Exercise, Cardiovascular Disease, and Chronic Heart Failure

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In addition to patients with coronary artery disease, high-risk patients with severe congestive heart failure can benefit from rehabilitation. Traditionally, such patients were excluded from rehabilitation, but resistive exercise, higher-intensity programs, and interval training have now been safely conducted. Emerging data indicate that exercise training results in a number of improved physiologic and psychologic indices, including neural control, quality of life, exercise tolerance, ventilatory function, skeletal muscle physiology, peripheral blood flow, and endothelial function. This review explores these beneficial outcomes through an assessment of therapeutic approaches, with special emphasis on the unique clinical characteristics of patients with congestive heart failure.

Overall Article Objective: To describe the benefits and the evolving role of cardiac rehabilitation for patients with congestive heart failure.

Key Words: Coronary disease; Heart-assist devices; Heart failure, congestive; Exercise; Rehabilitation

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OVER THE PAST 30 years, the effectiveness of rehabilitation for patients with coronary heart disease (CAD) has been established. In addition to traditional exercise, cardiac rehabilitation now includes risk factor modification and patient education. Recent literature has emphasized a variety of positive outcomes from secondary prevention programs, including improved exercise tolerance, skeletal muscle strength, psychologic status, and quality of life. Combined exercise and risk intervention programs have important implications for reduced health care costs and hospitalization. Yet, despite this volume of evidence, cardiac rehabilitation is often underutilized, especially for women.

Cardiac rehabilitation for CAD patients reduces mortality by as much as 25% in comparison with CAD patients not enrolled in such programs. Moreover, mortality rates are lower in CAD patients who receive multifactorial interventions than in those exposed to exercise only. Although the efficacy of cardiac rehabilitation in reducing morbidity is less clear, it is important to stress that exercise training does not increase morbidity. Exercise intervention has been shown to be safe, with a low rate of nonfatal cardiovascular events. In any case, cardiac rehabilitation improves function and quality of life.

Emerging evidence indicates that relatively intensive modification of lifestyle may slow or reverse CAD. The benefits of exercise in lowering CAD have confounded the contributions of dietary changes and lipid-lowering agents. The randomized trial by Niebauer et al of 113 male patients revealed that after 6 years of risk factor intervention, only improved physical work capacity independently contributed to angiographic evidence of regression in CAD lesions. It is important to note that exercise caloric expenditure in the Niebauer group's study was about 1800 kcal/wk, or nearly 4 hours of moderate physical exercise, well below the threshold of most supervised exercise intervention programs.

CHRONIC HEART FAILURE

Cardiac rehabilitation now includes higher risk patients, such as those with severe congestive heart failure (CHF). The prevalence of CHF is increasing worldwide, as indicated by the 116% increase in CHF mortality between 1929 and 1995. Experience gained through treating CAD patients can be applied to patients with severe CHF, especially those with ejec­tion fractions less than 30%, who have traditionally been excluded from rehabilitation. Despite a 6- to 9-times higher occurrence of sudden cardiac death in patients with severe CHF when compared with less severely ill CHF patients, emerging evidence demonstrates that exercise intervention is safe and effective in severe CHF.

Risk-stratification models exist for patients with severe CHF, but they are based on clinical characteristics and annual cardiovascular mortality risk, not on the risk of an exercise-induced event. The American Heart Association provides a risk-stratification model that is based on exercise event risk, and this model is useful in making decisions regarding supervision of exercise assessment and training. Although strongly associated with mortality, left ventricular dysfunction in severe heart failure is poorly related to exercise performance as measured by oxygen consumption.

Exercise does not worsen left ventricular performance in CHF. The data of Belardinelli et al suggest reduced mortality after exercise training. Moreover, emerging data indicate that exercise training is safe and that it results in improved physiologic and psychologic indices, including neural control, quality of life, exercise tolerance, ventilatory function, skeletal muscle physiology, peripheral blood flow, and endothelial function. Additionally, resistive exercise and higher-intensity programs, including interval training, have been safely conducted and are recommended as therapeutic options for CHF patients, including the elderly.

Improved fitness is attained by a combination of central (cardiac output) and peripheral (arteriovenous oxygen difference) adaptation, the latter being of fundamental importance because stroke volume and ejection fraction are reduced in the presence of CHF. A lowering of myocardial oxygen demands at equivalent workloads is achieved through improvement in peripheral circulation, oxygen extraction, and utilization in trained muscle. Increased oxidative capacity associated with skeletal muscle adaptation allows improved extraction and use of available oxygen to resynthesize adenosine triphosphate (ATP), delaying the exercise-limiting fatigue associated with excess accumulation of blood lactate. In addition, a training-
Table 1: Potential Changes Due to Exercise Training for Patients With CHF

<table>
<thead>
<tr>
<th>Increases or provides improvements in:</th>
<th>Decreases in:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measures of oxygen transport and endurance, including peak oxygen consumption, ventilatory anaerobic threshold, peak cardiac output, physical work capacity, and submaximal exercise endurance</td>
<td>Symptoms of dyspnea, fatigue, and weakness</td>
</tr>
<tr>
<td>Leg blood flow and arteriolar oxygen content</td>
<td>Submaximal exercise ventilation, carbon dioxide, and respiratory exchange ratio</td>
</tr>
<tr>
<td>Skeletal muscle aerobic enzyme activity, phosphocreatine, and ATP resynthesis</td>
<td>Neurohormonal activation and sympathetic nervous system activity</td>
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<tr>
<td>Muscle fiber size and skeletal muscle strength and endurance</td>
<td>Resting and submaximal exercise heart rate and blood lactate level</td>
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<tr>
<td>Parasympathetic nervous system activity</td>
<td>Ventricular arrhythmias</td>
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<tr>
<td>Respiratory muscle function</td>
<td>New York Heart Association functional class</td>
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<tr>
<td>Spontaneous daily activity and indices of quality of life</td>
<td>Morbidity and mortality in patients with coronary artery disease</td>
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Induced increase in blood volume and improved shunting of blood to skeletal muscle during exercise result in improved delivery of oxygen.

Improved central adaptation is also reported with exercise training in CHF. A higher rate-pressure product at the onset of ischemia has been observed, as has reduction in exercise ischemia as assessed by radionuclide technology. Central adaptation mechanisms have been postulated in explanation, including decreased blood viscosity and/or improved collateral coronary circulation, but these mechanisms remain unproven. Squires has provided an extensive compilation of evidence-based benefits of exercise training for severe CHF patients, as summarized in Table 1.

**FUNCTIONAL IMPROVEMENT AND APPLIED EXERCISE PHYSIOLOGY IN SEVERE HEART FAILURE**

A primary outcome of exercise training is improved functional reserve for safe participation in vocational and avocational activities. The ability to sustain activity is a function of oxygen consumption, cardiac output, oxygen transport, and the extraction of oxygen by active skeletal muscle, as described in the previous section. Improving functional reserve for activity is dependent on improving aerobic capacity. This is accomplished through exercise training to increase both peak oxygen consumption and the fatigue-limiting anaerobic threshold, with a lower relative oxygen cost and associated myocardial demand. Activities that were at or slightly above the anaerobic threshold become feasible after training, which is vitaly important for patients with severe CHF, who have lower peak oxygen consumption values as a result of diminished cardiac output.

Improved fitness from exercise training results in a critical reduction in heart rate and blood pressure for any specific activity. This improves the range of safety in patients with workload-induced ischemia. Clearly, the integrity of the coronary blood supply and the consequent degree of exercise-induced ischemia significantly influence the exercise profile for CHF patients. Since the myocardial demand associated with the ischemic threshold may vary for an individual patient, identification of this threshold from exercise assessment is essential for setting the safe upper limit of exercise. Through exercise, the metabolic equivalent (MET) level at which the heart rate is at anaerobic threshold increases, along with the mean arterial pressure (or rate-pressure product). This improvement in exercise capacity increases the range of functional activities in which the patient may safely engage, and it may be sufficient to permit return to work or a substantial increase in the range of tolerance of avocational activities.

Although left ventricular ejection fraction alone does not correlate well with oxygen uptake, normal right ventricular and mitral valve function are important for optimal physical performance in the presence of CHF. Additionally, patients with a low left ventricular ejection fraction increase their exercise capacity less with exercise training than do those with better myocardial function. If cardiac function were the sole limiting factor, a stronger association between exercise tolerance and left ventricular ejection fraction would be expected. The poor correlation emphasizes the importance of training in skeletal muscle adaptation in severe CHF. For patients with severely impaired cardiac output, the adaptation of skeletal muscle through exercise training can often compensate for central cardiac dysfunction.

**Approaches to Exercise Intervention for Patients With Severe CHF**

Because of the profound exercise-induced fatigue experienced by most CHF patients, the patient must be carefully prepared for exercise. Defining cardiac and noncardiac limitations to exercise is critical. Exercise programs must be complemented by optimal pharmacologic measures, nutritional support, dyspnea management (supplemental oxygen, mobilization of secretions), hemoglobin stabilization, and pain management.

Assessment of body mechanics is important in the selection of appropriate exercise modalities to lessen dyspnea or fatigue. Since recurrent or semirecumbent exercise may lead to decreased diaphragmatic excursion, lower lung volumes, increased venous return, and pulmonary edema, it is important to maintain adequate body position. Since recumbent or semirecumbent exercise may lead to decreased diaphragmatic excursion, lower lung volumes, increased venous return, and pulmonary edema, it is important to maintain adequate body position.

**Exercises (pursed-lip breathing, inspiratory muscle training, diaphragmatic breathing, inhibition of accessory muscles) because they decrease dependency on accessory muscles and the associated higher oxygen cost of ventilation.**

Not all CHF patients are appropriate candidates for exercise training. Patients should be able to speak without signs or symptoms of dyspnea (peak comfortably with a respiratory rate of less than 30 breaths/min); have no more than moderate fatigue by subjective clinical impression; have rales present in less than half of the lungs; and, for invasively monitored patients, have a cardiac index of more than 2L/min/m2 and a central venous pressure of less than 12mmHg.

CHF patients who are hospitalized for inotropic support of an exacerbation and patients with severe heart failure who are taking intravenous inotropes while awaiting heart transplantation have been involved in rehabilitation programs. Exercise to maintain and improve function can safely be prepared in this setting, with close monitoring.

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Community-based patients with stable CHF can be enrolled in outpatient cardiac rehabilitation programs. General exercise guidelines can be applied to these patients with individually designed programs that include 20 to 60 minutes of aerobic reconditioning, circuit weight training, and gentle resistive exercises. Recent studies have suggested alternative formats of exercise training. Meyer et al have shown significant improvement in exercise capacity for patients with severe heart failure after only 3 weeks of high-intensity interval training. They postulated that the improvement is associated with greater reduction in venous return and left ventricular end diastolic pressure during interval work than during continuous activity. Additionally, recent investigations suggest that endothelial function is enhanced by exercise programs approximating 60% to 70% exercise intensity.5,36

While the work of Meyer and others has expanded the options for exercise training in heart failure patients, high-intensity interval training does not facilitate weight management, which may be an important risk factor requiring modification in many patients. The most effective reduction in body mass associated with exercise occurs when the weekly volume of exercise exceeds 1200 to 1500 kcal. Interval training performed on alternate days with continuous exercise training may be the most pragmatic approach to optimizing training effect and weight control.

Role of Cardiovascular Exercise Testing in Rehabilitation of CHF

The preferred protocol for cardiovascular exercise testing for CHF patients is a modified ramped protocol of progressive exercise loads of 0.2 to 0.4 METS per 30-second stage. Patients with poor exercise tolerance should be tested with continuous protocols not exceeding 1 to 2 METS per 3 minute stage. Criteria for test termination are consistent with traditional criteria for all cardiac patients, special attention being paid to signs and symptoms associated with CHF, including dyspnea, weakness, and abnormal blood pressure responses, particularly hypotension with signs and/or symptoms of exertional intolerance. Less sophisticated exercise assessments, such as the 6-minute walk test, are useful in assessing exercise tolerance and monitoring progress during therapy.

NEW FRONTIERS IN THE REHABILITATION OF CHF

Nitric Oxide and Exercise

New understanding of the physiologic mechanisms underlying dyspnea in CHF has led to a new appreciation of the benefits of exercise training for these patients. The more we comprehend this physiology, the clearer will the goals of exercise in CHF become. Evidence shows that functional improvement from cardiac rehabilitation in CHF patients is related to improved peripheral vascular resistance and muscle metabolism, particularly the vascular flow of muscle tissue. The mechanisms of vascular dilation are partially associated with nitric oxide–mediated pathways. Measurement of urinary nitric oxide metabolites indicates that increasing systemic levels of nitric oxide are reflected in improved vascular tone. This improvement in vascular balance indicates exercise-induced normalization in the physiology of patients with CHF. As more is learned about the role of nitric oxide and other vasoactive substances in exercise training, there may be a role for interventions to be tailored to favorably alter the balance of these compounds.58

Dyspnea and Exercise

Altered pulmonary physiology in CHF plays a part in the observed symptomatic and physiologic limitations, particularly the respiratory factors that contribute to fatigue and dyspnea. The model of decreased exercise tolerance because of dyspnea in CHF is based on the mechanism of decreased cardiac output causing increased pulmonary vascular resistance and leading to interstitial and alveolar edema. This, then, impairs gas exchange and pulmonary compliance, and triggers J-fiber juxta-capillary receptors. The resulting stimulation of central nervous system receptors causes the subjective sensation of dyspnea. However, no clear correlation has been found between pulmonary wedge pressure or resting ejection fraction and dyspnea in patients with CHF.55,56 Treatments that decrease filling pressures do not alter the symptoms of dyspnea or relieve the exaggerated ventilatory response. Measures of ventilatory parameters reveal a better correlation. This constellation of findings leads to the observation that peripheral and pulmonary physiologic factors play prominent roles in dyspnea-induced exercise intolerance.

The pulmonary contribution to dyspnea lies partly in the inability of the lungs in cardiac failure to accommodate the increased blood flow that accompanies a dynamic exercise response. With exercise, there is an increase in the disparity of blood flow in the upper and lower lung fields, with a resultant increase in ventilation-perfusion mismatch.57 There is increased physiologic dead space and an increased ratio of dead space to tidal volume.55,35 These changes in blood flow are chronic, and they contribute to parenchymal changes in the lung, with the development of hypertrophy of the media in small arteries, arterioles, and pulmonary veins, and interstitial fibrosis.59 Additionally, these changes may be superimposed on pulmonary parenchymal disease in CHF patients who have a history of tobacco use, further exaggerating the pathophysiology observed in heart failure.60

Pulmonary compliance is also reduced in CHF, as a result of increased vascular stiffness associated with fluid overload. This decrease in compliance increases the work of breathing, contributing to dyspnea at all levels of activity.61 In patients with obstructive airway disease and CHF, treatment of the underlying congestion and pulmonary edema has yielded an increase in forced expiratory volume in 1 second.62 Impaired diffusion capacity, which also contributes to dyspnea, does not respond to treatment for heart failure.

In addition to the peripheral vascular and muscular adaptations discussed above, there is a direct effect on the respiratory musculature in CHF. Maximal voluntary ventilation and maximal sustainable ventilatory capacity are lower in patients with heart failure.63,64 To treat these alterations in lung function, selective respiratory muscle training has been tried in these patients, such as inspiratory muscle training against resistance, sustained (10s) peak inspiratory and expiratory force generation, and muscle endurance training with isocapnic hyperventilation. Marked improvements in respiratory muscle strength, maximal inspiratory and expiratory pressures, maximal voluntary ventilation, and respiratory muscle endurance are reported when these exercises were performed 3 times weekly over 3 months. These improvements were accompanied by significant gains in exercise capacity and decreases in subjective dyspnea.63 These interventions often are not included in cardiac rehabilitation programs for CAD. Yet patients with CHF clearly could benefit from the addition of respiratory muscle training and careful assessment and treatment of any concomitant pulmonary disease.
Exercise in Combination With Medical Therapy

The medical treatment of the cardiac limitations of CHF has improved significantly in the last few years, including an increased use of beta blockers, improved afterload reduction, and better inotropic support. With the favorable vascular alterations from better medical management, exercise may prove to have a synergistic role in normalizing vascular tone and improving survival in CHF. Furthermore, survival in CHF patients has improved through control of chronic life-threatening arrhythmias with automatic internal cardiac defibrillators and better antiarrhythmic regimens.

Intravenous inotropic therapy has been used in selected patients as an adjunct to exercise training. Limited data suggest that exercise is both safe and beneficial in the presence of dobutamine administration. For patients with CHF that is refractory to maximized inotropic therapy, a left ventricular assist device (LVAD) should be considered while awaiting transplantation. LVAD can support successful transition to cardiac transplantation and improve outcome. It provides virtually all the cardiac output at rest and most of it during exercise. The maximum output of the device with exercise is 11L/min (averaged between pneumatic and electric), which is sufficient for most daily functions and moderate exercise. Depending on the degree of left ventricular dysfunction, the LVAD-supported native left ventricle can augment exercise output. Pneumatic or vented electric systems are used to drive the pump. In the pneumatic device, an external console delivers pulses of pressurized air to drive blood flow, which does preclude some functional activities, such as climbing stairs. The electrical device, which has a driveline that is connected to a small battery-powered control shoulder harness, allows improved functional mobility.

Since an LVAD chamber volume is fixed and it empties when full, the increased rate during exercise provides a normal cardiac output up to moderate workloads, simulating a normal physiologic response to differing amounts of physical effort. Although the native heart rate and the LVAD rate do not match, there is a parallel increase in response to exercise. Likewise, diminished preload, such as would be experienced with orthostatic intolerance, slows the LVAD rate to permit chamber filling.

Exercise testing and training of LVAD patients are safe. Available data indicate improved physiologic and functional status. Exercise, Cardiovascular Disease, and Chronic Heart Failure, Humphrey S79

SUMMARY

The field of cardiac rehabilitation is evolving. The importance of cardiac rehabilitation in the patient with CAD has been well established, but the evolving frontier is the rehabilitation of patients with CHF. Current evidence indicates an important role for rehabilitation to increase function and quality of life in these patients. The functional improvements are not unique to CHF patients in CHF do not arise from changes in central cardiac physiology, but rather emerging mechanisms seem to indicate improved efficiency of peripheral blood flow and muscle metabolism. Although the effects on morbidity and mortality are not yet clear, recent evidence shows that cardiac rehabilitation programs in CHF patients can be undertaken safely. With the functional improvements that can be achieved in combination with emerging medical treatments, the effort of establishing cardiac rehabilitation programs for all persons with cardiac disease and proving the efficacy of these interventions is worthwhile.

References


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