Exercise and Coronary Heart Disease

11

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Abstract

Coronary artery disease (CAD) can be obstructive or nonobstructive. Patients with nonobstructive and stable angina pectoris are usually women. Nonobstructive CAD is caused by endothelial dysfunction at the microvascular level, such as cardiac syndrome X and coronary slow flow syndrome. Even if coronary anatomy is nonobstructive, the presence of myocardial ischemia is a major determinant for the exercise program. CAD is a chronic inflammatory disease, and the progression of the disease can lead to a rapid change in the functional capacity of CAD patients. Exercise training is a major component of cardiac rehabilitation and reduces cardiovascular mortality, morbidity, and rehospitalization as well as improves psychological stress and controls risk factors of CAD, such as diabetes mellitus, hypertension, and obesity. It is possible that the quality of life of patients with CAD can be improved by using appropriate exercise therapy. However, the exercise programs among CAD patients are highly underutilized. This chapter will summarize the research progress of exercise in the prevention and treatment of CAD as well as how to create safe exercise programs and the importance of exercise for patients with CAD. In addition, exercise training has fundamental beneficial effects on ischemic and nonischemic heart failure.

Keywords

Coronary heart disease · Dynamic exercise · Static exercise

11.1 Background

William Heberden, who first described the angina pectoris, noted that "If we give a task of sawing to a patient for half an hour every day, we may cure him." Hippocrates declared 2500 years ago, "the right amount of exercise, not too little and not too much, is the safest way to health." Currently, all CAD patients should be encouraged to regular exercise for long life even though they are symptomatic.

Age, hyperlipidemia, hypertension, cigarette use, diabetes mellitus, and sedentary activity are risk factors for the development of CAD. Some of these factors can be modified such as diet, smoking, and still life activity [1]. Sedentary behaviors increase the risk of cardiovascular mortality [2]. CAD has been reported as a cause of death in one in five people and its annual cost is more than $160 billion [3]. CAD is likely to cause death, especially over the age of 35 [4].

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Acute myocardial infarction (AMI), unstable angina pectoris, cardiac arrest, and heart failure may occur as a result of CAD [5, 6]. Atherosclerosis not only relates to be a cholesterol storage disease characterized by the collection of cholesterol and thrombotic debris in the artery [7], but it also associates with chronic inflammation and endothelial dysfunction [8]. Physical activity levels decrease systemic markers of inflammation, thrombosis, and endothelial dysfunction [9–11]. Genetic inheritance and lifestyle are important determining factors for CAD development [12, 13]. Therefore, physical activity has a key role in preventing CAD development via decreasing endothelial dysfunction and inflammation. Avoiding a sedentary lifestyle during adulthood not only prevents cardiovascular disease independently of other risk factors, but it also substantially expands the total life expectancy and the cardiovascular disease-free life expectancy for both sexes. This effect is seen at moderate levels of physical activity, and the gains in cardiovascular disease-free life expectancy are highly increased at higher activity levels [14]. Franco et al. [14] also found that life expectancy for sedentary people at age 50 years was found to be 1.5 years shorter than for people engaging in moderate daily physical activity and more than 3.5 years shorter than for people with high physical activity levels. These differences were similar for both sexes' CAD severity, and the number of coronary artery vessels' involvement, the degree of myocardial ischemia, the severity of angina, left ventricle function, and general health condition are important determinants of life expectancy and quality in patients with CAD [15]. In the treatment of CAD, many methods are used together, such as physical activity, weight control, smoking cessation, blood pressure control, control of lipid levels in the blood, diabetes control, and drug use (acetyl salicylic acid, beta-blockers, nitrates, etc.) [15]. It is also recommended that patients with CAD receive annual influenza vaccines [16]. Regular exercise is not only beneficial for both CAD prevention and treatment, but it also helps in the modification of CHD risk factors such as diabetes, hypertension, and hyperlipidemia [17–20]. Increased myocardial and peripheral artery perfusion and higher exercise capacity are related to lower mortality and morbidity of CAD [21, 22]. However, the basic mechanism of these positive effects is not fully understood. It is stated that this situation may be due to the improvement of endothelial functions and decrease of inflammation [23–25].

11.1.1 Exercise Definition

While dynamic exercise increases heart rate, static exercise increases blood pressure. For example, running is a dynamic exercise, and weight lifting is a static exercise. However, most of the sports include both dynamic and static exercise (Table 11.1) [26]. The effect of dynamic

Table 11.1 Classification of sports

	Dynamic/static	
1A	Low/low	Bowling, cricket, curling, golf, riflery, yoga
1B	Moderate/low	Baseball, softball, fencing, table tennis, volleyball
1C	High/low	Badminton, field hockey, running (long distance), soccer, race walking, squash
2A	Low/moderate	Archery, auto racing, diving, motorcycling, equestrian
2B	Moderate/moderate	American football, jumping, rugby, surfing, running (sprint)
2C	High/moderate	Basketball, ice hockey, lacrosse, running (middle distance), swimming, team handball, tennis
3A	Low/high	Gymnastics, martial arts, rock climbing, sailing, weight lifting, windsurfing, bobsledding/luge, water skiing
3B	Moderate/high	Bodybuilding, downhill skiing, skateboarding, snowboarding, wrestling
3C	High/high	Boxing, canoeing, kayaking, cycling, decathlon, rowing, triathlon, speed skating

Dynamic: Low (<50%), moderate (50–75%), high (>75%), static low (<10%), moderate (10–20%), high (>20). The estimated percentage of maximal oxygen uptake (VO_2 max) reflects the increasing dynamic exercise and relates to an increasing cardiac output. The increasing static exercise is defined in terms of the estimated percentage of maximal voluntary contraction achieved and leads to an increasing blood pressure exercise is evaluated by its effect on both maximal oxygen consumption and the percentage of cardiac output. The effect of static exercise is assessed by the increase in blood pressure and its effect on muscle strength. According to dynamic or static exercises' features, the classification of sports was categorized by the American Heart Association and American College of Cardiology (Table 11.2) [27].

11.2 Dynamic (Isotonic-Aerobic) and Static (Isometric-Resistance) Exercise and Cardiovascular Response

The exercise capacity is often consistent with the CAD severity. However, CAD patients may respond to dynamic exercise in various ways, such as myocardial ischemia, irreversible myocardial necrosis, and conduction abnormalities or normal [28–30]. Because the difference in coronary arteriovenous oxygen is unchanged, reduced exercise tolerance is often attributed to the decrease in heart rate and stroke volume. The arterial blood pressure response may be increased, normal, or decreased. A decrease in blood pressure is critical for patients with impaired left ventricular function due to myocardial ischemia. Myocardial lesions may cause left ventricular dysfunction. When left ventricular dysfunction progresses, the increase in heart rate does not fully meet the decrease in stroke volume. If more than 50% of the coronary artery diameter is affected by atherosclerosis, coronary insufficiency is encountered during exercise. The increased oxygen requirement of the peripheral tissue can be supplied by increasing the arterio-venous oxygen difference. Therefore, the absence of symptoms associated with exercise does not mean that there is no atherosclerosis in the coronary arteries [31]. Because the CAD severity increases, the probability of the coronary insufficiency triggered by exercise increases. The number of coronary vessels involved is also important, and as the number increases, the exercise capacity also decreases. Lesion complexity may not be directly proportional with the symptoms. The patient with a single coronary artery stenosis may be more symptomatic during a mild exercise, while a patient with two to three coronary vessel involvement may be asymptomatic at higher work capacity due to having good coronary collaterals. For this reason, functional classifications may be more guiding for the evaluation of patients' exercise capacity [31, 32]. The possibility of ischemia is higher in patients with CAD as the oxygen requirement of myocardium increases during exercise. This happens due to the higher end-diastolic volume and lower left ventricular ejection fraction caused by ischemia. The ST changes in ECG can be seen. Stress nuclear imaging or echocardiography should be performed for the evaluation of ischemia degree. Ischemia usually occurs on a specific exercise threshold in patients with CAD. This threshold can be assessed by the double product response calculated by multiplying the heart rate and systolic blood pressure. Dynamic upper extremity exercises may be useful to increase exercise threshold where ischemia begins [33]. In the supine position exercise, the threshold level decreases due to the increase in the end-diastolic volume of both ventricles. Because static exercises increase diastolic blood pressure and coronary flow in diastole, static exercise may increase threshold of ischemia [34, 35]. Therefore, CAD patients should do both dynamic and static exercises together.

Table 11.2 New York Heart Association classification

	VO_2 max (MET)	Exercise capacity-symptom
Class 1	>6	No limitation in normal physical activity
Class 2	4–6	Mild symptoms only in normal activity
Class 3	2–4	Marked symptoms during daily activities
Class 4	<2	Severe limitations, symptoms even at rest

Canadian Cardiovascular Society grading of angina pectoris is not compatible with VO_2 (MET) in any patient with CAD

11.3 Exercise and Inflammatory Response

Coronary artery atherosclerosis has different stages of the development. These stages include circulating plasma oxidized low-density lipoprotein cholesterol (LDL-C) entering subintimal area in the coronary vessel; upregulation of some adhesion molecules, such as vascular cell adhesion molecule-1 (VCAM-1), intercellular adhesion molecule-1 (ICAM-1), E-selectin, and P-selectin; upregulation of some chemotactic molecules, such as monocyte chemoattractant protein-1 (MCP-1); upregulation of metalloproteinases; influx of coagulation proteins; monocyte and T-lymphocyte movement to the arterial vessel wall; expression of some chemokines and cytokines, such as MCP-1, interferon gamma, tumor necrosis factor alpha (TNF-α), and interleukin-6 (IL-6); migration of smooth muscle cells from media into the intima; vascular endothelial growth factor (VEGF) production; and fibrous cap formation, subsequently [36, 37]. Palmefors et al. [38] have shown in their meta-analysis that physical activity decreases TNF-α, IL-6, VCAM-1, ICAM-1, C-reactive protein (CRP), and VEGF levels in patients with atherosclerosis. Some studies have presented the findings of exercise positive effects on coronary artery atherosclerosis [39, 40].

11.4 Exercise and Brain Natriuretic Peptides

Recently, there is growing interest in the evaluation of the relationship between exercise and ischemia. Plasma levels of brain natriuretic peptides (BNP) significantly increased during acute myocardial ischemia associated with dynamic exercise [41]. BNP levels can show the degree of left ventricular systolic dysfunction [42]. It was reported that BNP is a strong predictor of mortality in acute coronary syndromes and may be a strong prognostic marker in chronic coronary syndromes [43]. BNP show a positive correlation with peak exercise and anaerobic threshold in CAD patients, and it can improve the diagnostic accuracy of exercise testing [44, 45].

11.5 Benefits of Exercise Training and Secondary CAD Prevention

Regular physical activity improves exercise capacity [46]; increases estimated metabolic equivalents (+35%) [47, 48], peak oxygen consumption (+15%) [49], and peak anaerobic threshold (+11%) [49, 50]; decreases total cholesterol (−5%) [51, 52], triglycerides (−15%) [52], and LDL-C (−2%) [51, 52]; increases high-density lipoprotein cholesterol (+6%) [53]; reduces insulin resistance and body mass index (−1.5%) [54, 55], metabolic syndrome (−37%) [56, 57], and high-sensitivity CRP (−40%) [57, 58]; decreases anxiety [59], hostility [59], somatization [59], and mental depression [60]; improves autonomic tone (increased heart rate recovery and variability) [61]; reduces resting heart rate [61]; improves blood rheology [38], and reduces hospitalization costs, morbidity, and mortality [62–64].

11.6 Exercise Training and Cardiovascular Response

Higher intensities of exercise may not be sustainable for longer periods. Therefore, interval training was proposed by physicians [65]. Traditional training methods include continuous training (30–60 min) at moderate intensity (40–80% of VO_2 peak) (aerobic continuous training), leading to gains in VO_2 peak of approximately 20% after 12 weeks of three times-weekly exercise sessions [66, 67]. Even within the high-intensity training zone, exercise intensity was an important determinant for improving VO_2 peak in patients with CAD [68]. An increase of 1 mL/kg/min in exercise capacity yields an almost 15% increase in survival [69]. Villelabeitia et al. [70] have shown that high-intensity interval training (HIIT) results in a significantly greater increase in VO_2 peak compared with moderate continuous training (MCT). The aerobic threshold increased by 21% in HIIT and 14% in moderate continuous training (MCT). HIIT consists of a repeating series of high-intensity (peak interval) exercises, alternating with periods of low-intensity exercise (recovery interval). MCT program consists of aerobic dynamic exercise and aims at 60–80% of VO_2 peak. The studies on the benefits of MCT exercise have shown a significant improvement in terms of VO_2 peak [49].

11.7 Exercise Programs in Primary and Secondary Prevention of CAD

Both dynamic (aerobic) and static (resistance) exercise mode are proposed for all CAD patients. Dynamic exercise should be at least 20–30 min (preferably 30–45 min), and static exercise should be 10–15 repetitions, 1–3 sets of 8–10 different exercises for all extremities. The frequency of dynamic exercise should include most days (at least 4–5 days/week and preferably 6–7 days/week). The frequency of static exercise should include two to three sessions weekly (nonconsecutive days). The intensity of dynamic exercise should be close to anaerobic threshold: 50–75% peak VO_2, 65–85% of maximal heart rate or 60–80% of heart rate reserve, and 10–15 beats/min below the level of ischemia. Borg Rating of Perceived Exertion (BORG) scale can be used for this purpose. The recommended intensity of walking is a perceived exertion of 11–13 on the BORG scale. The intensity of static exercise should be moderate intensity [46, 71–73]. A CAD patient may have some symptoms during exercise, such as muscle overload, fatigue, muscular pain, dyspnea without oxygen desaturation, dyspnea with desaturation <94%, muscle injury, vasovagal conditions, ischemia, ventricular arrhythmia, or hypertensive emergencies. In these circumstances, exercise program should be reconsidered by the patient's physician.

11.7.1 Telehealth Interventions in CAD Exercise Program

Huang et al. [74] have shown that telehealth (such as the telephone, computer, Internet, and videoconferencing) interventions have a beneficial effect on risk factor reduction and secondary prevention for CAD patients. Telehealth intervention-delivered cardiac rehabilitation does not have significantly inferior outcomes compared to center-based supervised program in low to moderate risk CAD patients. Telehealth models may be helpful for the secondary prevention, especially among CAD patient who do not access cardiac rehabilitation [75].

11.7.2 Exercise-Based Cardiac Rehabilitation After AMI

Patients presenting with AMI should be encouraged for early ambulation (day 1). After early ambulation, the intensity of the exercise program should be quite low. Walking or mild level of gymnastic can be used for this purpose. If extensive myocardial damage, heart failure, hypotension, or arrhythmias exists initially, ambulation should be deterred for clinical stabilization. All AMI patients should be included in the exercise program after AMI [64]. A standard exercise-based cardiac rehabilitation must take account of patients' age, pre-infarction level of activity, and physical limitations. Exercise training, risk factor modification, education and stress management, and psychological support should be major determinants of the cardiac rehabilitation [76]. The best approach is to perform a low-level treadmill test after discharging and decide on the appropriate exercise program. The type, duration, frequency, and severity of the planned exercise should be prescribed for all CAD patients. Static or resistance exercise types such as weight lifting or push-up exercises are not recommended after early discharge. The exercise intensity can be increased after 3 months of AMI or surgery according to the presence of symptoms. Before and after the exercise, the warm-up and cooling periods should be 5–10 min. In this period, it is recommended to avoid competing sports [31]. An outpatient program should be 2–6 months' duration [77, 78]. Home-based rehabilitation is like centre-based cardiac rehabilitation in terms of the mortality of the patients with a low risk after AMI or revascularization [77].

11.7.3 The Selection of Exercise Program

In the selection of exercise, the risk classification of the CAD patients should be taken into consideration (Table 11.3). In general, the dynamic exercises, in which large muscle groups participate, are well tolerated by patients with CAD. The CAD patients' clinical condition, exercise tolerance, interest, and ability are the important variables influencing the selection of the exercise type. In the period after AMI or revascularization, bicycle ergometer or treadmill can be used. When planning an exercise prescription, it is very important to calculate the appropriate exercise intensity for each patient. Exercise should be intense enough to be beneficial for health fitness and performance, but this intensity should not lead to fatigue or cardiovascular symptoms, such as angina pectoris or dyspnea. The intensity, frequency, and duration of the exercise should be planned appropriately [31]. Heart rate and energy expenditure are directly proportional and very useful in determining the intensity of exercise for CAD patients. The prediction of energy expenditure from heart rate during exercise is possible [79]. Target heart rate during exercise is generally can be calculated with the formula (220 − age), and the target exercise heart rate of 50–80% is an optimal range [80]. The exercise test can be used to determine the appropriate heart rate. For example, if the symptoms of a patient begin at 130 beats/min, the safe interval is less than 130 beats/min. In this case, exercise should be done below the heart rate of 110 beats/min. This heart rate can be increased up to 10% per week according to the presence of symptoms. In patients with low exercise capacity (<5 MET), the exercise should be started with a target exercise heart rate of 40–50%, and the walking will be most useful for the exercise choice. Aerobic and dynamic exercise training sessions should be performed at least 3 days a week, and 250–300 kcal should be spent in one session. The weekly exercise frequency should be increased as much as possible. Approximately 1600 kcal of weekly energy expenditure with a moderate intensity exercise provides significant benefit in patients with CAD [81]. Exercise should not be done more than 5 days per week, which may increase orthopedic problems [31].

Table 11.3 The risk classification of CAD patients in the selection of exercise type

	Risk factors	
Patients with low risk	NYHA functional capacity >8 METs	No exercise-induced ischemia
	Left ventricle ejection fraction >50%	No arrhythmias
Patients with moderate risk	NYHA functional capacity <8 METs	Exercise-induced ischemia (<0.2 mV ST depression in exercise electrocardiogram)
	Left ventricle ejection fraction >30–50%	No severe arrhythmias, such as sustained ventricular tachycardia or fibrillation
Patients with high risk	Left ventricle ejection fraction <30%	Exercise-induced ischemia (>0.2 mV ST depression in exercise electrocardiogram)
	Hypotension at low exercise intensity (systolic arterial blood pressure >20 mmHg)	Persistent severe arrhythmias, such as sustained ventricular tachycardia or fibrillation, or history of cardiac arrest

11.8 Exercise and CAD Patients According to Guidelines

Exercise programs are important for the prevention and treatment of CAD patients, and the American Heart Association, the American College of Cardiology, and the European Society of Cardiology give a Class I recommendation as a fundamental therapy [82–84]. CAD patients may present their heart disease as asymptomatic (silent ischemia) or symptomatic. However, asymptomatic patients can be documented after exercise testing, stress nuclear imaging, or echocardiography. If necessary, the coronary artery anatomy is evaluated with computerized angiography and calcium score and imaging or coronary angiography in both groups' patients. Stenosis greater than 50% is considered significant. Maximal exercise test is taken under medical treatment in order to determine if there is exercise tolerance, electrical instability, and inducible ischemia in patients with known CAD. Echocardiography should also be performed for the evaluation of left ventricle functions. Patients with CAD should strongly consider deferring their possible return to highly intensive exercise to permit lesion regression and regression of lipid from the plaque. In these patients, statin therapy should be performed well according to guidelines for at least 2 years to reduce the risk of plaque rupture (Class 1; Level of evidence A). CAD patients should undergo an evaluation of left ventricular function (Class I; Level of evidence C). Asymptomatic CAD patients with the left ventricle resting ejection fraction (%) (EF) value of >50% and coronary artery stenosis of less than 50% can do competitive sports or intensive exercises if they are electrically stable during exercise and/or with induced ischemia by exercise (Class IIb; Level of evidence C). Patients should be given detailed information on the sudden outbreak or change of symptoms and should be checked regularly. According to the workforce (MET value) obtained in the exercise test and their clinical features, patients with electrically unstable or EF value <50% during the exercise test can do their exercise programs with 1A (bowling, cricket, curling, golf, riflery, yoga) and 1B (baseball, softball, fencing, table tennis, volleyball) (Class IIB, Evidence level C) sports or at low intensity (20–40% of VO_2 peak). If the patient with symptomatic CAD has undergone a revascularization procedure or has had an acute coronary event, he/she should stay away from any competitive sport within the next 3 months (Class IIb; Level of evidence C). If the duration and frequency of their symptoms increase, their exercise programs should never be competitive (Class IIb; Evidence Level C). Those who have coronary artery spasm and who do not have significant CAD disease can participate in competitive sports or higher-intensity exercise if complete relief is provided by medical treatment, but this indication is weak according to new clinical studies (Class IIb; Level of evidence C). Sports activities should be kept at 1A–B or 2A–B level according to their clinical features in patients with a history of spontaneous coronary dissection [26]. CAD patients with complete revascularization and without ischemia or myocardial depression can do competitive sports or do exercise at higher intensity according to their symptom threshold.

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