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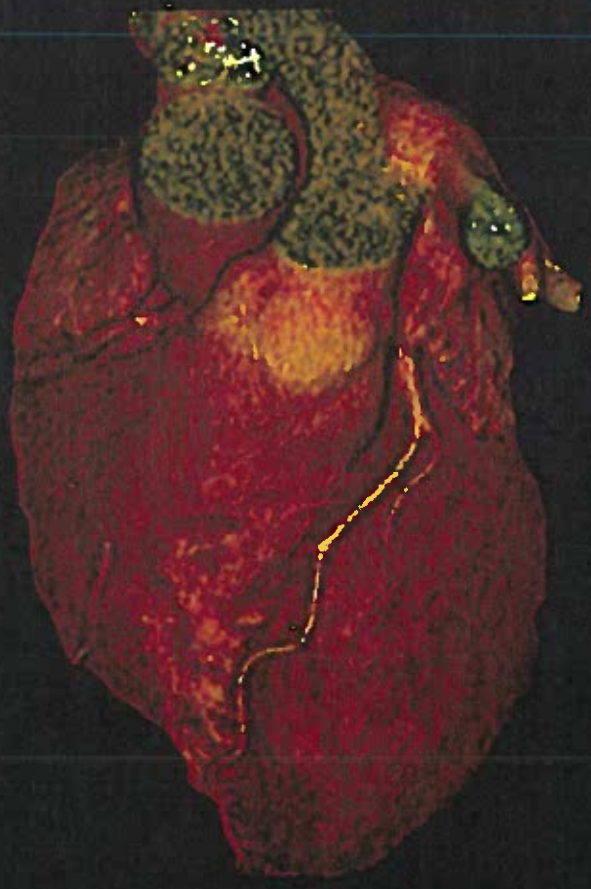

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CHAPTER 32

Exercise Training After an Acute Coronary Syndrome

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CLINICAL BENEFITS

Numerous publications have documented the efficacy of exercise-based cardiac rehabilitation (CR) after myocardial infarction (MI) or coronary artery bypass surgery. Because most studies published were underpowered to detect significant mortality reductions, many meta-analyses were performed to address this issue. Three recent meta-analyses[1-3] have confirmed earlier reviews published in the late eighties.[4,5]

In their publication, Clark and colleagues[1] reviewed 63 randomized trials including a total of 21,295 patients. For the 40 trials that reported all-cause mortality, representing 16,142 patients, the overall mortality reduction was 47% at 2 years. The risk of recurrent MI was reduced by 17% over a mean follow-up of 12 months. Seven trials reported a follow-up of at least 5 years and documented a sustained long-term benefit with a reduction of all-cause mortality of 23%. The treatment effect did not differ between the different types of interventions, that is, exercise only or exercise associated with a comprehensive risk factor reduction program.

Taylor and coworkers[2] reviewed 48 trials with a total of 8940 patients in their systematic review. Their results show that exercise-based CR is associated with a 20% reduction in all-cause mortality and a 26% reduction in cardiac mortality (Fig. 32-1). There was no significant reduction in the incidence of recurrent nonfatal MI.

A systematic review by the Cochrane collaboration published initially in 2001 and revised in 2005[3] studied 51 trials for a total of 8440 patients. They reported a 27% reduction in all-cause mortality and a 31% reduction in cardiac mortality. Combined events (nonfatal MI, coronary artery bypass surgery, and angioplasty) were reduced by 19%. There was no evidence of risk reduction for recurrent nonfatal myocardial infarction.

COST-EFFECTIVENESS OF EXERCISE-BASED CARDIAC REHABILITATION

A review of 15 studies on the economic impact of exercise-based CR was published by Papadakis and colleagues in 2005.[6] The authors concluded that the range of cost per life-year gained was between $2193 and $28,193 and from $668 to $16,118 per quality-adjusted life-year gained.

Ades and colleagues[7] studied the cost effectiveness of CR after myocardial infarction. Their results show a cost of $2130 per life-year saved in the late 1980s and $4950 per life-year saved in 1995. They concluded that exercise-based CR is more cost effective than thrombolytic therapy, coronary artery bypass surgery and cholesterol-lowering medication, although less cost effective than smoking cessation programs.

Fidan and coworkers[8] performed an economic analysis of treatments to reduce coronary heart disease mortality in England and Wales, and concluded that exercise-based CR was among the most cost-effective interventions. The cost per life-year gained was 1957 pounds sterling compared to angiotensin converting enzyme inhibitors at 3398 pounds, and to statins at 4246 pounds per life-year gained.

A Canadian government[9]–sponsored study concluded that exercise-based CR was cost-effective with an estimated cost of 4950 canadian dollars per life-year gained.

Underutilization of Exercise-Based Cardiac Rehabilitation

Despite the proven benefits of exercise-based CR, it is still greatly underutilized in North America and Europe. Recently Suaya and coworkers[10] studied the use of CR in 267,427 Medicare beneficiaries and found that CR was used in 13% of post-myocardial infarction patients and 31% of post-coronary artery surgery patients. The adjusted CR use rate varied greatly

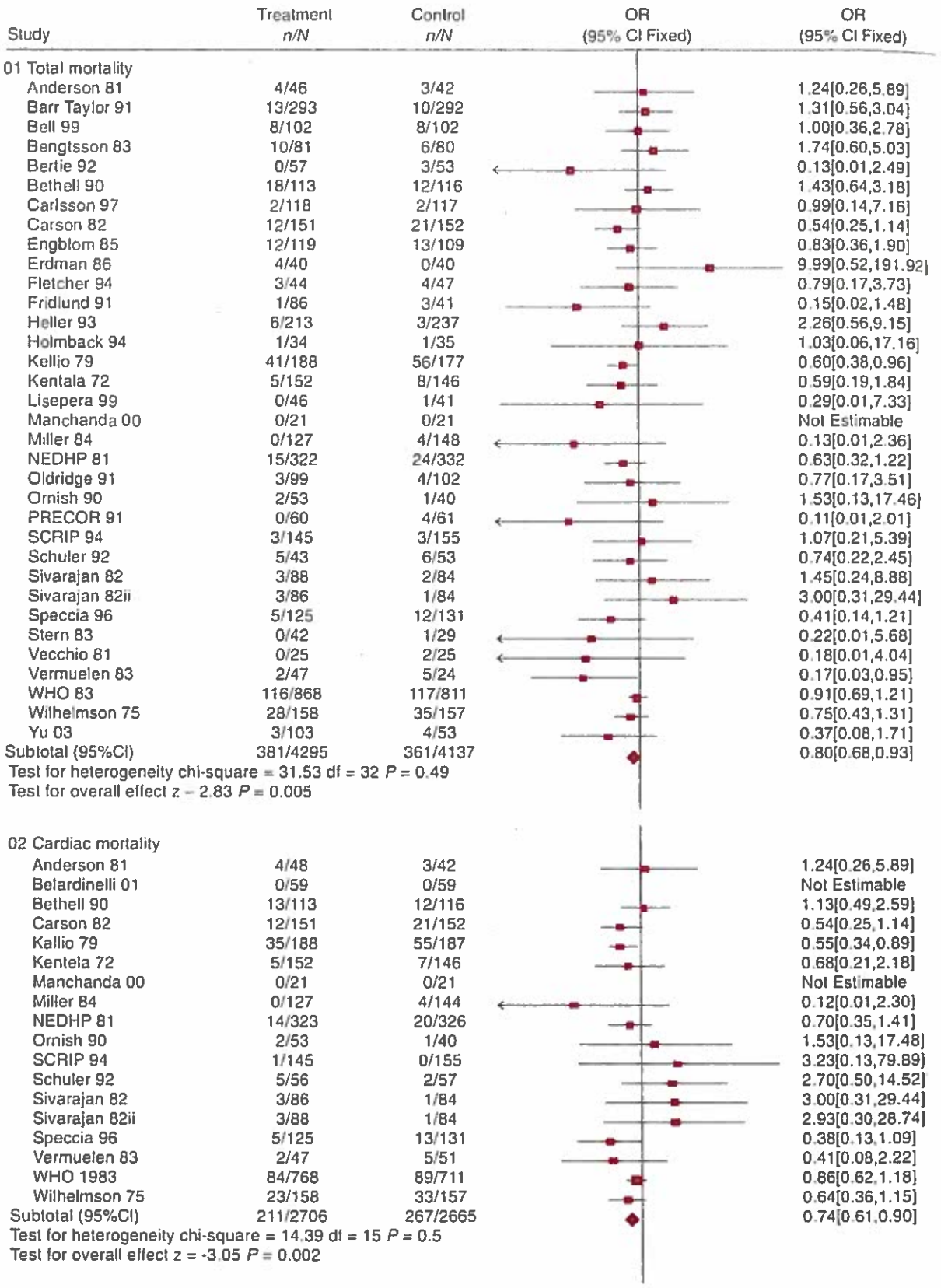

FIGURE 32–1 Summary of the effects of exercise training on total and cardiac mortality in patients with coronary heart disease. *(With permission from Taylor RS, Brown A, Ebrahim S, et al. Exercise-based rehabilitation for patients with coronary heart disease: Systematic review and meta-analysis of randomized controlled trials. Am J Med 2004;116:682-692.)*

(ninefold) among states from 6.6% in Idaho to 53.5% in Nebraska. Underuse in this study and others[11] was associated with older age, female gender, nonwhite ethnic origin, significant comorbidities, and long distance from the CR program.

CARDIOPROTECTIVE MECHANISMS OF EXERCISE

The cardioprotective effects of exercise in patients following acute coronary syndromes (ACS) as well as in those with stable coronary heart disease (CHD) are multifactorial and appear to be related to improvements in endothelial function, inflammation, autonomic regulation of cardiovascular function, and risk factor control, as well as potential antithrombotic effects and effects related to ischemic preconditioning (Box 32-1).

The Endothelium

Both acute and chronic exercise have been shown to improve endothelial function by increasing shear stress-induced flow-mediated arterial vasodilatation.[12,13] Increased shear stress on the arterial wall during exercise leads to increased production and release of nitric oxide (NO) from endothelial cells.[14] A single bout of vigorous exercise was recently shown to improve endothelial function in the rat, with regular exercise for 6 weeks further improving endothelial function.[12] Hambrecht and colleagues in a randomized, controlled trial involving 19 patients with stable CHD, demonstrated that an intensive in-hospital aerobic exercise training program of 4 weeks duration was able to improve coronary endothelial function and coronary blood flow.[15] A follow-up study assessing the effect of a 5-month home-based exercise training program in the same participants showed that home-based training (albeit at lower intensity and frequency) was sufficient to partially sustain the improvements in endothelial function achieved after the initial 4-week in-hospital program, suggesting the effects of exercise on endothelial function are dose-dependent.[16] In a randomized, controlled trial of 12 weeks' duration in 18 patients with stable CHD, Edwards and coworkers showed that CR with aerobic exercise training was able to improve peripheral endothelial function as measured via brachial ultrasonography.[17] Similarly, in a case-control study of 58 patients with stable CHD, a 10-week supervised exercise training program involving predominantly lower-limb activities (treadmill, stationary bicycling), resulted in an improvement in lower limb endothelial function while endothelial function remained unchanged in the non-training control group.[18] Walsh and coworkers also showed in a randomized, controlled, crossover study in 10 patients with stable CHD that an 8-week combined aerobic and resistance training program was able to improve conduit vessel endothelial function, indicating the effects of exercise on the endothelium are not limited to a single vascular bed but are systemic.[19] Two studies have specifically assessed the effect of exercise training on endothelial function following acute coronary syndromes. Firstly, Hosokawa and colleagues in 41 patients with recent myocardial infarction, showed that subjects performing regular exercise had improved coronary endothelial function after 6 months relative to non-exercisers.[20] Finally, Vona and colleagues in a randomized, controlled trial in 52 patients with a recent uncomplicated first myocardial infarction, demonstrated that a 3-month moderate-intensity aerobic exercise program improved brachial artery endothelial function, while detraining resulted in a deterioration in vascular function.[21]

Several mechanisms have been put forth to explain the beneficial effects of chronic exercise on endothelial function, namely by re-establishing the balance between NO production and degradation. Firstly, Hambrecht and coworkers showed in patients with multivessel CHD undergoing coronary bypass surgery, that a 4-week in-hospital aerobic exercise training program led to increased shear stress-induced Akt-dependent phosphorylation of endothelial nitric oxide synthase (eNOS) and eNOS expression in left internal mammary endothelial cells relative to inactive controls.[22] Exercise training also appears to reduce NO degradation by reducing oxidative stress through decreased expression of angiotensin-II (ATII) subtype I receptor, reduced nicotinamide-adenine dinucleotide phosphate (NADPH) oxidase-derived production of reactive oxygen species (ROS) and prevention of ATII-induced vasoconstriction of conduit arteries.[23] Finally, aerobic exercise might improve endothelial function by stimulation of endothelial progenitor cell (EPC) formation and release from bone marrow, resulting in repair of damaged vascular endothelium. Adams and colleagues showed in CHD patients with exercise-induced ischemia that a single bout of exercise was sufficient to increase blood EPC levels, whereas EPC levels remained unchanged in CHD patients without ischemia and in healthy volunteers.[24] In work by the same group, a 4-week exercise training program in patients with symptomatic peripheral vascular disease was shown to significantly increase blood EPC levels, whereas EPC levels remained unchanged in revascularized patients as well as in CHD subjects who trained below the ischemic threshold.[25] These data suggest that ischemia plays an important role in promoting EPC formation and release, perhaps through increased levels of vascular endothelial growth factor. Finally, in 20 patients with CHD and/or cardiovascular (CV) risk factors, a 12-week running program was shown to significantly increase circulating EPC levels, which correlated with improved endothelial function.[26] No studies have evaluated the effect of exercise training on EPC levels in patients following an acute coronary syndrome.

BOX 32-1 Cardioprotective Mechanisms of Exercise

1. Improved endothelial function and passivation of atherosclerotic plaques
2. Reduction in systemic inflammation
3. Beneficial effects on the autonomic regulation of cardiovascular function
4. Improvement in risk factor control
   - Increase in HDL-cholesterol concentrations
   - Reduction in triglyceride concentrations
   - Reduction in blood pressure
   - Reduction in body weight
   - Reduction in insulin resistance and improvement in glucose metabolism
5. Potential anti-thrombotic and anti-platelet effects
6. Intrinsic mechanisms
   - Ischemic preconditioning with reduced myocardial damage during prolonged ischemia
   - Prevention of reperfusion-induced ventricular arrhythmias

Atherosclerosis Progression/Regression

Three studies have evaluated the effect of exercise training in combination with lifestyle interventions on angiographic coronary artery disease. The first was the study by Schuler and colleagues in which 113 patients with stable angina were randomly assigned to either a usual care group or to an intervention group consisting of daily exercise training (approximately 4 hours per week) in combination with a low-fat diet.[27] After 12 months of treatment, atherosclerosis progression was significantly reduced in the intervention group relative to the

control group. In the Stanford Coronary Risk Intervention Project, 259 men and 41 women with angiographically documented coronary atherosclerosis were randomly assigned to either a usual care control group or to a multifactor risk reduction program which included a low-fat diet, exercise training, smoking cessation, weight loss, and lipid-lowering medication.[20] After 4 years, the progression of atherosclerosis was reduced by 47% ($P < .02$), and hospitalization for cardiac events was reduced by 39% ($P = .05$) in the multifactor risk reduction group. Finally, in the Lifestyle Heart Trial, 48 patients with moderate to severe coronary heart disease were randomly allocated to either a usual care group or to an intensive lifestyle intervention group (low-fat vegetarian diet, regular aerobic exercise, smoking cessation, stress management, and group psychosocial therapy) and followed for 5 years.[21] At the end of follow-up, average percent diameter stenosis was reduced by 8% in the intervention group, while this parameter increased by 28% in the usual care group ($P = .001$ between groups). Importantly, the risk of a cardiac event was 2.5-fold higher in the control group relative to the intervention group. These studies highlight the dramatic reduction in cardiac events with a multifactor risk reduction program including regular aerobic exercise, despite only modest changes in angiographic atherosclerosis burden. More recently, Hambrecht and colleagues randomized 101 men with class I to III angina pectoris and evidence of one coronary artery with greater than or equal to 75% diameter stenosis to either aerobic exercise training for 1 year or percutaneous coronary intervention (PCI).[28] Subjects in the exercise training group had a higher event-free survival relative to those in the PCI group (88% vs. 70%, $P = .023$) and better functional capacity at the end of 1 year. As with early statin studies that showed a significant reduction in clinical events despite modest changes in plaque burden, the striking clinical benefits with exercise training are now attributed to improved endothelial function and passivation of atherosclerotic plaques.[29-32] No studies have evaluated the impact of regular exercise on progression or regression of atherosclerosis following ACS.

Inflammation

Inflammation plays a major role in the pathogenesis of atherosclerosis and CHD.[33] A very sensitive marker of inflammation and one of the most studied biomarkers in patients with CHD is the acute-phase reactant C-reactive protein (CRP).[34] Elevated CRP levels are associated with a significantly higher risk of morbidity and mortality in otherwise healthy men and women.[35,36] A recent meta-analysis of studies evaluating the relationship between exercise and CRP in healthy men and women showed that regular exercise produces an anti-inflammatory effect associated with lower CRP levels.[37] A 12-week aerobic exercise training program was shown to significantly reduce levels of several inflammatory markers including CRP in patients with stable CHD.[38] Similarly, a 12-week aerobic training program conducted in 32 patients with CHD and/or CV risk factors demonstrated a reduction in chemokines, interleukin-8, and monocyte chemoattractant protein-1 as well as a reduction in matrix metalloproteinase-9.[38] In 39 patients randomized to either a control group or exercise training consisting of 1 month high-frequency aerobic training (90 minutes per day) followed by home-based moderate-frequency training (30 minutes per day), high-frequency training was associated with a significant reduction in several proinflammatory cell adhesion molecules, with a blunted response at 5 months after moderate-frequency training.[39] These data suggest a dose-response effect of chronic exercise on inflammation. Finally, in 101 male patients with symptomatic CHD randomized to exercise training or PCI and followed for 2 years, exercise training was associated with a significant reduction in both CRP and interleukin-6 levels while no changes were observed in inflammatory parameters in the PCI group.[21] No studies have specifically assessed the impact of exercise training on inflammatory markers in patients after ACS.

The Autonomic Nervous System

Measures of autonomic regulation of CV function and cardiac vagal activity including heart rate variability (HRV) and baroreflex sensitivity (BRS), have been shown to be powerful, independent prognostic indicators in post-MI patients.[40] Both decreased HRV and BRS, indicative of a sympathovagal imbalance, are associated with an increased risk of ventricular arrhythmias and sudden cardiac death following myocardial infarction.[41] To date, nine studies have been performed in post-MI patients to study the effects of chronic exercise training (3-6 month programs) on cardiac autonomic control, of which the majority showed a decrease in resting heart rate and improved sympathovagal balance.[42-51] While the mechanism of exercise-induced augmentation of cardiac vagal tone remains to be elucidated, data suggest that both peripherally and centrally produced NO (in neuronal cells) may exert a facilitation effect on baroreflex afferent-mediated activity in the nucleus tractus solitarius and increase central and peripheral vagal nerve activity.[42]

Risk Factor Control

Lipid Control

A recent review of the impact of exercise on blood lipid levels in the noncoronary population indicates a predominant effect of exercise training on high-density lipoprotein (HDL)-cholesterol and triglycerides with few and variable effects on total and low-density lipoprotein (LDL)-cholesterol.[52] Cross-sectional and prospective studies indicate that a training volume of 15 to 20 miles (24-32 km) per week of brisk walking or jogging corresponding to 1200-2200 kcal/week energy expenditure can increase HDL-cholesterol levels by 2 to 8 mg/dL, while reducing triglyceride levels by 8 to 20 mg/dL. A threshold value of 900 kcal appears to be required to raise HDL-cholesterol with a subsequent dose-response effect.[52,53] In a meta-analysis of randomized trials in patients with CV disease, aerobic exercise training was associated with a 9% (3.7 ± 1.3 mg/dL) increase in HDL-cholesterol, and an 11% (19.3 ± 5.4 mg/dL) reduction in triglycerides with no significant change in total or LDL-cholesterol.[54]

Blood Pressure

In a meta-analysis of 54 randomized trials conducted in individuals with and without hypertension, aerobic exercise training for 2 weeks or more was shown to lower systolic blood pressure by 3 to 4 mm Hg and diastolic blood pressure by 2 to 3 mm Hg, with a greater blood pressure-lowering effect noted in hypertensive patients.[55] Although less well studied, resistance training has been shown to lower diastolic blood pressure by 3 to 4 mm Hg.[56] Similarly, a regular walking program of ≥4 weeks or more duration was shown to significantly lower diastolic blood pressure by 2 to 3 mm Hg with no significant effects on systolic blood pressure according to a recent systematic review.[57] Finally, in a review of studies on exercise-based CR programs in patients with CHD including prior MI, exercise training (median program duration of 3 months) was associated with a significant 3.2 mm Hg reduction in systolic blood pressure ($P = .005$) with no significant reduction in diastolic blood pressure.[2]

Weight Loss

Several systematic reviews have evaluated the impact of aerobic exercise training on weight loss in overweight and

obese subjects.[58,60] All showed significant weight loss ranging from 2 to 11 kg with programs lasting 12 weeks to 1 year. Exercise training was also more effective for weight reduction if combined with a dietary intervention. Two studies of the effects of exercise-based CR of 3 months' duration on weight loss found either no weight loss or modest weight loss (2%) solely in obese subjects.[61,62] A long-term (≥6 months' duration) exercise training program was recently shown to result in modest but significant weight loss in CHD subjects with metabolic syndrome.[63]

Insulin Resistance Syndromes

A large body of literature has demonstrated the beneficial effects of exercise on insulin resistance syndromes including metabolic syndrome and type 2 diabetes mellitus. The subject is beyond the scope of this book and the reader is invited to consult one of the many excellent review articles on the subject. In a randomized trial of 29 patients with CHD, a 12-week supervised exercise training program in the absence of weight loss was not associated with an improvement in insulin sensitivity.[64] As noted earlier, a long-term exercise training program in CHD patients with the metabolic syndrome was shown to reduce obesity-related parameters including body weight, body mass index, and insulin resistance (Fig. 32-2).[63]

Antithrombotic Effects of Exercise

The effects of exercise training on hemostasis and coagulation remain unclear. Paradoxically, acute vigorous exercise has been shown to cause activation of blood coagulation, acceleration of blood fibrinolysis, and effects on platelet function, whereas moderate-intensity exercise results solely in activation of fibrinolysis.[65,66] Whether these findings possess clinical relevance, however, remain unclear. Information regarding the effects of chronic exercise training are incomplete and contradictory, most probably due to differences in study populations, training duration and intensity, and the analytical methods used.[65,66] Similarly, acute exercise has been shown to potentially increase platelet activation, whereas the effects of chronic exercise training on platelet function remain unclear.[65] Future studies are required to evaluate the effects of both aerobic and resistance training on hemostasis and platelet function in patients with CHD.

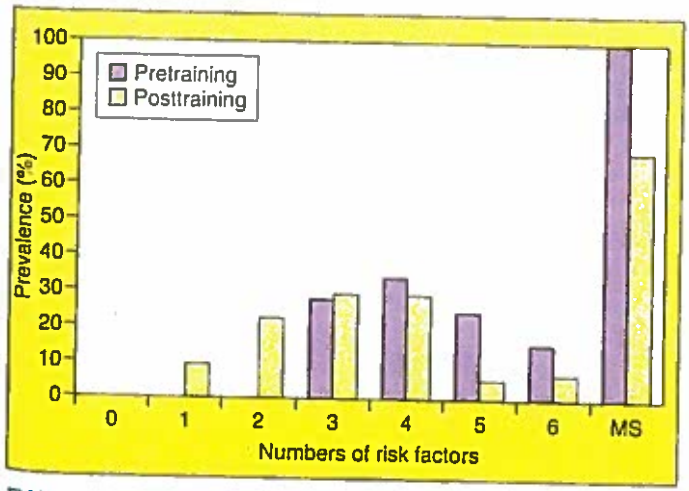

FIGURE 32-2 Frequency distribution of metabolic syndrome risk factors (ATP III criteria) among CHD patients before and after a long-term (6-month) cardiac rehabilitation program. $P < .0001$. MS, metabolic syndrome. *(Adapted with permission from Gayda M, Brun C, Juneau M, et al. Long-term cardiac rehabilitation and exercise training programs improve metabolic syndrome patients with and without coronary heart disease. Nutr Metab Cardiovasc Dis 2008;18:142-151.)*

Cardioprotective Effects of Exercise: Intrinsic Mechanisms

Ischemic preconditioning refers to the phenomenon whereby exposure to brief episodes of ischemia prior to a prolonged ischemic period followed by reperfusion leads to delayed myocardial injury and smaller infarct size.[67,68] This phenomenon was first described in the rat model in 1978 and has since been confirmed in a series of animal studies, although the exact underlying mechanisms remain unclear.[69,70] Several lines of evidence suggest the same phenomenon occurs in humans. For example, preinfarction angina is associated with smaller infarct size, a lower incidence of congestive heart failure, and decreased mortality.[71,72] During PCI, successive balloon inflations have been shown to result in decremental ST-segment elevation.[73] Finally, the phenomenon of warm-up angina whereby patients may present angina upon initiation of exercise, which then fails to return upon resumption of exercise, is also thought to be a manifestation of ischemic preconditioning,[74] which theoretically could provide protection during longer periods of ischemia such as during myocardial infarction.

Summary

The mortality benefits of exercise-based CR following ACS appear to be related to multiple cardioprotective mechanisms, including effects on endothelial function, autonomic tone, inflammation, and improved risk factor control. The final common pathways of risk reduction presumably operate through improved endothelial function, leading to plaque passivation and thereby reducing the risk of recurrent ischemic events, as well as effects on autonomic control of cardiovascular function leading to a reduced risk of sudden cardiac death. Future work will be required to enhance our understanding, particularly of the antithrombotic potential of exercise training, which at this time remains unclear.

EXERCISE PRESCRIPTION

The main components of exercise prescription include the mode of exercise, the intensity, the frequency, and the duration (Table 32-1). To develop an individualized exercise training program, a complete risk stratification must be performed. Since post-ACS risk stratification is discussed elsewhere in this textbook, only the principal components of the pretraining risk stratification will be presented here. This topic is discussed in details in published guidelines.[75,76]

TABLE 32-1 Exercise Prescription for Subjects with Coronary Heart Disease

Aerobic Training
Intensity:*
• Heart rate: 65%-85% of maximal HR** or 40%-60% of the HR reserve (HR reserve = (maximal HR − resting HR) + resting HR).
• Gas exchange measurements: 40%-60% of maximal VO_2.
• Perceived exertion: Borg scale 12-14.
Frequency: 3-5 sessions/week.
Duration: 20-45 minutes/session.
Resistance Training
Intensity: 30%-40% of 1-RM for upper body exercises, 40%-60% of 1-RM for lower body exercises.
Repetitions: 10-15 per set.
Number of sets: 8-10 sets of different exercises.
Frequency: 2-3 sessions/week.

*As measured during a symptom-limited exercise test.
**See text if exercise-induced ischemia is present during the exercise test.
HR, heart rate, 1-RM, maximum weight that can be lifted to complete one repetition

366 A symptom-limited exercise test[77] must be performed to evaluate exercise tolerance, perceived exertion (Borg scale), blood pressure and heart rate responses, as well as the presence or absence of exercise-induced angina, ischemia, and arrhythmias. An individualized Ramp protocol (treadmill or ergo cycle) is preferred since it provides a better estimation of exercise capacity[78] and can be better adapted to older patients or those with poor exercise capacity. An echocardiogram should be performed to evaluate left ventricular function, valvular abnormalities, presence of thrombus, etc.

32 Both aerobic (endurance) and resistance exercises are recommended.[76] For aerobic exercise, activities that use large muscle groups such as walking, jogging, running, swimming, and cycling are adequate.

Intensity

In general, exercise training should be undertaken at a moderate intensity. Several methods may be used to determine the target heart rate during exercise. The simplest one is to use 65% to 85% of the maximal heart rate achieved on the symptom-limited exercise test performed with the patient taking their usual medication including beta-blocking agents. A second method is to use 40% to 60% of the heart rate reserve (maximal heart rate – resting heart rate) and add this figure to the resting heart rate. For a patient with a maximal heart rate of 160 and a resting heart rate of 60, this would mean a target heart rate of 100 to 120 beats/min (160 – 60 × 40% – 60% + 60).

A third and more complex method since it necessitates the measurement of gas exchange during a cardiopulmonary exercise test, is to use a percentage (usually 40%-60%) of measured maximal oxygen uptake (VO_2).

Finally, exercise intensity may also be prescribed based upon the rate of perceived exertion measured with the Borg scale. This scale is used during the pretraining exercise test to specify the rate of perceived exertion during exercise training, and has been shown to be superior to the heart rate method for determining a precise exercise intensity.[79] This method also enables the patient to train at the desired intensity in many conditions where heart rate measurement is impractical (swimming, skiing, sailing, etc). The patient who uses the rate of perceived exertion to judge exercise intensity also learns to be aware of his or her symptoms and warning signs (chest pain, palpitations, dyspnea, etc.) rather than relying only on target heart rate. The 15-level original scale ranges from 6 (very light) to 20 (maximum) and the recommended target levels during training are 12 to 14. Level 14 on the Borg scale of perceived exertion generally corresponds to the ventilatory threshold, that is, the highest level of oxygen consumption during exercise in the absence of a significant increase in blood lactate.[79] Since it is not recommended for coronary patients to train above this threshold, the rating of perceived exertion on the Borg scale grade should be limited to 14 during training sessions.[76]

Patients with exercise-induced ischemia, that is, presenting a horizontal or downsloping ST-segment depression of greater than or equal to 1 mm, represent a special challenge for prescribing exercise intensity. Current recommendations state that in the presence of exercise-induced ischemia, the maximal heart rate during exercise training should be at least 10 beats per minute below the heart rate associated with greater than or equal to 1 mm ST-segment depression.[80] Unfortunately for patients with a relatively low ischemic threshold, this recommendation does not allow for a sufficient training stimulus.[81,82] Training coronary patients above the ischemic threshold when this threshold is relatively low is a controversial issue and requires medical supervision. Since 1991 at the Montreal Heart Institute Cardiovascular Prevention Centre, we have been prescribing exercise training in coronary patients at a target heart rate range of 65% to 85% of maximal achieved heart rate regardless of the presence or absence of exercise-induced ischemia. In 2002 we reported the chart review of 605 patients with documented coronary artery disease who trained from 3 months to 10 years representing a total of 295,000 patient-hours of training.[81] In this retrospective analysis, exercise training above the ischemic threshold was not associated with a higher incidence of documented coronary events relative to exercise training in the absence of exercise-induced ischemia. The event rate was 1/55,000 patient-hours of training versus 1/50,000 patient-hours, respectively. To evaluate the possibility of myocardial damage after a training session above the ischemic threshold, we measured troponin T levels in 20 patients with stable coronary disease after 2 training sessions: one above the ischemic threshold and the other under this threshold. We found no evidence of myocardial damage following either training session.[83]

The recommended frequency of training is between 3 and 5 sessions per week and the duration is usually from 20 to 45 minutes of continuous or discontinuous exercise. The exercise sessions must be preceded by a warm-up period of 5 to minutes and by an equivalent cool-down period.

Resistance Training

Resistance training, because its health benefits and safety are well documented, is now part of exercise-based CR[76,84] for stable coronary patients and for patients after an ACS.[85] Resistance training enhances muscular strength, endurance, and muscular mass. It also has beneficial effect on most CV risk factors. The prescription of resistance training is based on the maximum weight that can be used to complete one repetition (1-RM). The usual prescription is to perform 30% to 40% of 1-RM for upper body exercises and 40% to 60% of 1-RM for lower body exercises. Each set of exercises includes 10 to 15 repetitions, and usually 8 to 10 sets of different exercises are performed. The resistance training sessions are repeated 2 to 3 times per week.[86]

Risk of Exercise-Related Major Cardiac Events

The risk of cardiac events during exercise-based CR has been the subject of numerous studies. The reported range of major cardiac events is between 1/50,000 to 1/120,000 patient-hours of exercise in medically supervised programs.[80] In a recent publication, Pavy and colleagues[87] reported the data of a prospective registry of 65 CR programs in France representing 25,420 patients. During 1 year, the major cardiac event rate was 1/49,565 patient-hours of exercise training and the cardiac arrest rate was 1/1.3 million patient-hours of exercise. No deaths occurred during the 1-year period. Franklin and coworkers[88] reported a single center experience of 16 years of exercise-based CR. Two cardiac arrests and three nonfatal myocardial infarctions occurred. Accordingly, the rate of cardiac arrest was 1/146,127 per patient-hours of exercise and for acute myocardial infarction, the rate was 1/97,418 patient-hours of exercise. The authors concluded that the risk of major cardiovascular events during CR is very low and that current risk stratification criteria can identify patients at risk of exercise-related cardiovascular events.

Risk Stratification and Level of Supervision

Risk stratification after an ACS is discussed in Chapter 18. Risk stratification for exercise training in healthy individuals and in cardiac patients is also recommended.[12] Class A represents apparently healthy individuals. Patients with a recent ACS can be categorized as low risk (class B) or moderate to high risk (class C). In summary, class B patients have the following characteristics:

- New York Heart Association (NYHA) or Canadian Cardiovascular Society (CCS) class 1 to 2
- Exercise capacity ≥6 metabolic equivalents (METS)

- No clinical heart failure
- No angina or ischemia <6 METS
- Ejection fraction >30%

Class C patients present the following characteristics:

- NYHA or CCS class 3 to 4
- Exercise capacity <6 METS
- Angina or ischemia <6 METS
- Nonsustained ventricular tachycardia (VT)
- Ejection fraction <30%

Low-risk patients (class B) can safely train in a structured program but do not require direct medical supervision. They can also train at home with prior evaluation and instructions if they are capable of monitoring their exercise intensity by the rate of perceived exertion method or heart rate.

Moderate- to high-risk patients (class C) should be referred to a medically supervised program with all the necessary personnel and equipment. The personnel must be trained to provide advanced cardiac life support and defibrillation.

Air Pollution and Risk of Coronary Events During Exercise

A very large number of epidemiologic and experimental studies have demonstrated the link between atmospheric pollution and CV events.[87] Miller and coworkers studied the effect of particulate matter (less than 2.5 μm in aerodynamic diameter) exposure in 65,893 postmenopausal women initially free of previous CV disease in 36 U.S. cities during a mean follow-up of 6 years. They reported that each increase of 10 μg per cubic meter of particulate matter was associated with a 24% increase in the risk of a CV event and a 76% increase in the risk of CV-related death.[90] Short-term exposure to atmospheric particulate matter also significantly contributes to increased mortality and morbidity, especially in high-risk individuals.[91-93] Peters and colleagues showed that transient exposure to traffic may trigger an acute MI in high-risk individuals.[94] This is especially important for patients who exercise in cities with poor air quality. In a recent study of patients with prior MI exposed to diesel smoke during exercise, Mills and coworkers[95] demonstrated that diesel exhaust increases myocardial ischemia and inhibits endogenous fibrinolytic capacity. These findings suggest that the risk of triggering an acute coronary event may be increased when exercising in polluted areas, and some authors recommend avoiding exercise training near traffic when possible to "optimize the risk-benefit ratio" of exercise.[96] Potential mechanisms to explain the effect of poor air quality on triggering ACS include a reduction in myocardial oxygen supply secondary to vasoconstriction or a decrease in oxygen carrying capacity caused by increased carbon monoxide. Transient thrombus formation may also be involved since polluted environments with small particulate matter are proinflammatory and prothrombotic.[97]

CONCLUSION

Exercise training after ACS is a very effective nonpharmacologic intervention to reduce mortality and morbidity and also to improve quality of life. Its clinical benefits appear to be related to multiple cardioprotective mechanisms, including effects on endothelial function, autonomic tone, inflammation, and improved risk factor control. Unfortunately this therapeutic intervention is still greatly underused.

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