Chapter 1

Exercise is Medicine: The Importance of Exercise as Preventative Medicine for a Disease-Free Lifestyle

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Abstract

Currently, overweightness and obesity are the biggest health problem faced in the twenty-first century. The major causes of this problem are lack of physical activity and excessive consumption of processed food. Individuals who are overweight typically show abnormal cardiovascular function, and obesity is an independent risk factor for cardiovascular diseases, such as hypertension, heart disease, and type 2 diabetes. Hypertension has been found to occur more frequently in overweight compared to lean individuals and poses a risk for hypertension development in young overweight adults. Obesity has also been found to be associated with reduced life expectancy and sudden death largely through its negative effect on the cardiovascular system. Degradation of a number of key autonomic cardiovascular markers, such as reduced heart rate variability and baroreflex sensitivity, is associated with the development of these lifestyle diseases. Also alterations in the metabolic profile, such as dyslipidemia and hyperglycemia, can lead to impairment in cardiac structure and function. Regular exercise has been widely used as preventative medicine to reverse autonomic, cardiovascular, and metabolic decline. Thus, incorporating regular exercise into daily activity may prevent the development of these cardiovascular diseases and accompanying risk factors.

Keywords: exercise, cardiovascular health, metabolic health, arterial stiffness, heart rate variability, baroreflex sensitivity

1. Introduction

Physical inactivity has been shown to affect health by increasing cardiovascular and metabolic dysfunction. More and more people including children and adolescents are leading a sedentary lifestyle, which leads to a number of health problems. Overweightness and obesity are often accompanied by a lack of physical activity that can lead to more serious health problems, such as metabolic syndrome, type 2 diabetes, and hypertension. Lack of physical activity has also been found to be a major cause of morbidity [1] and mortality [2]. Overweight and obese individuals typically show abnormal cardiovascular function, and obesity has been found to be an independent risk factor for cardiovascular diseases, such as hypertension [3], type 2 diabetes, and cardiac complications (i.e., heart failure, heart disease). Obesity is associated with reduced life expectancy [4] and sudden death through its negative effect on the cardiovascular system [5]. Overweight and obese individuals usually develop hypertension. Compared to normal weight individuals, overweightness and obesity pose a potential risk for hypertension development in overweight individuals. It was found that a 10 kg excess in weight was associated with a 3 mmHg higher systolic and a 2–3 mmHg higher resting diastolic blood pressure. This can be translated into an estimated increased risk for coronary heart disease of 12% and an increased risk of stroke of 24% [6]. Alterations in the metabolic profile that are commonly found in overweight and obese individuals, such as dyslipidemia and hyperglycemia, can also lead to impairment in cardiac structure and function as adipose tissue accumulates [7]. It has been shown that left ventricular (LV) function and the ratio of the stroke index and LV end-diastolic pressure are reduced with overweightness and obesity [8]. These changes show that depressed LV function has already occurred even in young overweight and obese individuals.

Overwhelming evidence indicates that regular physical activity in the form of both acute and regular aerobic exercise reduces the severity and occurrence of diseases related to unhealthy lifestyles. One single bout of acute exercise has been found to improve vascular function even in normotensive young healthy individuals with a family history of hypertension [9]. Whereas regular aerobic exercise has been shown to improve physical fitness (cardiorespiratory fitness) in addition to improving vascular function [10]. Having high levels of physical fitness, assessed through a sub-maximal or maximal oxygen uptake test, is desirable as low cardiorespiratory fitness has been found to significantly increase the risk of cardiovascular diseases and mortality more so than other factors, such as hypertension, type 2 diabetes, and smoking, and regardless of body mass index [11]. High-intensity interval training (HIIT) is a form of interval sprinting exercise typically performed on a stationary bike and has also been found to improve cardiac and metabolic health of young overweight males [12] and females [13]. Physical activity is so important that failure to lead a physically active lifestyle can result in several abnormalities such as high blood pressure, metabolic syndrome, and type 2 diabetes [14]. Baroreceptor sensitivity (BRS) has also been found to decrease with age [15, 16], being hypertensive [17] and being overweight and obese [18].

Overall, regular exercise results in improvement of the pathogenesis and symptoms of specific conditions that include chronic heart failure, coronary heart disease, dyslipidemia, hypertension, insulin resistance, intermittent claudication, obesity, and type 2 diabetes [19]. Other health benefits of regular aerobic exercise include improvement in balance, cognitive functioning, life expectancy, and overall quality of life [20, 21]. The beneficial effects of regular aerobic exercise have been well known. Thus, modification of a sedentary lifestyle by incorporating regular exercise is paramount for maintaining and improving health. Exercise is a powerful stimulus and can reduce the severity of several conditions with its effects being similar to many drug therapies. In this regard, exercise has now been widely accepted as medicine [22]. Therefore, the purpose of the chapter is to summarize the major autonomic, cardiovascular, and metabolic changes associated with being physically inactive. Then, the ability of differing forms of exercise (aerobic, interval sprinting, and resistance) to reverse these negative changes will be described.

2. Cardiovascular problems associated with physical inactivity

A sedentary lifestyle, which is associated with overweightness and obesity, typically leads to an increased risk of cardiovascular disease. Currently, overweightness and obesity have been escalating at an alarming rate worldwide. Based on the World Health Organization (WHO, Global Health Observatory data) region data from 2010 to 2014 [23], the prevalence of overweightness (**Figure 1**) and obesity (**Figure 2**) for both males and females at the age of ≥18 years has significantly increased. The highest prevalence of overweightness and obesity, according to the WHO, was the Americas, followed by Europe and South Pacific, with Southeast Asia containing the lowest prevalence of overweightness and obesity. Also, women were more likely to be obese than men in 2014 in all WHO regions. Increased numbers of overweight and obese individuals put tremendous pressure and burden on healthcare providers and threatens world health in many countries. Approximately 20–30% of adults worldwide are categorized as clinically obese and numbers are progressively increasing [24, 25]. It has been well established that both high body mass index and a sedentary lifestyle are associated with greater risk of cardiovascular disease [26, 27].

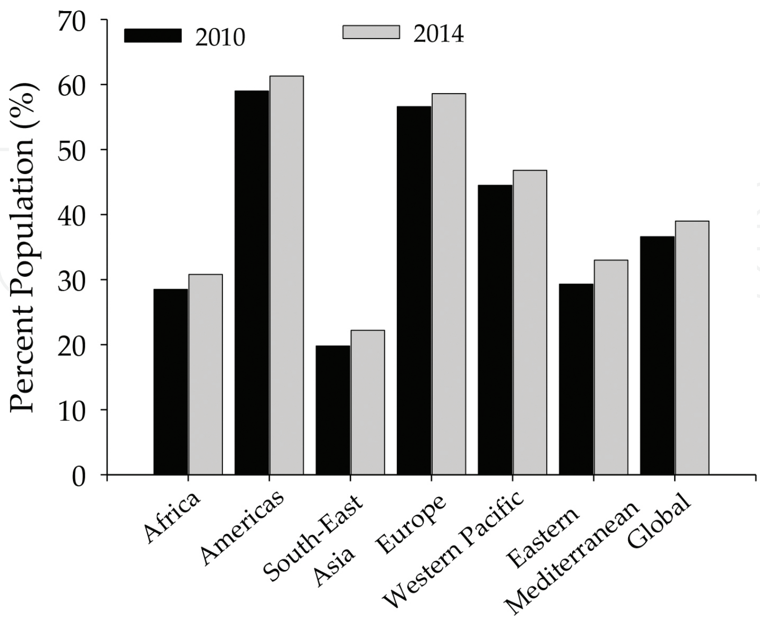

Figure 1. Prevalence of overweight based on WHO region for both sexes 2010–2014.

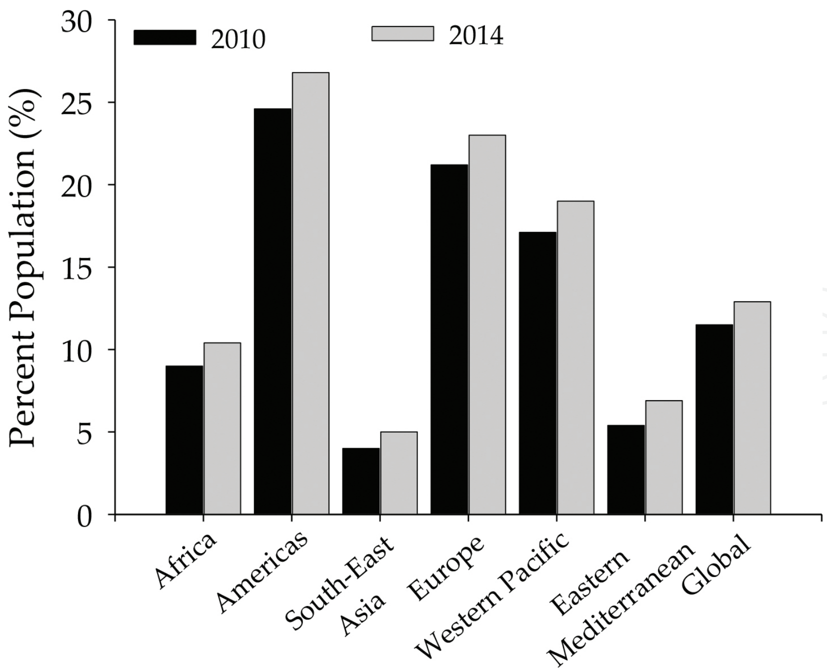

Figure 2. Prevalence of obesity based on the WHO region for both sexes 2010–2014.

It has been shown that overweightness and obesity are accompanied by a cluster of cardiovascular risk factors, which is termed metabolic syndrome and includes hypertension, glucose intolerance, hypertriglyceridemia, and visceral obesity. These conditions occur in approximately one out of four adults over the age of 40 [28]. The metabolic syndrome is also associated with insulin resistance and endothelial dysfunction [29, 30]. It is believed that in child obesity, as fat mass increases, insulin resistance develops, which is a determinant of impaired metabolic function at early age [31]. Other health problems accompanying overweightness and obesity include cardiac autonomic dysfunction and endothelial dysfunction. Aberrant cardiac autonomic function has been found in obese children [32] and increased adiposity during childhood increases the risk of obesity, type 2 diabetes, and cardiovascular disease in adulthood [33, 34]. Endothelial dysfunction can be defined as inadequate endothelial-mediated vasodilation, which is typically due to a deficiency of endothelial-derived relaxing factor, nitric oxide (NO) synthesis, and/or release. It is believed that NO deficiency is a primary factor linking insulin resistance and endothelial dysfunction. Thus, it is clear that being sedentary results in increased cardiovascular disease risk, aberrant metabolic, cardiac, autonomic, and endothelial function.

2.1. Cardiac autonomic function

It has been well established that cardiac autonomic dysfunction is associated with conditions, such as overweight, obesity, and type 2 diabetes [35, 36]. The decline of cardiac autonomic function is typically influenced by an accumulation of visceral fat [37]. Lowered autonomic function was also found to be correlated with higher abdominal-to-peripheral body fat distribution measured by dual energy X-ray absorptiometry in both young and old healthy men [38]. These results suggest that visceral obesity contributes to a decline in autonomic function. Also, young individuals with high abdominal adiposity seemed to undergo an early decline and a premature aging of autonomic function [37]. Thus, hypertension and high levels of central adiposity have an unfavorable effect on cardiac autonomic function, which is reflected by impaired heart rate variability (HRV) and baroreflex sensitivity (BRS).

HRV is a marker that is commonly used to assess cardiac autonomic function and can be defined as beat-to-beat variation in the heart rate of individuals possessing normal sinus rhythm [39]. HRV has been shown to be an indicant of healthy cardiac autonomic function as it has been found that reduced HRV predicts increased cardiovascular disease and mortality [40, 41]. High body mass index, which is commonly found in overweight and obese individuals, is also associated with reduced HRV, which contributes to decreased parasympathetic activity and increased sympathetic activity [42, 43]. BRS is another marker of cardiac autonomic function that provides information about the ability to increase parasympathetic or vagal activity and to decrease sympathetic activity in response to sudden increases in blood pressure [44]. BRS, which is typically reduced as people age, is an indicant of the body's autonomic nervous system sensitivity in responding to sudden blood pressure changes [44]. Low BRS is a marker of reduced compliance of the carotid artery [15, 16]. Overweight and obese individuals typically possess endothelial dysfunction that leads to reduced arterial compliance, which is accompanied with a low BRS compared to that of normal weight individuals. Lower BRS has also been found to be associated with high blood pressure, increased sympathetic activity, and diseases related to an unhealthy lifestyle. It seems that low HRV and BRS are affected by the accumulation of visceral fat and metabolic syndrome factors.

Studies have shown that obese children typically have decreased parasympathetic activity compared to normal weight children [45–49]. It has also been reported that an increased thickness of carotid intima-media in obese children represents a very early sign of atherosclerosis [50]. It has also been found that the earliest signs of atherosclerosis development are lipid deposits in the intimal layer of systemic arteries (aorta), which have been found in children as early as 3 years old and in the coronary arteries of adolescents [51]. Another aberrant change possessed by overweight and obese individuals is high levels of leptin. Several studies have shown that positive correlations among leptin, insulin resistance, and blood pressure existed in overweight children [52, 53]. A reduction in adiposity level, however, brought about a reduction in leptin, which further improved metabolic health, by decreasing insulin, cardiovascular function, and blood pressure [52]. Adiponectin has a major anti-inflammatory and anti-atherogenic effect [54] and has been found to be three times higher in normal weight children compared to overweight and obese children [34]. A 1-year follow-up, following a 1-year intervention, found that children with weight loss had similar adiponectin levels compared to normal weight children. Leptin levels, however, remained higher in overweight and obese children with weight loss. The increase in adiponectin appears to be an early biomarker of improvement in insulin sensitivity [34]. Thus, it is clear that overweightness and obesity in children result in early deposition of fat in the systemic arteries and thickening of arterial walls. These conditions can lead to more serious health complications later in their life if lifestyle modification is not introduced.

2.2. Vascular dysfunction

Overweight and obesity conditions not only result in metabolic dysfunction but also bring about vascular dysfunction. The balance between the ability of the vasculature (arterioles) to vasodilate and vasoconstrict is impaired with the development of overweightness and obesity. The loss of balance between vasodilators and vasoconstrictors is an indicant of endothelial dysfunction. Endothelial dysfunction is now regarded as a precursor of atherogenesis [55], which further leads to the development of atherosclerosis [56] and diabetic complications [57]. Arterial compliance, and its inverse arterial stiffness, can be defined as the ability of an artery to distend in response to intravascular (transmural) pressure [58] and is commonly termed as stiffening of the arteries. It is well known that overweight and obese individuals typically have high arterial stiffness [59], and this high arterial stiffness is associated with high body mass index and body fat [60]. Reduction in body mass index, however, has been found to be the strongest determinant of decreased arterial stiffness in severe obese young and middle-aged adults [61].

Arterial stiffness, which has been considered to be an independent predictor of cardiovascular disease, can be assessed through a reflection wave, commonly known as the augmentation index (AIx) and carotid femoral pulse wave velocity (PWVcf), which is considered to be the gold standard of arterial stiffness assessment. AIx, a reflection wave, is typically assessed by placing an applanation tonometry sensor (e.g., SphygmoCor) on either a radial or carotid artery. AIx then is derived from the ratio of augmented pressure (AP) and pulse pressure (PP), AP/PP [28]. PWVcf is obtained by dividing the distance from the carotid pulse and femoral pulse as measured by a tape measure by the time taken for the arterial pulse to propagate to the carotid and femoral arteries [62].

Arterial stiffness, which is an indicant of the stiffening of the large arteries, increases with age, especially in central arteries, such as the aorta and carotid artery. Arterial stiffness has also been found to increase with overweightness and obesity, which leads to an increased risk of arteriosclerosis [63]. Overweight and obese children have been found to have high arterial stiffness, assessed through pulse wave velocity [64]. Similar findings were also found in young overweight individuals who had higher arterial stiffness levels compared to the normal weight individuals [62]. Hemodynamic changes accompanying overweightness and obesity include increased arterial wall stress, smooth muscle cell proliferation, thickening of vessel walls, and eventually reduced arterial compliance/increased arterial stiffness. Thickening of vessel walls is likely caused by increased total blood volume and cardiac output to compensate for the metabolic requirements of excess fat [65, 66]. Alterations of hemodynamics, together with other markers of obesity, including chronic inflammation and endothelial dysfunction, have been shown to contribute to the impairment of vasculature structure and function in obese individuals [67]. Thus, the development of arterial stiffness seems to be due to coping mechanisms by the body to meet the metabolic demands caused by excess fat gain. In overweight and obese children, this mechanism seems to develop very early on and carries on until adolescence and adulthood if interventions to reverse this condition are not introduced.

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3. Health benefits of aerobic, interval sprinting, and resistance exercise

The health benefits of regular aerobic exercise are well known. Physical activity has been ranked as one of the leading health interventions, which is used to reduce sedentary behavior in children, adolescents, and adults [68]. Currently, exercise guidelines include 150 minutes of exercise per week that consist of moderate and vigorous physical activity combined with resistance training. It has been shown that performing 150 minutes of regular exercise per week results in a reduction of mortality risk by 30% and a decreased risk of diabetes, cancer, depression, and stroke [69]. Despite the positive benefits of regular physical activity, however, many people do not comply with the minimum exercise requirements to maintain health. Lack of motivation and time constrains are possibly the underlying reasons of not performing regular exercise. The importance of regular physical activity is so overwhelming that exercise now has been regarded as medicine.

Exercise has been widely used as preventative medicine to reduce the risk and incidence of cardiovascular and metabolic diseases related to sedentary and unhealthy living. Regular exercise has been shown to improve health and reduce the severity of diseases accompanying an unhealthy lifestyle. The benefits of exercise are overwhelming, and it has been shown that exercise can be used therapeutically for conditions, such as hypertension and insulin resistance [70], dyslipidemia [71, 72], type 2 diabetes, obesity [73], and endothelial dysfunction [74]. Exercise can also be used to improve cardiovascular and metabolic dysfunction that includes enhancing adipokine, cardiometabolic, and other clinical markers [75]. Thus, it is clear that exercise can be used as therapeutic or preventive medicine in order to alleviate lifestyle diseases.

The types of exercise used in past research include aerobic exercise (continuous walking, jogging, and cycling), high-intensity interval training (HIIT), and resistance training (e.g., weights). A study showed that either supervised or unsupervised aerobic exercise resulted in a reduction of body mass index in overweight and obese adolescents [76]. Whereas other studies have shown that moderate endurance training [77] and interval sprinting exercise [12] have a positive effect on HRV. Both HIIT and aerobic training have been used to induce improvement in HRV in different populations, such as young overweight individuals, type 2 diabetic patients, and older adults. Twenty minutes of HIIT on a stationary cycle ergometer, proceeded with 5 minutes of warm-up and 5 minutes of cool-down, three times per week, for 12 weeks have been found to improve parasympathetic activity [12] in young overweight males (**Figure 3**).

A study examining type 2 diabetic individuals has also found similar results when 30 minutes, four times per week for 12 weeks of HIIT training on a treadmill resulted in improvement in HRV by 19% [78]. This form of exercise consisted of 3 minutes of warm-up, 6×2 minutes of high intensity at 80–90% of heart rate maximum, separated by 6 minutes of moderate intensity at 50–60% of heart rate maximum with 2-minute recovery intervals, and 3 minutes of cool-down. The improvement of HRV in type 2 diabetes is significant as exercise could potentially prevent type 2 diabetic patients progressing to a condition called diabetic neuropathy later in life. Another HIIT study also showed that HRV was significantly improved in older individuals, whose average age was 74 years, following 14 weeks of cycle ergometer HIIT exercise [79]. Thus, both continuous aerobic exercise and HIIT had positive effects on autonomic function by increasing HRV levels. However, HIIT is currently regarded as a type of exercise that is superior to a typical continuous moderate intensity of aerobic exercise in terms of time efficiency and clinical benefits. The effectiveness of HIIT has been well established in youth [80] and in overweight adult men [12] and women [13]. Twelve weeks of HIIT have shown to improve cardiovascular function, physical fitness, assessed through a maximal oxygen uptake test, and body composition in young overweight women [81]. It seems that both continuous steady state aerobic exercise and HIIT are beneficial for health.

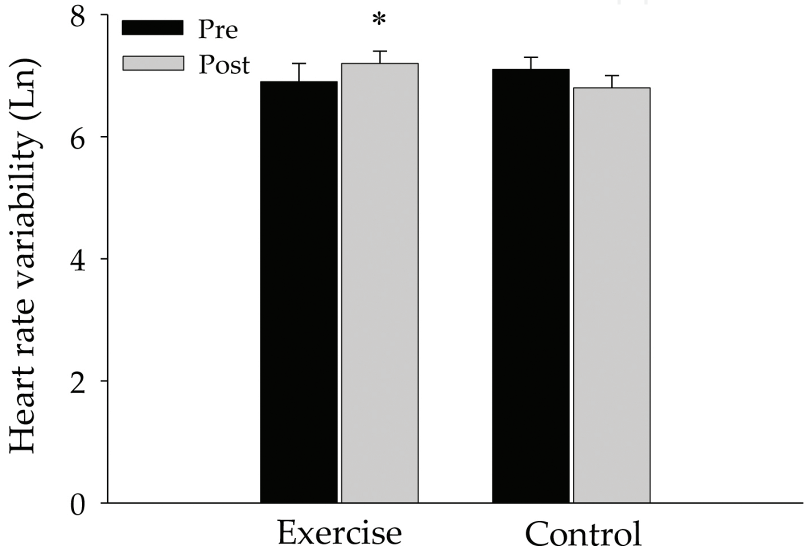

Figure 3. Heart rate variability of overweight young males at pre and post 12 weeks of interval sprinting exercise. *Significant difference between groups, $P<0.05$.

Modification of HIIT protocols, however, may be needed to suit different populations. For example, HIIT to induce athlete performance would be different with the HIIT used to induce cardiovascular health in healthy sedentary or diseased individuals. Certain exercise effects or adaptations that occur following HIIT training may not occur or be apparent after regular aerobic exercise. Depending on health markers and conditions examined, the magnitude of change following aerobic exercise may be smaller than that of HIIT. For example, it has been demonstrated that arterial stiffness, assessed through PWV [82] and autonomic function [82] are normalized following HIIT in hypertensive individuals, but not following continuous moderate exercise. With HIIT training, the exercise drop-out rate was found to be less [12, 83] compared to continuous steady state aerobic exercise. HIIT is also deemed to be superior in terms of improvement in cardiovascular health compared to regular aerobic exercise [84]. Thus, HIIT may be needed to be incorporated into daily life to induce extra health benefits. HIIT defined as repeated bouts of high-intensity exercise interspersed by rest for 20–30 minutes has also been used to prevent or to reduce severity of diseases related to unhealthy lifestyles. HIIT has been found to improve cardiac and metabolic health of young overweight males [12] and females [83]. The AIx was found to be reduced by 4% (**Figure 4**), whereas PWVcf velocity

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was also reduced by 0.4 $m.s^{-1}$ (**Figure 5**) following 12 weeks of HIIT in young overweight males [12].

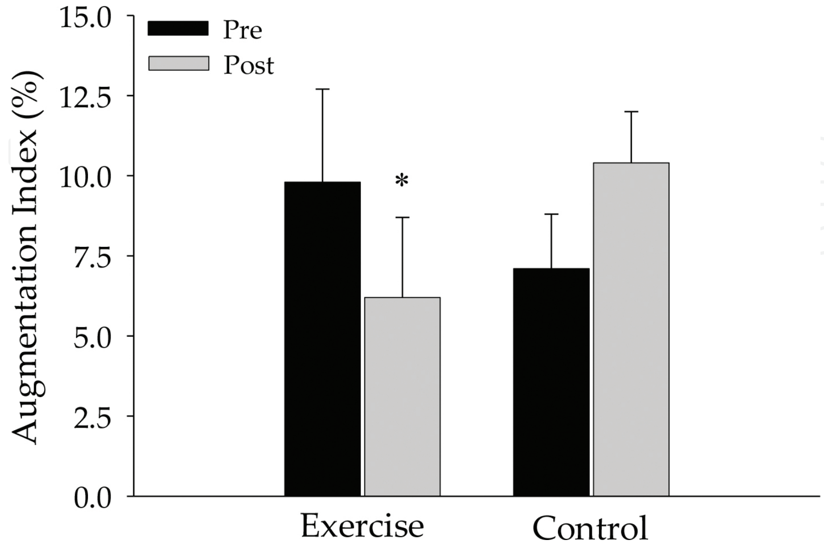

Figure 4. Augmentation index of young overweight males at pre and post 12 weeks of interval sprinting exercise. *Significant difference between groups, $P<0.05$.

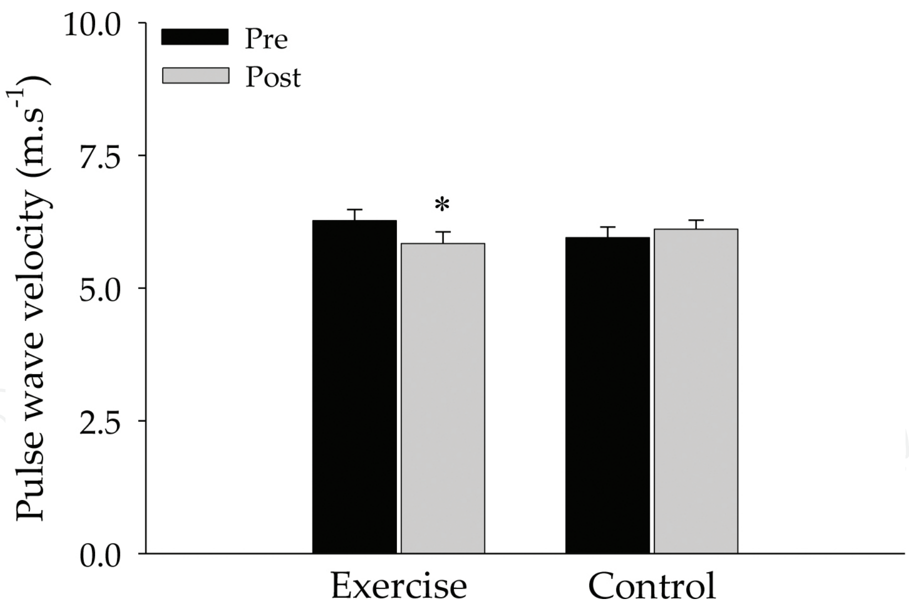

Figure 5. Pulse wave velocity of young overweight males at pre and post 12 weeks of interval sprinting exercise. *Significant difference between groups, $P<0.05$.

The HIIT employed was an 8-s pedaling sprint at a cadence of 100–120 revolutions per minute (rpm) at 0.5–1 kg of load, followed by a period of lighter intensity exercise at a cadence of 30–40 rpm for 12 seconds, repeated for 20 minutes. Another type of HIIT included cycling on a stationary bike at 80–85% of maximal oxygen uptake for 4 minutes with 5-minute rest intervals, repeated six to eight times [85]. HIIT has also been used in a number of clinical studies involving cardiac rehabilitation, chronic obstructive pulmonary disease, and intermittent claudication disease patients. Thus, a range of interval training exercise programs have been employed to improve cardiovascular and metabolic health.

Resistance exercise is another type of exercise that contributes to cardiovascular and metabolic health. Participating in resistance exercise can maintain muscle mass that declines with aging. Acute resistance training has been found to reduce systolic blood pressure by 11 mmHg and mean arterial pressure by 12 mmHg and systolic blood pressure by 13 mmHg and mean arterial pressure by 12 mmHg with 40 and 80% maximum weight, respectively [86]. The mechanisms underlying this reduction in blood pressure following resistance training is thought to be due to an increased blood flow and shear stress that act on vascular endothelial cells. The increased muscle contraction leads to an increased production of nitric oxide, an important vasodilator [87]. It appears that this mechanism occurs independently of the exercise intensity employed [88].

The effect of resistance training on arterial stiffness, however, is equivocal. Several studies [89, 90] have shown an unfavorable effect of resistance training on arterial stiffness, whereas others have shown no alteration in arterial stiffness [82, 91]. A reduction in central (increased arterial stiffness) but not peripheral arterial compliance was found following 4 months of resistance training in young and healthy middle-aged men [89]. However, only brachial artery endothelial function was improved following 1 year of resistance training, but body mass index, body composition, blood lipids, and lean muscle mass improved [92]. A meta-analysis [91] found that young adults had their arterial stiffness elevated from 14.3 to 20.1% following high-intensity resistance training. In contrast, it has been shown that progressive high-intensity resistance training without an increase in training volume did not alter arterial stiffness in young individuals [90]. Interestingly, the association between resistance training and arterial stiffness was not found in middle-aged individuals [90]. Although high-intensity resistance training has been found to increase arterial stiffness by 11.6%, moderate intensity resistance training did not seem to induce the same effect [90]. Another study showed an unexpected finding when improvement in the muscular strength of young individuals was inversely correlated with arterial stiffness [93]. This finding suggests that resistance training attenuates arterial stiffness. Different protocols and populations possibly could have contributed to the variability of results. Further studies looking at resistance training and arterial stiffness need to be carried out. Overall, regular HIIT is recommended, especially for people with time constraints. A combination of aerobic exercise and resistance training is also highly recommended as muscle wasting could occur with aging and a sedentary lifestyle.

4. Conclusion

A sedentary lifestyle leads to an increased risk of cardiovascular disease and dysfunction, such as high blood pressure, stiffening of the arteries, cardiac autonomic dysfunction, and metabolic dysfunction. If children become overweight or obese, these conditions described above appear to develop earlier. Lifestyle modification for children to avoid childhood obesity is paramount to further reduce the risk of health complications later in life. Therapeutic drug interventions can be introduced; however, overwhelming evidence suggests that regular exercise has been shown to prevent and to reduce the severity of disease-related lifestyle. Exercise is a powerful stimulus that can reduce and prevent the occurrence of cardiovascular and metabolic dysfunction. Therefore, exercise indeed is medicine that can improve the quality of life. Both regular aerobic exercise and HIIT are beneficial for health. HIIT, in particular, is highly recommended, especially for people with time constraints, and HIIT combined with resistance training is potentially highly beneficial. People of all ages should be encouraged to incorporate regular exercise into their daily lifestyle.

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