Clinical evidence for a health benefit from cardiac rehabilitation: An update

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The recent decision by the Centers for Medicare and Medicaid Services to expand the indications for cardiac rehabilitation (CR) provides an opportunity to review the clinical evidence of the efficacy of exercise in the CR setting for patients who have experienced an acute myocardial infarction, coronary artery bypass graft surgery, stable angina, percutaneous coronary intervention, chronic heart failure, cardiac transplant, or cardiac valve repair/replacement. Evidence shows that physician-directed, exercise-based CR positively affects the basic pathophysiology of coronary artery disease, the extent of disability and level of quality of life, and the ability to potentially impact events of both morbidity and mortality. The role of CR, including regular exercise, lifestyle modification, and appropriate medical therapy, is effective in younger and older men and women with cardiac diagnoses. The efficacy of this important therapeutic modality warrants its more widespread application. [Am Heart J 2006;152:835-41.]

Participation in cardiac rehabilitation (CR) is a valuable component of a multidisciplinary treatment strategy after the diagnosis of acute myocardial infarction (MI), coronary artery bypass graft (CABG) surgery, and stable angina.1,2 The recognition of the importance of CR in the treatment of various other cardiac disease diagnoses continues to evolve as evidenced in the recent decision by the Centers for Medicare and Medicaid Services3 to expand the indications for CR services and the adoption of expanded diagnosis codes for CR eligibility in at least one region of the country.4 Unfortunately, even with the apparent increasing need,5 CR remains underused6,7 with only an estimated 15% to 25% of eligible patients participating. This has occurred despite the evidence indicating that CR positively affects risk factors for heart disease8-11 and the disease process itself,12,14 reduces mortality and morbidity,15 and improves health-related quality of life (QOL),16 in younger and older men and women with cardiac diagnoses.17,18 The purpose of this review is to draw attention to the value of such programming by providing an update of the clinical evidence of the efficacy of CR for patients who have experienced an acute MI, CABG surgery, stable angina, percutaneous coronary intervention (PCI), cardiac transplant, chronic heart failure (CHF), or cardiac valve repair/replacement. The review will also update information provided in several earlier reports.8,11,19

Coronary heart disease

There has been significant progress in clarifying the pathophysiology of atherosclerosis and the benefits of comprehensive CR programs on coronary heart disease (CHD). Many of the multi-risk factor benefits occurring in CR mediate through the exercise training component of CR. Exercise training leads to increased fibrinolysis and decreased coagulability, thus promoting conditions that benefit patients with existing coronary artery disease (CAD).20,21 Inflammation is moderated and, thus, endothelial function is improved, as demonstrated by reduced C-reactive protein levels in patients undergoing CR.22 Endothelial dysfunction has also been shown to be a culprit in restenosis, and, therefore, the value of exercise training is underscored.23 Exercise training prevents and restores age-related declines in endothelium-dependent vasodilation in cardiac patients with a variety of diagnoses,24-26 which may also help to explain the improvement in hyperemic myocardial blood flow (flow reserve) seen in patients after CR.27 Exercise training accompanied by multifactor risk reduction, similar to that provided in supervised CR programs, has also been shown to slow CAD progression.27 Finally, because the disease processes of inflammation and endothelial dysfunction themselves are associated with the established risk factors for heart
Exercise-related benefits in autonomic function have also been reported. Autonomic dysfunction is associated with an increased risk of sudden death and exercise improves autonomic function in patients with CAD. Exercise has been shown to improve cardiovascular outcomes partially by increasing vagal activity and attenuating sympathetic hyperactivity. Significant improvements in autonomic markers of neural regulation of the sinoatrial node, such as increases in R-R variance and the gain of the overall spontaneous baroreflex, have been observed. These improvements may partially explain the increased survival demonstrated in exercise rehabilitation studies after MI.

Disability is also frequently associated with the aforementioned cardiac disease diagnoses. Participation in supervised CR programs has been shown to improve functional independence by improving fitness and reducing signs and symptoms of exercise intolerance. In addition, peak oxygen uptake (VO$_2$) is an important predictor of both cardiac and all-cause death. Thus, even a small gain in aerobic power should improve not only functional capacity but also survival prospects.

**Cardiovascular disease risk**

Cardiac rehabilitation facilitates a systematic approach to exercise training and risk factor management through regular patient evaluation and monitoring, and support of compliance and adherence. Intensive interventions directed at inactivity, dyslipidemia, metabolic syndrome, excess body weight, elevated blood glucose, hypertension, and tobacco addiction, as well as the reduction of stress, anxiety, and depression, are critical components of CR.

**Acute Myocardial Infarction**

Cardiac rehabilitation has long been recognized as integral to the comprehensive management of patients after a hospitalization for MI. The survival benefit after CR is well established. Meta-analyses of clinical trials of CR after MI documented a 24% and 20% decrease in total mortality, respectively, and a 25% and 22% decrease in cardiovascular mortality at 3 years of follow-up. The review of Jolliffe et al included more women and older patients, and included not only MI, but also patients with CABG surgery and patients who had undergone PCI. Cardiac rehabilitation exercise programming reduced all-cause mortality by 27% and cardiac mortality by 31%. A similar analysis using a shorter follow-up period of exercise-based CR also demonstrated significant reductions in all-cause mortality (20%) and cardiac mortality (26%). Finally, a study of patients after MI found that although women and persons ≥70 years old were less likely to participate in CR, overall survival benefit was better in CR participants compared with nonparticipants, along with a decrease in recurrent MI. Participants exhibited a 3-year survival of 95% compared with 64% among nonparticipants. Improved endothelium-dependent vasodilation of coronary arteries resulting from exercise training was hypothesized by the authors as the most important mechanism to explain the marked reduction of myocardial ischemia and coronary events, although many other mechanisms have been proposed including favorable effects on blood lipids, blood pressure lowering, and improvements in insulin sensitivity.

Cardiac rehabilitation improves prognosis after MI in a highly cost-effective manner by reducing recurrent hospitalization and health care expenditures, while prolonging life. It compares favorably in terms of costs per year life saved with other well-established preventive and therapeutic interventions in the treatment of CHD such as cholesterol lowering, thrombolysis with tissue plasminogen activator, and CABG surgery. Because CHD in the elderly is characterized by a greater severity of disease, more severe left ventricular dysfunction, and more medical comorbidities, it is not surprising that compared with younger patients, older coronary patients after MI have diminished exercise capacities and higher rates of disability. Because improvement in exercise capacity is one of its most predictable beneficial effects, exercise-based CR effectively combats physical disability in this population, particularly with long-term participation. Furthermore, a randomized controlled trial of resistance training in disabled older women with CHD documented improvements in physical functional performance, which included both household activities and measures of endurance activities such as stair climbing, grocery carrying, and 6-minute walk distance.

**Coronary artery bypass graft surgery**

At entrance to CR, patients who have undergone CABG surgery have a significantly reduced exercise capacity, and older patients, particularly women, are a severely disabled group. Consequently, a primary role of CR is to provide an effective means for returning these patients to an appropriate level of functional independence. The ability of CR to improve functional capacity in older patients, particularly women, has been consistently demonstrated.

A controlled trial of CR versus usual care after CABG surgery with 10-year follow-up documented significantly fewer total cardiovascular events for patients in CR (18.4% vs 34.7%) as well as reduced hospital...
readmissions.\textsuperscript{49} In a study of patients after CABG surgery or MI, improvements in peak exercise capacity after CR correlated with a decrease in long-term mortality rates.\textsuperscript{50}

**Stable angina**

It has been known for $>30$ years that exercise training improves exercise tolerance in patients with chronic stable angina by increasing the anginal threshold and delaying the onset of ischemia as identified by the electrocardiogram. Furthermore, in many patients, angina can no longer be precipitated even with maximal exercise after exercise training. Improved endothelium-dependent vasodilation of the coronary arteries resulting from exercise training may represent the most important mechanism to explain the marked reduction of myocardial ischemia.\textsuperscript{25,26} A randomized controlled 12-month study in patients with stable angina compared outcomes of patients randomized to PCI, primarily coronary stent placement, to patients receiving 12 months of exercise training.\textsuperscript{51} At the end of 1 year, patients in the exercise group had an increased exercise capacity compared with the PCI patients and had experienced fewer total coronary events requiring hospitalization. From a cost-effectiveness perspective, exercise training improved functional capacity at half the cost of the interventional approach.

**Percutaneous coronary intervention**

Between 1987 and 2002, the number of PCIs increased by 324% to 1.2 million cases per year.\textsuperscript{5} Fifty percent of these procedures were performed in patients age $\geq 65$ years old. Participation in CR post-PCI is associated with marked improvement in functional capacity, blood lipid profile, exercise tolerance and peak VO$_2$, and morbidity (decreased clinical events), decreased hospital readmission rate, improved sympathovagal balance, improved health-related QOL, and decreased inflammation as indicated by decreased levels of C-reactive protein.\textsuperscript{16,22,29,52} In a randomized trial of patients who underwent PCI, those participating in CR not only demonstrated significantly improved lifestyle variables, but these changes were more persistent over the 5-year follow-up than non-CR participants.\textsuperscript{30} Patients who underwent PCI in the presence of MI have been shown to have improved endothelial function as a result of 6 months of exercise training.\textsuperscript{24}

Belardinelli et al\textsuperscript{52} demonstrated that PCI patients who participated in CR experienced a significant increase in peak VO$_2$ and QOL compared with a control group that experienced no change in these variables. Total clinical events were significantly lower in the CR group than in the control group (11.9% vs 32.2%). Hospital readmission rate in the CR group was 18.6% versus 46% in the control group. It has also been demonstrated that lack of progression in functional capacity in a CR program may be an early indicator of restenosis in this population.\textsuperscript{55}

**Chronic heart failure**

Randomized clinical trials conducted over the last 15 years demonstrate that exercise-based CR favorably improves exercise tolerance, disease-related symptoms, and QOL in patients with CHF, without negatively impacting left ventricular function. No adverse exercise training-related effects have been reported despite that these patients would appear to be at higher risk for events given their left ventricular dysfunction and heightened state of sympathetic activity.

Exercise training contributes to a reduction of the fatigue- and dyspnea-limiting exercise intolerance that is common in these patients.\textsuperscript{54-56} The magnitude of improvement ranged from 15% to 30%, using peak VO$_2$ to measure exercise capacity, comparing favorably to gains in exercise capacity observed in clinical device and drug trials. The mechanisms responsible for the improved exercise performance are both central and peripheral adaptations. Central factors include exercise training-induced increases in peak cardiac output, heart rate, and stroke volume.\textsuperscript{57} Adaptations in peripheral function include improved flow-mediated vasodilatation among the active muscles, increased cellular oxidative enzyme activity, an improved neurohumoral axis, and decreased sympathetic nervous system activation.\textsuperscript{58-60}

Improvements in shortness of breath, ability to perform activities of daily living, anxiety, depression, and general well-being have been observed using both generic and disease-specific instruments.\textsuperscript{54,61,62} The magnitude of the improvement in each variable ranged between 15% and 50%. Improvements in QOL can occur as early as 2 months into the exercise program and parallel increases in peak VO$_2$.

Hospital readmission and subsequent cardiac mortality have also been evaluated. In one trial, risk for cardiac events was decreased by 67% in patients undergoing exercise training,\textsuperscript{54} whereas a separate trial reported no exercise training-related effect on clinical outcomes.\textsuperscript{56} Meta-analyses of the effect of exercise training in patients with CHF have shown a significant reduction of 28% in total mortality or hospitalization\textsuperscript{55} and a 29% reduction in death rate.\textsuperscript{63} Mechanistically, exercise training down-regulates sympathetic nervous system activity and plasma and tissue cytokine concentrations, all of which are typically increased and associated with a poorer prognosis and worsening disease in patients with CHF.

**Heart transplant**

Patients who undergo heart transplantation face a myriad of medical problems including persistent heart
The groups. 

Conclusion episodes, and weight gain did not differ between medications, the average number of rejection or infections, the side effects of immunosuppressive medications (sarcopenia, osteopenia, overall fat mass, particularly central body fat gain, and infections), and risk of organ rejection. Peak VO\textsubscript{2} among patients having undergone heart transplant is 40% to 50% lower compared with age-matched, healthy control subjects.\textsuperscript{35,64,65} The hemodynamic responses to exercise (heart rate, blood pressure, cardiac output) are also impaired due to cardiac denervation and medications. Furthermore, the ventilatory response to exercise is excessive and inefficient, and bone mass and density are significantly reduced.

Several well-designed studies have demonstrated that exercise training partially reverses many of the physiologic abnormalities observed in heart transplant patients.\textsuperscript{35,64-66} Most exercise training studies have been physician-directed CR programs where exercise is conducted 3 to 4 times per week for 12 to 16 weeks at “moderate” intensity levels. In these programs, endurance capacity has improved by approximately 20% to 50% because of both peripheral adaptations (muscle and vascular changes leading to increased oxygen extraction) and central hemodynamics, including an increase in heart rate and cardiac output. Ventilatory response to exercise improves, bone mineral density and muscle mass increase, and fat mass decreases.

Kobashigawa et al\textsuperscript{35} completed the first randomized trial of 27 heart transplant patients to either a 6-month medically supervised aerobic and resistance training CR program or an unstructured home exercise program. The CR group increased peak VO\textsubscript{2} by 49% versus 18% for the home exercise group. The CR group also showed a significantly greater increase in peak exercise workload and reduction in ventilatory response. The mean dose of prednisone, number of patients taking hypertensive medications, the average number of rejection or infection episodes, and weight gain did not differ between the groups.

Braith et al\textsuperscript{67} used 6 months of strength training in transplant patients and showed a return to pretransplant bone mineral density levels, whereas nonexercising patients had a decrease of 6%. This study demonstrated that resistance exercise training is essential for preventing and potentially reversing the glucocorticoid-induced bone loss.

### Heart valve replacement

Before cardiac valve surgery, patients are frequently extremely symptomatic as well as highly deconditioned, with most identified as New York Heart Association Functional Classification III to IV.\textsuperscript{58,69} This level of exercise capacity is 30% of that of age-matched control patients. In addition, the cardiovascular hemodynamics and symptoms in these patients are similar to those of patients with heart failure with elevated pulmonary capillary wedge pressures, depressed cardiac indices, and extreme dyspnea with minimal exertion. Although valve replacement or repair improves function, exercise capacity for most valve patients 6 months after valve surgery still approaches only 55% of normal controls.\textsuperscript{70} Abnormal rest and exercise cardiac hemodynamics persist up to a year after surgery.\textsuperscript{71} Older patients have longer hospital stays and more complications, which increase the level of disability.

Exercise training after aortic valve replacement increases peak VO\textsubscript{2} by 25% while improving cardiovascular response at submaximal workloads.\textsuperscript{71} Patients who participate in CR demonstrate improvements in performing activities of daily living and employment.\textsuperscript{72} Reemployment after valve surgery corresponds to a patient’s physical working capacity, with greater physical work capacity associated with higher rate of returning to work.\textsuperscript{73} In a nonrandomized study of patients who had undergone heart valve replacement, there was a significant improvement in QOL after 6 months of exercise training compared with the nonexercise group and this improvement correlated to increases in peak VO\textsubscript{2}.\textsuperscript{46} Improvement in functional capacity (25%) as a result of CR compared with a control group has also been documented in women after mitral valve replacement.\textsuperscript{74}

### Conclusions

Because of the aging population, and the shift of cardiovascular disease from an acutely fatal event to a chronic disease, there is a marked and growing need for medical services that help patients improve their QOL, lessen symptoms, increase functional capacity, decrease disability, and reduce the risk of subsequent morbidity

### Table I. Summary of impact of exercise-based cardiac rehabilitation by diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Functional capacity</th>
<th>QOL</th>
<th>Morbidity</th>
<th>Mortality</th>
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</thead>
<tbody>
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<td>AMI</td>
<td>+++</td>
<td>++</td>
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<tr>
<td>CABG surgery</td>
<td>+++</td>
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<td>Stable angina</td>
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<td>PCI</td>
<td>+++</td>
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<td>CHF</td>
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<td>Cardiac transplant</td>
<td>+++</td>
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<tr>
<td>Heart valve replacement</td>
<td>+++</td>
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+++, ++, + indicate clear evidence of benefit; ++, good evidence of benefit; +, limited evidence of benefit; ?, no clear evidence of benefit.
and mortality (Table 1). Although CR is currently underused in patients who had acute MI or undergone CABG surgery, PCI, heart transplantation, and heart valve surgery, and in patients with CHF, the efficacy of this important therapeutic modality warrants its more widespread application. Clinicians should recognize that referral to CR increases the likelihood of participation and long-term compliance beyond that which might be provided through “usual care.” In sum, the body of literature shows that CR with supervised exercise training positively affects the basic pathophysiology of CAD and the underlying disease process, the extent of disability and level of QOL, and has the ability potentially impact events of both morbidity and mortality.

References


