



Cardiac rehabilitation: not just exercise anymore

FREDRIC J. PASHKOW, MD

The treatment of older and sicker patients and decreasing length of stays are forcing a rethinking of approaches to cardiac rehabilitation. As a result, cardiac rehabilitation programs are becoming more flexible, emphasizing life-style changes and psychosocial support to meet patient needs.

KEYPOINTS Today's rehabilitation patients are likely to be older and to stay in the hospital fewer days than patients in the past, and they may have congestive heart failure or be candidates for cardiac transplantation. Newer therapies, such as angioplasty, result in some patients being diagnosed, treated, and discharged quickly. These patients often do not stay in the hospital long enough to undergo the first phase of cardiac With the decreasing length of stays for most rehabilitation. cardiac events, it is not reasonable to expect that inpatient rehabilitation will produce tangible improvement in physical capacity or significant retention of information and instructions. Rehabilitation programs need to be changed accord-Low-risk patients undergoing angioplasty may still need cardiac rehabilitation to decrease the risk of restenosis and to reduce cardiac risk factors. Programs that include aggressive risk-factor modification may produce regression in stenosis of coronary arteries, but compliance is difficult to elicit and maintain.

INDEX TERMS: CORONARY DISEASE; REHABILITATION; EXERCISE; RISK FACTORS CLEVE CLIN J MED 1996; 63:116–123

From the Department of Cardiology, The Cleveland Clinic Foundation. Address reprint requests to F.J.P., Department of Cardiology, F15, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195.

ARDIAC rehabilitation is not just exercise training anymore. Rehabilitation provides a golden opportunity to modify behavior that contributed to the development of coronary artery disease. Rehabilitation programs now try to motivate people in a way that is consistent with modern ethical medical practice, through the achieve ent of selfactualization and self-responsibility. Thus, current rehabilitative programs consist of exercise, psychosocial support, education, secondary risk-factor modification achieved through motivation, and compliance enhancement.

HISTORICAL PERSPECTIVE

Twenty-five years ago, patients with acute myocardial infarctions were confined to bed for up to 6 weeks. Since then, cardiologists have allowed their patients to get out of bed sooner and sooner. Now, only patients with large extensive infarcts who are hemodynamically unstable are confined to bed.¹

As physicians began to allow patients to ambulate sooner, they began to formalize stepped-ther-

apy protocols. Such a program might be very specific about what a patient should do and when. For example, on the fifth day after an infarction, patients would be allowed to get up briefly, and on the eighth day they would walk 100 feet in the hall at a slow pace. The nurse, physical therapist, or occupational therapist would provide education to accompany the particular level of physical activity.

Some authorities still advocate such a stepped approach2; however, our institution has dispensed with it. Instead, we prescribe activity on an individual basis and increase it as quickly as possible, depending on the patient's vital signs, pulse-rate response, subjective symptoms, and appearance.

Possibly as a consequence of earlier ambulation, patients do not stay in the hospital as long as they used to. Most patients now stay only 6 or 7 days after bypass surgery if the recovery is uncomplicated, and over the last decade the average length of stay decreased and is still decreasing by more than half a day per year. The same phenomenon is observed after uncomplicated infarction.

As length of stay declined and as patients were allowed to ambulate sooner, physicians began to pose questions about what patients should or should not do after they returned home. In the mid-1970s, patients began to undergo exercise testing shortly before being discharged. By the mid 1980s, the predischarge evaluation of patients to establish the appropriate amount of exercise had led to the concept known as "risk stratification."3,4 The risk stratification process, ostensibly performed to evaluate the patient's ability to safely perform activities outside the hospital, has become a paradigm of appropriate clinical cardiologic evaluation and management.⁵ Today, formal risk stratification begins almost at the moment a patient enters the coronary care unit with an acute coronary event. Typical criteria are listed in the *Table*.

TABLE

CHARACTERISTICS OF PATIENTS AT LOW, INTERMEDIATE, AND HIGH RISK OF ANGINA, RECURRENT MYOCARDIAL INFARCTION, AND DEATH

Low risk

After uncomplicated coronary revascularization ≥ 7.5 metabolic equivalents (METs) 3 weeks after an ischemic event No ischemia, left ventricular dysfunction, or significant arrhythmia

Intermediate risk

4.6-7.4 METs 3 weeks after an ischemic event Angina or 1- to 2-mm ST-segment depression with exercise Perfusion or wall-motion abnormalities with stress History of congestive heart failure More than mild but less than severe left ventricular dysfunction Late potentials present on signal-averaged electrocardiogram Nonsustained ventricular arrhythmia Inability to self-monitor exercise or comply with exercise prescription

High risk

Severe left ventricular dysfunction ≤ 4.5 METs 3 weeks after cardiac event Exercise-induced hypotension (≥ 15 mm Hg) Exercise-induced ischemia with > 2-mm ST-segment depression Ischemia induced at low levels of exercise Persistence of ischemia after exercise Sustained ventricular arrhythmia, spontaneous or induced

*From Pashkow, reference 5

NEW CANDIDATES FOR CARDIAC REHABILITATION

The median age of patients undergoing cardiac rehabilitation at our institution is now over 70 years, and this figure has been increasing by 1 year of age each year. Further, the indications for rehabilitation are expanding, and sicker patients are entering our program.

As recently as 5 years ago, heart failure was considered a relative contraindication for exercise training. Today patients with heart failure undergo rehabilitation. Patients awaiting heart transplants are also undergoing rehabilitation. In this institution in 1992–1993, patients with implantable left ventricular assist devices began formal exercise training in preparation for cardiac transplantation. This has reduced length of stay following transplantation by more than 20%.6

Another new group of candidates for cardiac rehabilitation, patients with antiarrhythmic devices and bradycardia pacemakers, need exercise training to compensate for the deconditioning they often experience with the associated loss of chronotropic competence and restricted activity before device implantation.

THE CLASSIC REHABILITATION MODEL CHANGES

Until relatively recently, rehabilitation has consisted of four phases. Phase 1 takes place in the hospital and begins as soon as the patient is able to resume activities of daily living. Rehabilitative specialists usually supervise the patient's activity while the patient undergoes continuous ambulatory telemetric electrocardiography. The goal of this phase is to prepare the patient physically and psychologically for discharge.

Phase 2 training begins as soon as possible after the patient goes home, as soon as 1 week or as late as 6 weeks after myocardial infarction or surgery. The patient undergoes exercise training under direct supervision and continuous or intermittent electrocardiographic monitoring.

Phase 3 rehabilitation can take place in the home, a facility in the community, or in a hospital. There is no monitoring, but experienced specialists directly supervise the sessions, anticipate problems, and follow up the patients to help them maintain compliance. A typical session in phase 2 or 3 consists of 5 to 10 minutes of warm-up, 20 to 45 minutes of aerobic activity, and a cool-down phase. In group programs, the warm-up helps patients adjust psychologically and socially after the acute event. It is often a form of "group therapy" and is one of the advantages of community vs home-based programs.

Phase 4 can take place within a sheltered environment such as a hospital, in the community, or at home. Ideally, help is less than a phone call away. These relatively unsupervised programs are entirely appropriate for primary as well as secondary prevention.

Coping with shorter stays

New therapies have accelerated the process. A patient may experience unstable angina, come to the hospital, have an acute myocardial infarction ruled out, go to the cardiac catheterization laboratory, have critical disease discovered in one or more vessels, undergo an angioplasty, and go home the next day. Under these conditions, a patient may not completely comprehend what has happened and may go through this process in a state of denial. Patients no longer stay in the hospital for enough time to undergo comprehensive phase 1 therapy. Rehabilitative programs need to adapt to the patient's psychologic state, education, level of understanding, and capacity for physical exercise.

With hospitalization for only a day or two follow-

ing angioplasty now becoming commonplace and with such declining lengths of stay for other acute coronary events, we must rethink the objectives and goals of inpatient cardiac rehabilitation. We cannot possibly produce tangible improvements in physical capacity or realistically expect significant transfer and retention of educational content in such a short period of time. Should inpatient rehabilitation serve primarily as a bridge to some form of outpatient experience?

The reality is that only a small percentage of eligible patients find their way into outpatient cardiac rehabilitation programs. The obstructions to such participation are multiple. Home programs seem to be a logical means of overcoming many of these obstacles and have been shown to be feasible and reasonable in cost.

BENEFITS OF EXERCISE TRAINING

Improved functional capacity

Functional capacity is measured in metabolic equivalents (METs). One MET equals 3.5 mL oxygen consumed per kilogram body weight per minute, which is the average oxygen requirement for a middle-aged white man at rest. Most daily activities require only 2 to 5 METs, and most people spend most of their time within this exercise-capacity "window." Walking at 1.7 miles per hour on a 10% grade (stage 1 of the Bruce protocol)^{10,11} requires 5 METs. Athletes in good condition are capable of much higher MET levels. However, training programs for patients usually focus on lower levels.

A typical older patient who has been sedentary and acutely ill for an extended period may be able to exercise at only 2 METs at first. After 8 to 12 weeks of exercise training, such a patient may be capable of 4.5 to 5 METs. This represents a significant success, as this patient could live a relatively normal life with this functional capacity and can perform most activities of daily living, including cooking, light housework, shopping, and, possibly, dependent care. This would be entirely adequate for most people, because few persons want to achieve levels of conditioning appropriate for competitive-level recreation.

Whereas formerly one had to estimate oxygen consumption from MET tables (which are inherently inaccurate because they are generally based on middle-aged white men instead of on all patients who undergo testing), oxygen consumption can

now be measured directly. In addition, one can determine a patient's ability to function within a reasonable and appropriate activity window. That level coincides closely with the anaerobic threshold the level of exercise at which lactate begins to build up and carbon dioxide production increases in a nonlinear fashion. When patients are told to increase exercising until they feel tired and want to stop, they almost always stop within 5% to 10% of their anaerobic threshold.

Does rehabilitation help patients who have heart failure? A growing body of literature indicates that it does, but the conditioning effect is caused by improved peripheral utilization of metabolic substrate and more efficient peripheral muscle activity, not improvement in the central hemodynamic parameters.12

Decreased mortality

In a meta-analysis of prospective trials, Oldridge et al¹³ found that rehabilitative programs consisting of exercise, education, and psychosocial support were associated with a decrease in mortality of 8% when patients participated for less than 12 weeks. The mortality rate declined by 24% when patients participated between 12 and 52 weeks and by 38% after 36 months. The decrease in the death rate achieved statistical significance only after 12 months. Unfortunately, most rehabilitative programs are prescribed (and paid for by third-party payers such as Medicare) for only 8 to 12 weeks.

In another meta-analysis, O'Connor et al14 documented a similar overall reduction in mortality and also found a highly statistically significant association between exercise training and a 37% decrease in the incidence of sudden cardiac death in the first year. This effect, however, wears off over time after patients leave the program. By the third year, the incidence of sudden death is approximately the same in patients who have undergone exercise rehabilitative training as in those who have not.

This reduction in the incidence of sudden cardiac death is probably attributable to two consequences of exercise training. First, the program is supervised: the staff is likely to note any early symptoms or signs of destabilization and take appropriate action. Second, heart rate variability appears to correlate inversely with the incidence of subsequent sudden death in coronary disease patients. 15 Thus, the reduction in mortality may also be related to the decrease in catecholamine concentrations and the increase in heart-rate variability associated with exercise training. 16

What, in practical terms, is the potential impact of rehabilitative programs on mortality after myocardial infarction, now that we are starting to observe tremendous improvements related to more aggressive therapies? The current incidence of mortality after myocardial infarction is about 8%, 17 and there are approximately 1.5 million myocardial infarctions per year. 18 A 25% reduction in mortality attributable to rehabilitation would thus amount to 30 000 lives saved per year in the United States alone.

Cost-effectiveness

Oldridge and associates¹⁹ studied the effect of cardiac rehabilitation on costs of care and quality of life in a randomized trial. They found that patients who underwent an 8-week rehabilitation program spent an estimated \$790 more on rehabilitation during the first year than did those assigned to usual care, but this was partly offset by a savings of \$310 on other health-care costs. Quality of life improved in both groups, but it improved more in the rehabilitation group—a difference of 0.052 quality-adjusted life years (95% confidence interval 0.100 to 0.007). Cardiac rehabilitation was as cost-effective as betaadrenergic antagonist therapy, and considerably more cost-effective than drug therapy for hypercholesterolemia. The cost-utility estimate was considerably lower than that for single-vessel bypass surgery and similar to the estimate for bypass surgery in patients with left main vessel disease. These data provide some preliminary evidence that cardiac rehabilitation after acute myocardial infarction is an efficient use of health-care resources and can be economically justified.5

Modification of risk factors

Exercise can have statistically significant effects on plasma lipid and lipoprotein concentrations. Numerous studies demonstrate that high-density lipoprotein (HDL) concentrations increase with exercise, 20,21 and triglyceride concentrations decrease in some individuals.²¹ Low-density lipoprotein (LDL) concentrations seem to change very little, but some research in animals has documented that the concentration of small, dense LDL particles seems to decrease with exercise, even if the overall LDL concentration does not change.²²

Exercise also changes the ratio of body fat to overall body mass, which may be more important than weight per se as a risk factor.²³ Physicians are starting to record their patients' waist-to-hip ratio (the waist circumference divided by the hip circumference), which should be 0.8 or less in women and 1.0 or less in men. The waist-to-hip ratio appears to correlate nicely with percent body fat, much better than even the body mass index.

STRATIFYING RISK

The mortality rate after myocardial infarction has progressively declined since the 1950s.¹⁷ The prognosis after an acute infarction depends on the extent of myocardial damage, the persistence of active ischemia, and the presence of significant electrical instability. Knowing this, one can predict if a patient is likely to experience untoward events (mainly recurrent infarction) and left ventricular dysfunction, particularly clinical manifestations such as congestive heart failure and death.

Exercise testing, performed before or soon after discharge from the hospital, helps one assess the need for future interventions, formulate the exercise prescription, and establish a baseline from which to measure progress.²⁴ One will also need this baseline information to determine whether other interventions and therapies have been successful, to monitor the progression of disease, and especially to reassure the patient and the family.⁵

On the basis of the results of exercise testing, one can determine if the patient is at high, intermediate, or low risk. The Figure shows a simple algorithm appropriate for use after a myocardial infarction. Patients who have recurrent angina after an infarction usually undergo coronary arteriography and do not need exercise testing, as their functional capacity is already known to be less than 1 MET. Patients with left ventricular dysfunction and an ejection fraction of less than 30% need evaluation with Holter monitoring or telemetry, since they clearly are at risk for sudden death. They may undergo signal-averaged electrocardiography, and on the basis of this test and other factors such as the presence of active ischemia and the extent of left ventricular dysfunction, they may need to undergo electrophysiologic testing. If they are not candidates for an implantable defibrillator, they may receive medical therapy and follow-up with subsequent Holter and exercise testing to monitor their progress.

Patients who have mild or moderate left ventricular dysfunction undergo exercise testing and subsequently undergo medical therapy (if no ischemia is evident), coronary arteriography (if gross ischemia is evident), or further evaluation with nuclear imaging techniques such as thallium or rubidium positron-emission tomography or echocardiographic studies (if the initial studies are equivocal).

High-risk patients (*Table*) need close supervision and monitoring after their acute event, either in an institution-based group program or at home. Equipment for home therapy is now available that can provide phase II-equivalent cardiac rehabilitation with both real-time monitoring and supervision to patients who live far away and cannot come in for an appointment three times a week.⁸

As a result of angioplasty and improved techniques of revascularization, more low-risk patients are candidates for cardiac rehabilitation. Low-risk patients have a relatively high exercise capacity (usually > 7.5 METs 3 weeks after their event), no evidence of active ischemia, no significant left ventricular dysfunction, and no manifestations of arrhythmia. Why then do they need cardiac rehabilitation?

Angioplasty patients commonly experience restenosis, and supervision in this group will likely help detect this problem. ²⁵ Low-risk patients also need instruction in exercise training, especially in how to follow a prescription based on heart rate or on a perceived exertion scale. They need to know how to select appropriate exercises and equipment, particularly if they have any musculoskeletal limitations. Most important, they need risk-factor intervention to slow or reverse the coronary disease process.

BENEFIT OF LIFE-STYLE MODIFICATION

Although some risk factors are modifiable and some are not, one must not acquiesce if nonmodifiable ones are present. Even if the patient is a man and every male member of his family died before the age of 45 (or especially if this is so), one should emphasize to him that he can do something to reduce his risk.

Ornish and colleagues²⁶ conducted a study in which 28 patients with coronary artery disease were randomly assigned to undergo a comprehensive lifestyle intervention program that included a vegetarian diet in which fats made up only 10% of the caloric intake. The program also included stress management, moderate aerobic exercise for 30 to 45

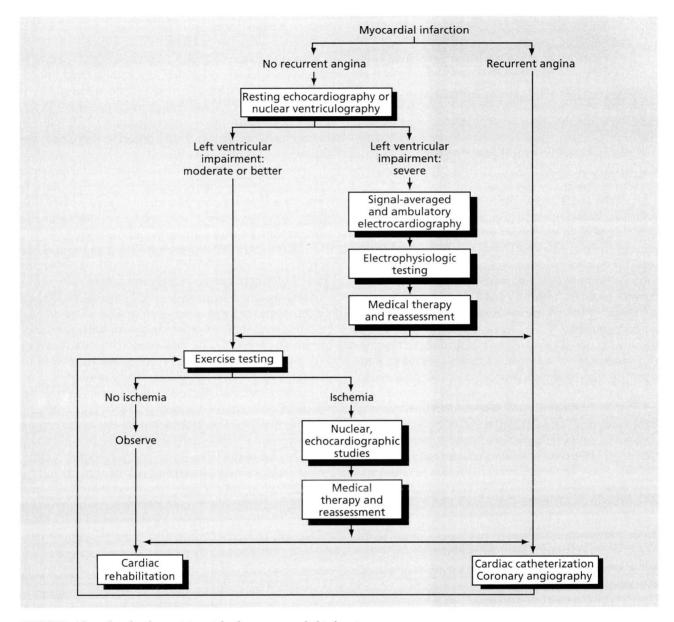


FIGURE. Algorithm for determining risk after a myocardial infarction.

minutes three or four times per week, and group psychosocial support. Another 20 patients received usual care, for a total enrollment of 48 of 98 eligible patients invited to participate. In all, 195 coronary artery lesions were analyzed by quantitative angiography.

In the experimental group, the stenotic arteries were occluded by an average of 40.0% at baseline, but at the end of 1 year this had declined to 37.8%. In contrast, in the usual-care group, the stenotic arteries were occluded by an average of 42.7% at baseline, and the occlusion progressed to 46.1% at 1 year (P = .001, two-tailed t test). In the subset of arteries that were obstructed by more than 50% at baseline, stenosis regressed in the experimental group from 61.1% at baseline to 55.8% at 1 year but progressed in the usual-care group from 61.7% at baseline to 64.4% at 1 year (P = .03, two-tailed test). The investigators divided the experimental group into three subsets of patients according to adherence to the program and found that stenoses decreased by an average of 4.5 percentage points in the

most adherent group but decreased only slightly in the least adherent group.

When patients in the usual-care group were combined with those in the experimental group (which was necessary because some patients crossed over from the experimental group into the usual-care group when they did not adhere to the program), the stenoses were found to have decreased by an average of approximately 4 percentage points in the most adherent group but progressed by more than 6 percentage points in the least adherent group.²⁶

At least some of the patients volunteered in desperation because surgery or interventional procedures were believed to be poor alternatives. Even patients who conformed to the regimen said the diet was difficult to follow because the specified low-fat foods were not readily available and took too much time to prepare. This raises the question of whether such a program is a truly practical alternative for the average patient with coronary artery disease. Indeed, when we attempted to confirm these findings in a similar study, we were unable to recruit a sufficient number of patients because of the rigor of the treatment.

Schuler and associates²⁷ also documented significant regression of atherosclerotic lesions following aggressive, nonpharmacologic lipid-lowering treatment. The patients were recruited after routine coronary angiography for stable angina pectoris and were randomized to an intervention group (n = 56) or to "usual care" (n = 57). Treatment consisted of intensive physical exercise in group training sessions for a minimum of 2 hours per week, daily home exercise periods for at least 20 minutes per day, and a low-fat, low-cholesterol diet (the American Heart Association phase 3 diet).

After 12 months, coronary angiography was again performed, and coronary lesions were measured by quantitative image processing. Myocardial perfusion was assessed by thallium 201 scintigraphy. In the intervention group, body weight decreased by 5% (P < .001), total cholesterol by 10% (P < .001), and triglycerides by 24% (P < .001); high-density lipoproteins increased by 3% (NS). Physical work capacity improved by 23% (P < .0001), and myocardial oxygen consumption, as estimated from the maximal rate-pressure product, improved by 10% (P < .05). Stress-induced myocardial ischemia decreased concurrently, indicating improvement of myocardial perfusion. Progression of coronary lesions was noted in nine patients (23%), no change

was noted in 18 patients (45%), and regression occurred in 13 patients (32%).

In the control group, metabolic and hemodynamic variables remained essentially unchanged, whereas progression of coronary lesions was noted in 25 patients (48%), no change in 18 patients (35%), and regression in nine patients (17%). These changes were significantly different between the groups (P < .05).

Recently, Haskell and associates²⁸ have reported that an intensive home-based program of multiple risk factor reduction can significantly reduce the rate of progression of atherosclerosis and decrease hospitalizations for clinical cardiac events.

Three hundred patients (259 men and 41 women, mean age 56 ± 7.4 years) with angiographically defined coronary atherosclerosis were randomly assigned to receive usual care (n = 155) or enter a risk-reduction program analogous to a comprehensive long-term cardiac rehabilitation program (n = 145). The risk-reduction program was individualized and included a low-fat and low-cholesterol diet, exercise, weight loss, smoking cessation, and medications to favorably alter lipoprotein profiles. Computer-assisted quantitative coronary arteriography was performed at baseline and after 4 years.

The risk-reduction group enjoyed highly significant improvements in several risk factors, including a decrease in body weight of approximately 4% and a 20% increase in exercise capacity, compared with relatively small changes in the usual-care group. The risk-reduction group also showed a rate of narrowing of diseased coronary artery segments that was 47% less than that in the usual-care group. Three patients died in each group. There were 25 hospitalizations in the risk-reduction group that were initiated by clinical cardiac events, compared with 44 in the usual-care group (rate ratio 0.61; P = .05; 95% confidence interval 0.4 to 0.9).

SUMMARY

The structure and content of rehabilitative programs have evolved with changing patient populations and patterns of care. Today's patients are likely to be older and to stay in the hospital fewer days than patients in the past, and they may have congestive heart failure or be candidates for cardiac transplantation. One can use the principles of risk stratification to individualize the rehabilitative

process and meet the patient's needs. Contemporary rehabilitative programs increase functional capacity and decrease mortality. Programs that include aggressive risk-factor modification as well may actually produce regression in stenosis of coronary arteries.

REFERENCES

- Hurst J. "Ambulation" after myocardial infarction. N Engl J Med 1975; 292:746-748
- Fletcher BJ, Lloyd A, Fletcher GF. Outpatient rehabilitative training in patients with cardiovascular disease: emphasis on training method. Heart Lung 1988; 17:199-205
- Krone RJ, Gillespie JA, Weld FM, Miller JP, Moss AJ. Lowlevel exercise testing after myocardial infarction: usefulness in enhancing clinical risk stratification. Circulation 1985; 71:80–89
- Topol EJ, Juni JE, O'Neill WW, et al. Exercise testing three days after onset of acute myocardial infarction. Am J Cardiol 1987; 60:958-962.
- Pashkow FJ. Issues in contemporary cardiac rehabilitation: a historical perspective. J Am Coll Cardiol 1993; 21:822-834.
- McCarthy PM, James KB, Savage RM, et al. Implantable left ventricular assist device. Approaching an alternative for end-stage heart failure. Circulation 1994; 90:II-83-II-96.
- Pashkow FJ, Pashkow PS, Schafer MN. Successful cardiac rehabilitation: the complete guide for building cardiac rehab programs. 1st ed. Loveland, CO: The Heart Watchers Press, 1988:329.
- Squires RW, Miller TD, Harn T, Micheels TA, Palma TA. Transtelephonic electrocardiographic monitoring of cardiac rehabilitation exercise sessions in coronary artery disease. Am J Cardiol 1991; 67:962-964.
- DeBusk RF, Haskell WL, Miller NH, et al. Medically directed at-home rehabilitation soon after clinically uncomplicated acute myocardial infarction: a new model for patient care. Am J Cardiol 1985; 55:251-257.
- Bruce RA. Exercise testing of patients with coronary heart disease. Principles and normal standards for evaluation. Ann Clin Res 1971; 6:323-332.
- Froelicher V, Marcondes G. A manual of exercise testing. Chicago: Year Book Medical Publishers, 1989.
- Sullivan MJ, Higginbotham MB, Cobb FR. Exercise training in patients with chronic heart failure delays ventilatory anaerobic threshold and improves submaximal exercise performance. Circulation 1989; 79:324-329.

- 13. Oldridge NB, Guyatt GH, Fischer ME, Rimm AA. Cardiac rehabilitation after myocardial infarction. Combined experience of randomized clinical trials. JAMA 1988; 260:945-950
- 14. O'Connor GT, Buring JE, Yusuf S, et al. An overview of randomized trials of rehabilitation with exercise after myocardial infarction. Circulation 1989; 80:234-244.
- Kleiger RE, Miller JP, Bigger J Jr, Moss AJ. Decreased heart rate variability and its association with increased mortality after acute myocardial infarction. Am J Cardiol 1987; 59:256-262.
- De Meersman RE. Heart rate variability and aerobic fitness. Am Heart J 1993; 125:726-731.
- Hopper JL, Pathik B, Hunt D, Chan WW. Improved prognosis since 1969 of myocardial infarction treated in a coronary care unit: lack of relation with changes in severity. Br Med J 1989; 299:892-896.
- 1993 Heart and Stroke Facts Statistics. Dallas: American Heart Association, 1992:18.
- 19. Oldridge N, Furlong W, Feeny D, et al. Economic evaluation of cardiac rehabilitation soon after acute myocardial infarction. Am J Cardiol 1993; 72:154-161.
- Cowan GO. Influence of exercise on high-density lipoproteins. Am J Cardiol 1983; 52:13B-16B.
- 21. Lavie CJ, Milani RV. Factors predicting improvements in lipid values following cardiac rehabilitation and exercise training. Arch Intern Med 1993; 153:982-988.
- Stucchi AF, Terpstra AH, Foxall TL, Nicolosi RJ, Smith SC. The effect of exercise on plasma lipids and LDL subclass metabolism in miniature swine. Med Sci Sports Exerc 1991; 23:552-561.
- 23. Bonora E, Zenere M, Branzi P, et al. Influence of body fat and its regional localization on risk factors for atherosclerosis in young men. Am J Epidemiol 1992; 135:1271-1278.
- **Krone RJ.** The role of risk stratification in the early management of a myocardial infarction. Ann Intern Med 1992; 116:223-237.
- Foley JB, Chisholm RJ, Common AA, Langer A, Armstrong PW. Aggressive clinical pattern of angina at restenosis following coronary angioplasty in unstable angina. Am Heart J 1992; 124:1174-1180.
- 26. Ornish D, Brown SE, Scherwitz LW, et al. Can lifestyle changes reverse coronary heart disease? The Lifestyle Heart Trial. Lancet 1990; 336:129-133.
- Schuler G, Hambrecht R, Schlierf G, et al. Regular physical exercise and low-fat diet. Effects on progression of coronary artery disease. Circulation 1992; 86:1-11
- Haskell WL, Alderman EL, Fair JM, et al. Effects of intensive multiple risk factor reduction on coronary atherosclerosis and clinical cardiac events in men and women with coronary artery disease. The Stanford Coronary Risk Intervention Project (SCRIP). Circulation 1994; 89:975-990.