	12	Individualized protocol	None during training
(7) Belardinelli et al (1995)[134]	16	31	8	40% $\dot{V}O_2$	None during training
(8) Belardinelli et al (1995)[58]	36	28	8	60% $\dot{V}O_2$	Atrial fibrillation (n=1); hypotension (n=2)
(9) Hambrecht et al (1995)[59]	12	26	24	70% $\dot{V}O_2$	Atrial arrhythmia (n=1)
(10) Keteyian et al (1996)[60]	15	21	24	60% to 80% HR	None during training
(11) Kavanagh et al (1996)[96]	15	22	52	50% to 60% $\dot{V}O_2$	None during training but worse HF (n=5) after training
(12) Kiilavuori et al (1996)[135]	12	24	24	50% to 60% $\dot{V}O_2$	Not reported
(13) Wilson et al (1996)[89]	32	23	12	60% to 70% HR	Extreme exhaustion (n=3)
(14) Demopoulos et al (1997)[136]	16	21	12	50% to 80% $\dot{V}O_2$	None during training
(15) Dubach et al (1997)[61]	12	32	8	70% to 80% $\dot{V}O_2$	None during training
(16) Meyer et al (1997)[137]	18	21	3	50% $\dot{V}O_2$	None during training
(17) European Heart Failure Training Group (1998)[74]	134	25	6 to 16	70% to 80% HR	None during training
(18) Hambrecht et al (1998)[37]	10	24	24	70% $\dot{V}O_2$	None during training
(19) Belardinelli et al (1999)[62]	50	28	52	60% $\dot{V}O_2$	None during training
(20) Hare et al (1999)[138]	9	26	11	Resistance training	None during training

HR indicates heart rate (bpm).

purposes has not been established and is not recommended. In such patients, a program of low-intensity (<50% maximum predicted heart rate or <45% heart rate reserve or peak $\dot{V}O_2$ on exercise testing) may be considered to foster physical activity, limit skeletal muscular atrophy, and promote caloric expenditure in overweight or diabetic patients.

Risks

Although many factors affect the risk of exercise, three of the most important are age, presence of heart disease, and intensity of exercise.[148] Sudden cardiac death during exercise is rare in apparently healthy individuals. Individuals with cardiac disease seem to be at a greater risk for sudden cardiac arrest during vigorous exercise (such as jogging) than are healthy individuals.[148] The incidence of major cardiovascular complications during outpatient cardiac exercise programs has been estimated to be 1 in 60 000 participant-hours.[149] The type and intensity of exercise and the use of monitoring affect incidence of sudden cardiac arrest.[150–152] In cardiac subjects, the incidence is lowest during activities that are largely controlled, such as walking, cycling, or treadmill walking. Activities performed with continuous ECG monitoring have the lowest rates of sudden cardiac arrest compared with those that are unmonitored or only intermittently monitored.[148]

Myocardial infarction is another risk associated with participation in exercise and is more likely to occur than sudden cardiac death. Exercise is a potent trigger of myocardial infarction. Approximately 4% to 20% of myocardial infarctions occur during or soon after exertion.[153–155] Physical exertion at a level of ≥6 metabolic equivalents (METS) has been reported within 1 hour of acute myocardial infarction in 4% to 7% of patients. The adjusted relative risk, however, has been found to be greater in persons who do not regularly participate in physical activity.[153,154] It is clear that the least active patients are at greatest risk for myocardial infarction during exercise and that both leisure-time physical activity and cardiorespiratory fitness have a strong inverse relationship with the risk of acute myocardial infarction during exercise.[156]

Patients with chronic HF have greater overall morbidity and mortality rates than those of healthy persons and people with most other forms of heart disease. Thus, current practice guidelines stratify those patients with HF at the highest level of risk.[148,157,158] However, on careful evaluation of 21 exercise training studies conducted in a total of 467 patients with chronic HF (Table 3), the overall adverse event rate seems to be low.[37,56–62,74,86,89,90,96,132–138] The most common events in such patients include postexercise hypotension, atrial and ventricular arrhythmias, and worsening HF symptoms. This finding points to the need for careful patient selection and follow-up. In a population of patients in which functional class often changes, it is difficult to determine whether worsening HF may be related to the frequent variability of symptoms or to the exercise program. The adverse event rates in those studies of patients with HF who performed home exercise[37,57–62,74,86,89,90,96,134–138] are also low. To date, however, no randomized trial has been designed specifically to evaluate adverse event rates relative to the level of supervi-

sion during training. Patients with chronic HF can participate in a supervised training program for a brief time to obtain instructions for self-monitoring before proceeding with a program of unsupervised exercise. A brief supervised period will serve to enhance patient confidence in his or her ability to exercise with safety.

LV remodeling is a dynamic process that occurs after acute myocardial infarction and can affect the size and shape of the LV. Questions have been raised about possible detrimental effects of regular exercise on LV remodeling in patients after myocardial infarction. One small, nonrandomized study has shown that patients with >18% asynergy after first anterior Q-wave infarction experienced a further increase in asynergy and a decrease in EF after 12 weeks of exercise training when compared with nonexercising controls.[75] However, 2 subsequent randomized controlled trials of moderate- to high-intensity exercise training patients after large myocardial infarction have not demonstrated adverse effects on regional wall motion, LV systolic function, or LV chamber dimensions after several months of exercise.[87,159] In the larger Exercise in Anterior Myocardial Infarction (EAMI) trial,[159] exercise training in patients after first anterior Q-wave infarction did not result in any significant changes in global or regional LV size for the group as a whole. Among patients with EF <40%, spontaneous global and regional LV dilatation was seen similarly in both the exercise and control groups but was not influenced by exercise training. In another study[87] of 25 patients with reduced LV function (mean EF 32%), serial LV measurements obtained from MRI indicated no detrimental effects from 2 months of moderate-intensity cycle exercise training on LV volume or EF.

Musculoskeletal injuries are common and include direct injuries such as bruises, sprains, and strains and indirect problems such as arthritis and back pain. Low-impact exercises (walking, cycling, and swimming) cause little stress on bones and joints, whereas high-impact exercises (running and aerobic dancing) cause repeated impact on the knees, ankles, and feet. Studies of injuries during exercise indicate that intensity and biomechanical impact of the activity performed are the two most important factors in determining the frequency of injuries.[148]

IV. Exercise Training Recommendations

The Agency for Health Care Policy and Research Guidelines on Cardiac Rehabilitation[160] recommended exercise training for patients with chronic stable HF. As can be noted from the review of available studies of exercise training in HF, the exercise training regimen has varied among studies from a low level to a more moderate intensity. Interval training[161] at various intensities (50%, 70%, and 80% of maximal capacity) has also been shown to be beneficial. Of interest, training intensity does not seem to directly influence the magnitude of the increase in exercise tolerance.[161] Others have chosen isolated muscle training involving major muscle groups. The setting has varied from supervision to home training. Modality has also been variable, more commonly treadmill or bicycle ergometry. Similarly, the length of the program has been as short as several weeks to as long as a year.

Because agreement on a universal exercise prescription for this population does not exist, an individualized approach is recommended. Exercise training guidelines for patients with cardiovascular disease should be followed as provided in the AHA Standards.[148] Gas exchange measurements offer an objective assessment of functional capacity and should be used when feasible to derive the exercise prescription and to monitor changes in functional status.[150] Alternatively, baseline exercise testing can be performed according to protocols that optimize the estimation of functional capacity, such as ramp protocols or others that utilize small increments in work rate. Heart rate–derived exercise prescriptions may be inaccurate in patients with more advanced disease. In these patients, chronotropic reserve may be limited. In the current era of β-blockers, heart rate alone as a measure of intensity may not be practical. The most frequently used intensity range has been 70% to 80% of peak $\dot{V}O_2$ (see Tables 1 and 3) determined from a symptom-limited (but of sufficient effort) exercise test. Very debilitated patients or those who are not accustomed to aerobic activity may need to initiate the program at a lower intensity, eg, 60% or 65% of peak $\dot{V}O_2$, and perform interval training with periods of rest. It is essential that progression be built into the prescription to allow the rehabilitation staff to adjust the exercise intensity as the patient becomes better conditioned. The Borg scale can also be quite useful in prescribing exercise intensity, especially in patients on β-blockers. The ventilatory or anaerobic threshold generally occurs at a rate of perceived exertion (RPE) of 13 to 15. RPEs of 12 to 13 are usually well tolerated by the stable patient.

Duration of exercise should include an adequate warm-up period. The warm-up period may need to be longer in the most debilitated patients. Usually, a period of 10 to 15 minutes is recommended. The exercise duration most frequently used is 20 to 30 minutes at the desired intensity (see Table 1). A cool-down period is also advised. Most studies have used 3 to 5 times per week as the optimal training frequency. Patients who develop exhaustion after training may need a day of rest between sessions. Supplemental walking should be encouraged on the nontraining days.

The need for monitoring has not been systematically studied. The studies that have been referenced have ranged from monitored to supervised to home programs without supervision. In many instances, the patient with more advanced HF has not been included in these studies. Per the recommendations of the American Association for Cardiovascular and Pulmonary Rehabilitation, the setting should be one of direct monitoring and supervision, especially during initial training sessions.[150,158] Telemetry monitoring is also recommended initially.[150,158] A supervised program would also allow for education, including advice on recognition of symptoms, nutrition guidelines, the disease process, and the importance of compliance. Home training can follow this early supervised period, which may vary from patient to patient according to the level of deconditioning and disease stability. It would be particularly prudent to monitor patients who have demonstrated exercise-induced arrhythmias and those patients with more advanced forms of HF, who to date have not been included in smaller trials. Patients who are

stable and well medicated can initiate a home program after a baseline exercise test with guidance and instructions. Frequent follow-up, which is common for this group of patients, can serve to assess the benefits of the home exercise program, determine any unforeseen problems, and advance to higher levels of exertion if lower levels of work are well tolerated.

It is not clear whether the benefits that can be obtained from exercise training are sustained should exercise be stopped. Most exercise training reports have not terminated the exercise program and reassessed functional capacity 6 months or a year later. Willenheimer and colleagues[162] randomized patients with stable HF to either an exercise program or to a control nonexercising group and assessed QOL and physical function 6 months after the termination of the exercise program. The trained patients had a decrease in habitual physical activity similar to the nonexercising control group. Therefore, there was no sustained benefit 6 months after termination of training. Only a small improvement in QOL was sustained in the exercise group.[162] It is recommended that patients with HF continue to remain active either in a formal exercise program or one at home for an indefinite period of time. It is hoped that the patients will enjoy their activity and want to continue it.

Although the safety and efficacy of resistive training has not been established in this population,[150] resistive training can offer the opportunity to strengthen individual muscle groups. Small free weights (1, 2, or 5 lb), elastic bands, or repetitive isolated muscle training can be used.[163] In addition, the upper body should not be ignored because many activities of daily living require arm work. These muscle groups are often neglected in exercise training. Resistive training benefits and rationale can be found in the AHA Science Advisory.[163] In a group of 9 patients with chronic HF, Hare et al[138] found an increase in strength and endurance associated with a lower O_2 consumption at submaximal workloads with no improvement in peak $\dot{V}O_2$. There were no safety issues during the training. A program of combined aerobic and resistance training administered as a circuit weight training program can increase voluntary contractile strength in addition to increasing peak $\dot{V}o_2$ significantly.[71] The safety of resistance training in patients with HF needs to be further established in larger trials.

Exercise Training in Patients Before and After Heart Transplantation

Before Transplantation

Candidates for transplantation are usually among the most debilitated and deconditioned patients with HF. As waiting times for transplantation increase and the level of sickness inevitably rises in the pretransplantation patient, deconditioning will play a major role in the total clinical picture. Ideally, transplantation candidates should initiate an exercise program soon after listing. In accordance with the Agency for Health Care Policy and Research Guidelines on Cardiac Rehabilitation,[160] exercise training is recommended both before and after transplantation.

The program should include both aerobic training and resistive exercise.[164,165] If the program is instituted before transplantation, the patient will be familiar with exercise modes such as range of motion and be able to reinitiate these with minimal reeducation shortly after transplantation. Inspiratory muscle training has also been shown to improve ventilatory muscle strength in a group of patients awaiting transplantation.[166] For those patients who become dependent on inotropic therapy and are listed as Status Ia or b, the same type of program can be instituted in the hospital. A set routine consisting of bicycle, treadmill, upper body ergometry, and free weights can be carried out safely in the controlled intensive care setting. The exercise intensity may need to be determined by patient symptomatology rather than by heart rate or RPE.

Left Ventricular Assist Devices

Although recent to the care of patients with advanced HF, LV assist devices (LVADs) are currently serving as viable options to bridge patients to transplantation and in the near future may be considered as destination therapy for a select group of patients. These devices should offer a unique opportunity to improve conditioning in a group of very ill patients who may have been extremely limited before implantation. In spite of the drive lines and implanted pumps, exercise training has been shown to be safe and efficacious, although published reports have included small numbers of patients. The Experience with Left Ventricular Assist Device with Exercise (EVADE) trial evaluated exercise capacity in a group of LVAD patients who had recovered after surgery and undergone rehabilitation 1 to 2 months later.[167] Peak $\dot{V}O_2$ by treadmill was 14.1 ± 2.9 mL $\cdot$ kg^{-1} $\cdot$ min^{-1} during maximal testing, and cardiac output rose from 5.0 to 7.8 L/min during exercise. None of the patients were limited by right ventricular dysfunction. The extensive experience of Morrone et al with LVADs has shown that with ambulation at 7 to 10 days after implantation and treadmill training starting on day 21, followed by 6 to 8 weeks of 20 to 30 min/d training, significantly improved functional capacity, which peaked at 6 weeks after surgery.[168]

After Transplantation

Persistently abnormal exercise capacity early after cardiac transplantation can be caused by marked deconditioning before transplantation, surgical denervation, skeletal muscle weakness, and corticosteroids.[165,169,170] Kavanagh et al[171,172] reported reduced exercise capacity after transplantation as demonstrated by a reduction in ventilatory threshold and greater minute ventilation and perceived exertion. Subsequent reports of rehabilitation programs showed improvements in peak $\dot{V}O_2$ from 16.7 to 20 mL $\cdot$ kg^{-1} $\cdot$ min^{-1} after 10 weeks of outpatient exercise training.[173] A randomized study of 27 posttransplantation patients who were assigned to either a 6-month structured exercise program or unstructured home therapy showed an 18% increase in peak $\dot{V}O_2$ in the trained group versus the non trained group. The improvement seemed to be independent of weight gain, prednisone dose, or number of rejections.[164]

Exercises can be performed in a supervised setting early and patients transferred to a home program once an adequate level of activity is achieved. A walking program is recommended for alternate days. Duration of the program can vary

from 4 to 6 weeks up to 6 months.[164] An extension of the timetable is often necessary to take into account early episodes of rejection or infection, which may preclude exercise for several days at a time. It is important to outline a progressive increase in exercise activity to account for improvement in function that may occur early in the program. The RPE at the anaerobic threshold is a useful tool to prescribe intensity because the heart rate will not be reflective of effort.[174] Warm-up and cool-down periods are essential, with a minimum of 20 minutes at the prescribed intensity. An initial low RPE of 11 to 13 will allow for the early deconditioning after surgery and take into account steroid-induced myopathy. Patients who have early rejections and are treated with additional steroids may need an extended period of low work rates. Every effort should be made to gradually increase the intensity to at least an RPE of 13 to 15 to approach the ventilatory threshold, which may also be improving with training. Patients should be encouraged to adopt exercise and activity as a way of life. Adherence to physical activity prescriptions should be monitored in a fashion similar to that of the medical regimen.

Future Research

Several areas require further research in light of the studies noted in this statement, which have involved primarily single-center trials and have included only small numbers of patients. These include the following:

(1) Do short-term benefits of exercise training in HF translate into long-term effects?

(2) Does training affect hospitalization rates as a morbidity index of disease progression?

(3) Does training improve mortality rate beyond the improvement noted with the use of ACE inhibitors and β-blockers?

(4) Does training lessen the incidence of sudden death and reduce ventricular arrhythmias?

(5) Are the physiological benefits noted in small studies applicable to the larger population of patients with HF?

(6) Are there populations of patients with HF who will not benefit from exercise training or in whom exercise training could be potentially harmful?

These questions can only be answered by large prospective randomized trials to investigate the impact of exercise as a treatment option on mortality and morbidity. Such a trial, called HF-ACTION (Heart Failure—A Controlled Trial Investigating Outcomes of exercise TraiNing), is currently being organized in the United States and Canada. A similar trial is being developed in the European continent. If both of these trials are successfully initiated and completed, they will add much-needed information in this area.

Recommendations

The Committee on Exercise, Rehabilitation, and Prevention of the American Heart Association Council on Clinical Cardiology concludes that exercise training in patients with HF seems to be safe and beneficial overall in improving exercise capacity, as measured by peak $\dot{V}O_2$, peak workload, exercise duration, and parameters of submaximal exercise performance. In addition, QOL improves in parallel to the improvements in exercise capacity. Furthermore, benefits have been reported in muscle structure and physiological responses to exercise, such as improvements in endothelial function, catecholamine spillover, and oxygen extraction in the periphery, among others. In summary, this position statement will serve as guide to health professionals to better understand the exercise limitations of the patient with HF and aid in directing their patients to engage in physical activity. Therefore, insurers and third-party payers should support exercise training programs in patients with chronic HF that follow recommendations and patient selection as discussed in this position statement.

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