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REVIEW ARTICLE

PHYSICAL ACTIVITY AND EXERCISE IN CARDIOVASCULAR DISEASE

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ABSTRACT

Cardiovascular diseases (CVD) are the leading cause of death in the world. Physical inactivity is one of the important risk factors for the development of CVD. It is thought that increasing physical inactivity and sedentary lifestyle in recent years will result in an increase in CVD and mortality due to CVD. Therefore the importance of physical activity (PA) programmes which are both preventive and treatment approaches in the disease process is increasing day by day. Regular exercise has been shown in many studies to improve endothelial function, increase aerobic capacity, improve autonomic function and blood pressure, reduce lipid accumulation and inflammation, improve vascular health, prevent sarcopenia, and increase muscle strength and endurance. However, discussions continue in the literature on which of the different PA programs such as aerobic exercise, resistance exercise, yoga, and pilates are more effective for people with CVD. For exercise programs in CVD, it is critical that health professionals choose a patient within the framework of guidelines, ensure the safety of patients during exercise, and making the patient feel safe. It should not be forgotten that the evidence-based benefits mentioned require a sustainable exercise habit and it is important to ensure exercise compliance of people with CVD. In this review, the effectiveness of PA and exercise programs in the CVD, studies on coronary heart disease, heart failure and peripheral artery disease, safety of exercise programs, patient selection, importance of PA and compliance with exercise programs were discussed. As a result, it has been shown that PA and exercise program are effective in CVD and strategies to improve compliance with the programs should be used.

Keywords: Cardiovascular disease, physical activity, exercise, exercise contraindications, self-efficacy.

INTRODUCTION

Cardiovascular diseases (CVD) are a group of heterogeneous diseases that commonly originate from atherosclerosis and concern the heart and circulatory system (1, 2). It has been the leading cause of premature death for years. It is predicted that 23.6 million people will die from CVD each year until 2030 (2).

It is thought that one of the problems related to the risk of CVD development is a lifestyle away from healthy lifestyle behaviors. In this context, it is known that physical inactivity is an important risk factor for the development of CVD. It has been shown that a sedentary lifestyle increases the risk of CVD 1.5 times, causing 2 million deaths per year and 22% of all ischemic heart diseases (3). Due to increased physical inactivity and sedentary lifestyle in recent years, a higher increase in CVD is expected.

The 2008 Physical Activity Guidelines Advisory Committee Report showed that the amount of moderate-to-severe PA was inversely proportional to all-cause death, CVD mortality, and CVD-related events (4). In Physical Activity (PA) guidelines, PA programs consisting of 150-300 mins of moderate-intensity PA, 75-150 mins of vigorous-intensity PA, or a combination of these at an equivalent intensity are recommended (5).

The benefits of regular PA on cardiovascular health can be seen at levels up to about 5 times the recommended amount, even at activity levels well below. Although potentially harmful effects have been reported at relatively moderate activity levels in those with CVD, the maximum benefit may be achieved in healthy individuals at higher moderate-intensity PA levels (approximately 14.000 steps per day). In contrast, combined exercise programs, especially combining endurance and strength training, are more effective at improving cardiovascular health (6).

Exercise and PA are not only the preventive approaches for CVD but also as therapeutic methods in disease process. The evidence in the literature regarding preventive and therapeutic effects on CVD is quite convincing (7). Cumulative exposure to hemodynamic stimulus in regular aerobic PA produce antiatherogenic adaptations in vascular structure and function. Regular PA reduces the chronic inflammatory status by releasing myokines from muscles. These functional adaptations are before structural adaptations in vascular structures are dilated during exercise. The content of atherosclerotic plaque, collagen, and elastin increase, the volume of necrotic core declines, and general plaque loads reduce. Coronary collateralization which increases myocardial perfusion is achieved. It prevents arrhythmia resulting in death by inducing cardiac preconditioning, which protects the heart against ischemia-reperfusion injury. Cardioprotection can be stimulated by a single session of exercise and maintained for months with regular exercise (6). Exercise capacity, skeletal muscle strength, and endurance, left ventricular function, diaphragm function, decreased endothelial function, and many similar systemic effects improve quality of life and reduce morbidity and mortality (8).

In PA guidelines, it is recommended that people with clinically stable CVD aim for 30 mins or more of moderate-intensity PA on most, if not all, days of the week (9). Exercise programs with less intense, shorter sessions, and including more rest periods may be sufficient for patients with CVD and severe symptoms. Additionally, regular low-to-moderate resistance activities, preferably initiated under the supervision of an expert, are recommended (10). An important point to consider is that the potential for functional benefit in persons with CVD is most in those who were least active before starting regular PA, and this benefit can be achieved even at relatively low PA levels (7). Within the scope of this review, PA and exercise program recommendations, benefits, and effectiveness of these programs will be discussed in light of the literature on coronary heart disease, heart failure, and peripheral artery diseases.

Coronary heart disease

Coronary heart disease (CHD) is a group of diseases that includes angina, myocardial infarction, ischemic cardiomyopathy, and sudden cardiac death. The main cause of CHD is the progression of coronary atherosclerosis and thrombosis. The pathogenesis of atherosclerosis is explained not only in the form of lipid accumulation in the vessels but also in the gradual increase of endothelial dysfunction and chronic inflammation. Therefore, correction of endothelial dysfunction and inflammation become priority targets for the prevention of CHD (11, 12). Although it is emphasized that genetic predisposition is important, it should not be ignored that the lifestyle shaped by the effect of environmental conditions is among the determining factors (13). PA and exercise habits are also important in lifestyle.

The "dose" of endurance exercise that will provide the most benefit in coronary artery disease is unclear. However, it is said that the presence of cardiovascular risk factors should be specific to each individual according to their response to exercise training and the progression of the disease. However, many studies suggest that the best functional adaptations occur over 1 year. Besides it requires frequent exercise sessions at relatively higher intensities (14).

It is seen that the superiority of high-intensity intermittent exercise and moderate-intensity continuous exercise programs over each other in aerobic exercise studies in CHD are discussed. Conraads et al. compared the two training programs in terms of peak VO_2 (oxygen consumption), peripheral endothelial function, cardiovascular risk factors, quality of life, and safety in their study of 200 patients. They trained for 12 weeks at 70-75% of maximal heart rate for continuous training and 90-95% of maximal heart rate for interval training. In conclusion, they reported that aerobic interval training and continuous training equally improved peak VO_2, peripheral vascular function, quality of life, and some cardiovascular risk factors (15). Another study, a systematic review and meta-analysis of 12 studies, compared the two trainings. It was found that high-intensity interval training programs were superior to continuous training programs at peak VO_2 gain. However, when a sub-analysis of isocaloric protocols was performed in patients with CHD, this superiority disappeared and there was no difference between the effects of the two training programs on quality of life (16).

Resistance training is one of the recommended exercise modalities along with aerobic training. While it is emphasized that combined training provides the best benefit in CVDs, it is very important to know the benefits of these two trainings separately. In a study in which only resistance training was examined in patients with CHD, it was shown that eight-week high-repetition low-resistance training was effective enough to improve important results such as heart rate change, muscle strength, and endurance (17). A meta-analysis reporting the results of resistant training in middle-aged and older people with CHD included 22 studies, 17 of which were conducted in the middle-aged and 5 of which were performed in the elderly. In middle-aged patients, it was observed that lower and upper extremity muscle strength and peak VO_2 develop but no improvement in mobility. However, mobility also improved significantly with the aforementioned parameters in elderly patients (18).

Today, home-based practices have gained importance both to reduce the cost of health expenditures and to overcome the barriers to accessing treatment under current conditions. Although the problems related to the compliance of the patients continue in these programs, home-based exercise training programs carried out with the appropriate patient group give convincing results. Three groups, namely the home-based exercise group, the center-based exercise group, and the control group, were included in the study of Avilla et al. (19). The home-based group applied an individualized exercise program of at least 150 mins per week at a target heart rate of 70-80% of the heart rate reserve (HRR). They uploaded their data on software, and feedback was received from the patients once a week via telephone call or e-mail. The center-based training group was advised to maintain an exercise program consisting of approximately 45 mins of endurance training at 70-80% of HRR followed by relaxation. The control group was asked to maintain a physically active lifestyle. After three months of intervention, all groups were encouraged to continue exercising and no interviews were conducted for nine months. As a result of the study, it was shown that exercise capacity, PA, anthropometric measurements, muscle strength, and health-related quality of life were similar in home-based and center-based exercise training.

Heart Failure

Heart failure (HF) caused by the impaired systolic or diastolic performance of the heart is characterized by exercise intolerance due to many causes (20). The most common cause is due to symptoms of fatigue and/or breathless. The main causes are attributed to abnormal gas exchange, abnormal cardiac output, and myopathy of the peripheral muscles and diaphragm (21).

Although the New York Heart Association (NYHA) Functional Classification was developed to categorize the level of exercise limitation in patients with HF. It is useful in the initial evaluation of PA programs, the subjective nature of this system and the difficulty of defining intermediate functional classes (II-III) are among the disadvantages (22). It is of great importance that it is used in many stages of treatment planning for patients with HF as well as in PA and exercise prescribing.

Despite these PA and exercise recommendations, it has been reported that only 10.4% of eligible patients with HF are referred to cardiac rehabilitation and included in exercise programs after hospitalization for HF (23). Raising awareness on this issue and including patients in cardiac rehabilitation programs as soon as possible plays a key role in both controlling the disease as soon as possible and minimizing health expenditures.

Sociodemographic features such as age, gender, comorbidities, previous PA level, and clinical features such as orthopedic/musculoskeletal system factors should be taken into consideration while creating an exercise plan. There may be various patient and treatment-related obstacles related to the continuity of exercise programs. For this reason, any problem that may concern compliance should be defined carefully, patients should be informed about the benefits, effectiveness, and safety of exercise training. Furthermore the patient's exercise program and compliance with these programs should be evaluated during the controls, and the patient should be encouraged(15). Klompstra et al. reported that 42% of stable patients with HF were active less than 1 hour a day. However, in the same study, they found that motivation led to a higher self-efficacy, which resulted in higher levels of PA in patients with HF. In addition, they emphasized that it is important to adapt PA and exercise programs and present various formats according to the motivation and self-efficacy of the patients (24). At this point, it should not be ignored that the self-efficacy-exercise relationship is in a bidirectional interaction and should be taken into consideration when it comes to exercise programs.

In a meta-analysis that included 6 studies, it was examined the effects of exercise training in patients with HF. It was observed that exercise training provided significant improvements in peak VO_2 and quality of life, which are important parameters of cardiorespiratory fitness but no significant changes in left ventricular systolic or diastolic function (25). As in many disease groups, the effectiveness of different exercise modalities in patients with HF has been the topic of research. A review of 20 studies including different exercise types showed that interval training is more effective for improving left ventricular ejection fraction and left ventricular end-diastolic volume. Additionally, it presents evidence that it is not clear which type of exercise is more effective on cardiorespiratory fitness and quality of life (26). These results show that active participation of patients with HF in any exercise training program will be sufficient to improve disease prognosis, quality of life, and anatomical function.

One of the secondary consequences of many heart problems is impaired autonomic function balance. This imbalance is basically in the form of increased sympathetic nervous system activity and parasympathetic nervous system being in the background (27). The effect of exercise training on autonomic functions is one of the subjects investigated in patients with HF. A review and meta-analysis of 20 studies examining this autonomic effect included exercise interventions such as aerobic training, strength training, combined training, Tai-chi, yoga, pilates, and hydrotherapy. After exercise training, heart rate recovery (HRR1), heart rate variability (HRV), and muscle sympathetic nerve activity (MSNA) at 1 minute, which are important parameters of autonomic function, were examined. In this study, in which different exercise types were included, increased parasympathetic (vagal) tone and decreased sympathetic activity in patients with HF suggestively improves HRR1, HRV, and MSNA, thus helping to restore autonomic function (28). However, this meta-analysis, which included many different types of exercise training, raises questions about exercise prescription for optimal results of autonomic function. These questions have not yet been answered clearly.

A significant point for PA and exercise programs is the variability of compliance with the programs due to seasonal transitions. Klompstra et al., in their study examining seasonal variability in PA, concluded that one-third of patients with HF performed less PA in winter than in summer, this situation was associated with symptom severity and decreased PA was not associated with motivation and self-efficacy. Furthermore, it was emphasized that self-efficacy was low in both seasons (29). These results highlight the need for personalized PA programs that also assess symptom severity and variation in symptom severity depending on seasonal conditions. The effects of seasonal changes on PA and exercise compliance is an unregarding issue and it is needed more research especially in patients with CVD.

Peripheral artery disease

Peripheral arterial disease (PAD) is a clinical condition caused by atherosclerotic changes in the vascular structures distal to the aorta. Despite its high prevalence, PAD is often diagnosed late. There is insufficient awareness of its clinical manifestations, including gait disturbance, intermittent claudication, critical limb ischemia, and associated adverse cardiovascular events and limb findings (30). The most common symptom of PAH is intermittent claudication, which manifests as pain in the leg muscles triggered by exercise.It is seen in 2% of people with PAD and older than 65 years (31).

PAD is accompanied by several problems. Muscle atrophy, changes in capillary density, type I/type II muscle fiber ratio, increase in arteriogenesis and mitochondrial activity, decrease in muscle strength and endurance, decrease in walking distance, imbalance, and deviations in walking parameters are some of the problems seen (32). The problems such as increased oxidative stress, changes in metabolism, mitochondrial dysfunction, changes in myosin heavy chain expression, myositis apoptosis, muscle fiber denervations, and fat infiltration are observed in the stenotic vascular structure in the disease process (30). These problems may be caused by the frequently repeated ischemia-reperfusion cycle.

Structured exercise training programs are highly recommended for the treatment of PAD. It is stated that supervised exercise therapy reduces the risk of cardiovascular events along with reducing symptoms and improving quality of life. Even if people are not diagnosed with PAD, exercise habits are an essential protective component. Studies included in a guideline in which high-evidence data are shared have reported that exercise training provides improvements in fundamental problems affecting the daily life of patients, such as functional status, quality of life, leg symptoms, and walking ability (33).

In the review of Fakhry et al., it was shown that supervised walking programs provide improvement in maximum walking distance and pain-free walking distance in peripheral arterial patients with intermittent claudication (34). In Vun et al. study examining the effect of supervised exercise programs on lean muscle mass in people with intermittent claudication, they observed that 12-week standard treadmill training did not cause loss of calf lean mass, however, it caused a significant reduction in bilateral thigh lean mass even in patients with unilateral symptoms. They emphasized that these changes explain the lack of development of functions in which the thigh muscles are dominant, such as sitting and standing up from a chair with exercise training in previous studies. However further studies are needed to determine whether they affect functional performance, quality of life and survival, taking into account the exercise modality and limitations (35).

The effectiveness of aerobic and resistance training is one of the frequently studied topics in PAD. McDermott et al. examined cardiorespiratory fitness and many functional outcomes in their study in which they included treadmill, lower extremity resistance exercise, and control groups with 24-week follow-up (36). Treadmill training improved 6 min walking performance, treadmill walking performance, brachial artery flow-mediated dilation, and quality of life. However, this training did not improve short physical performance battery scores of patients with PAD with and without intermittent claudication. Lower extremity resistance training improved functional performance as measured by treadmill walking, quality of life, and stair climbing ability. In another review examining the effectiveness of combined training, they reported that there was insufficient evidence about the effects of combined aerobic and resistance exercise on walking performance compared to isolated aerobic exercise or classical care. In the same review, it was emphasized that although the quality of evidence was low, combined aerobic and resistance exercise programs seemed to be an effective strategy to improve walking performance in patients with intermittent claudication. Considering the limited data, it has been stated that randomized controlled studies assessed cardiovascular risk factors are needed to better determine the effect of combined exercise training (37).

In the clinical practice guidelines of the American Heart Association/American Institute of Cardiology published in 2006, it was emphasized that there is no evidence of the effectiveness of unsupervised home-based exercise programs in people with PAD. It was stated that was not correct to recommend that they "go home and walk" and it must be supervised exercise training programs. The studies in these guidelines appear to have resulted from a few small studies of home-based exercise in patients with PAD with claudication that do not include behavior modification techniques (38). Selecting patients suitable for this approach and following by encouraging them with some strategies will provide a fundamental step in the treatment process of patients. It is known that the best-known effects of exercise programs are on walking time and walking distance. An application was developed in recent years to monitor these parameters is encountered in the literature. Reis et al. developed remote monitoring-oriented software aimed at tracking exercise programs prescribed to patients with PAD. This software allows recording and monitoring many parameters such as number of steps during walking, duration of walking, pain-free walking time, pain-free walking distance, walking time until pause, walking distance to pause, number of pauses during walking, the time required to pause, maximum walking distance, duration of pain relief at the end of the walking session (39).

Safety of Exercise Programs in Cardiovascular Diseases

The concerns about the safety of exercise may come at the beginning of hesitations about participation in exercise programs in people with CVD. This concern can also be experienced by health professionals. In this case, defining the relative and absolute contraindications and following the patient well are the basis of a reliable exercise program. The indications for delaying and terminating activities stated in the current guidelines are as in Table 1 (40). The risk of major or fatal cardiovascular (CV) events among participants in supervised exercise is estimated to be one major event per 117.000 hours

Table 1. The indications of activity postponing and termination (40).

The Indications of Activity Postponing	The Indications of Activity Termination
Unstable angina	Tightness in the middle or back of the chest
Uncontrolled heart failure	Discomfort/typical pain or symptoms reminiscent of previous myocardial ischemia
Severe aortic stenosis	Dizziness, lightheadedness or feeling faint,
Uncontrolled hypertension or severe hypertension	Difficulty in breathing,
Symptomatic hypotension	Nausea,
Acute infection or fever or feeling unwell (including acute myocarditis or pericarditis),	Uncharacteristic excessive sweating
Resting tachycardia or arrhythmias	Palpitations associated with feeling unwell
Diabetes with poor blood sugar control	Over-fatigue,
	Leg pain that limits function
	physical inability to continue
	Shivering, tingling in the lips, hunger, weakness, palpitations in diabetics

of activity and one fatal event per 750.000 hours (41). However, it should be noted that exceeding the recommended dose may increase the risk of recurrent CV events (7).

There is a common idea that people with CVD are at increased risk of acute adverse CV events during dynamic high-intensity resistance training. In the early stages of cardiac rehabilitation, patients with CVD are directly mentored and supervised by clinicians who are familiar with the contraindications for dynamic resistance training and who are familiar with the patient's risk profile (42). In addition, environments where rehabilitation or exercise training is carried out are designed to be prepared for adverse events during exercise (43). For this reason, all equipment is provided for risk management and possible intervention.

Physical Activity and Exercise Compliance in Cardiovascular Diseases

All these recommendations together with the evidence-based benefits are very important for the sustainability of PA and exercise programs, the preservation of the benefits, and the emergence of long-term effects. Therefore, compliance with these programs plays a key role in the treatment process of the patient with CVD. Although it is easier to achieve this compliance in supervised programs, especially home-based programs which are the alternative approach of today's rehabilitation programs becomes more important to follow this compliance and to catch provider strategies.

There may be many barriers that may affect the PA and exercise compliance of people with CVD. Physical health-related problems brought by the disease (symptoms such as shortness of breath, fatigue, and more physiologically based factors such as low energy), psychosocial factors (level of understanding the need for self-care, social support, mental health, weak sense of self and/or lack of perceived benefit or perceived benefit) and the patient's knowledge level may inhibit exercise behaviors at various levels (44-46). In addition to these barriers, it was shown that lower adherence to PA is associated with advanced age, lower social and economic status, financial and medical concerns, and motivational limitations (47). Motivation is a critical factor for exercise commitment as well as influencing participation in exercise programs (48). The relationship of high motivation with the increase in self-efficacy levels opens a big door for ensuring the sustainability of exercise behavior (24).

The compliance with exercise requires long-term behavioral changes of the individual. Studies that include theory-based interventions that offer multiple behavior change techniques appear to have a greater impact than interventions that do not include such strategies (49). The studies often use Bandura's social cognitive theory to to improve exercise compliance. The social cognitive theory states that people learn from observation and that improved self-efficacy which influenced by performance achievements, vicarious experiences, verbal persuasion, and emotional stimulation is the key to behavioral change (50). Based on this theory developed by Bandura, many strategies are used and these strategies can also be applied for exercise programs.

CONCLUSION

One of the important risk factors for CVD which is one of the leading causes of death in the world is a lifestyle away from healthy lifestyle behaviors. Among the healthy lifestyle behaviors, PA and exercise habits occupy a critical place among both preventive and therapeutic approaches for CVD. The evidence indicates that aerobic exercise and resistance exercise programs provide significant benefits separately by different mechanisms. However it was observed that combine training programs will provide maximum benefit. It should not be forgotten that exercise is safe for people with CVD and that it will be more reliable with the precautions to be taken during exercise training, and this confidence should be given to the patient. However, the sustainability of PA and exercise is important to observe the long-term effects and prevent reversal of the benefits. The strategies to ensure compliance in different status seem to be lacking in studies prescribing exercise programs. For this reason, barriers of compliance should be identified and appropriate strategies should be created and added in PA and exercise programs.

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