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Review Article

Impact of Aging on The Cardiovascular System: A Practical Application of High Intensity Interval Training

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Introduction

Age is a primary determinant of cardiovascular health [1]. By the year 2040, approximately 22% of the United States' population will be aged 65 or older [2]. Although aging is associated with multiple chronic diseases, cardiovascular disease (CVD) is the leading cause of death in this age group, accounting for 40% of all deaths [3]. The prevalence of CVD is expected to increase by 9.9% from the year 2010 to 2030 [2]. Specifically, an additional 27 million people will develop hypertension, eight million will develop coronary heart disease, four million will develop stroke, and three million will develop heart failure during this time frame [2]. The increase in CVD, associated with a significant rise in the elderly population, will triple direct medical costs from $272.5 billion in the year 2010 to $818.1 billion in the year 2030 [2]. Thus, it is imperative for researchers to develop a better understanding of the impact of aging on the cardiovascular system.

Physical activity has shown to improve cardiovascular function, as well as reduce mortality and CVD incidence in older adults [4, 5]. In particular, research provides evidence to support the use of high intensity interval training (HIIT) among elderly populations in order to improve cardiac functioning [6-8]. During these HIIT studies, participants typically completed four bouts of four-minute aerobic exercise at 85-95% maximal heart rate. HIIT appears to promote positive cardiovascular adaptations, such as increased VO2-Max, which is associated with an improved aerobic profile [9]. Therefore, exercise should be an integral component in interventions aimed at improving cardiovascular health in older populations. Despite scientific evidence supporting health benefits associated with exercise, only 16% of adults aged 65 and older met national guidelines for physical activity in the year 2013 [10]. A comprehensive literature review is required in order to identify the pathophysiology of cardiovascular changes that occur with aging. Furthermore, the practical application of HIIT among elderly populations will be highlighted in this review of literature.

Typical outcome measures in this area of research include ejection fraction, VO2-Max, blood pressure, and arterial stiffness. Ejection fraction is a measurement that is often used in order to determine cardiac function. Specifically, ejection fraction refers to the amount of blood pumped out of the left ventricle with

each contraction of the heart [11]. An ejection fraction of 50% or lower indicates reduced cardiac functioning, as the heart is no longer supplying enough blood to meet the oxygen demands of the body [11]. Ejection fraction can be measured through a variety of diagnostic testing procedures, including computed tomography, echocardiography, and magnetic resonance imaging [11]. Arterial stiffness refers to the elastic properties of arteries, including the ability of an artery to expand and recoil with each heartbeat [12]. Increased arterial stiffness is associated with aging and contributes to a variety of pathological conditions, such as congestive heart failure, hypertension, and hypotension [12]. Pulse wave velocity (PWV) is the most common measure of arterial stiffness [13]. Increased arterial stiffness typically precedes hypertension.14 Hypertension is a term used to describe high blood pressure, when the force of blood against artery walls is elevated [14]. In addition, hypertension is associated with an increased risk of stroke and coronary artery disease.14 Blood pressure is typically measured using the auscultatory method, which involves the use of a stethoscope and blood pressure cuff. Finally, VO2-Max is a measurement of maximal aerobic capacity.9 Essentially, VO2-Max refers to the maximum amount of oxygen a person is able to utilize during exercise. VO2-Max is typically measured using computer-assisted open-circuit spirometry during a graded exercise test [7].

Despite a significant amount of research investigating age-related changes in the cardiovascular system, there are still gaps in knowledge. Healthy young adults can safely choose from a variety of exercise modalities; however, elderly populations may be sedentary and less fit. Thus, researchers need to explore the best strategies for planning exercise interventions aimed at improving cardiovascular functioning in older adults. Sampling issues and exercise measurement are two common methodological challenges experienced by researchers in this field [15]. In addition, age-related cardiovascular changes do not always occur in a generalized structural or functional decline.16 Therefore, age-related cardiovascular changes and underlying mechanisms must be studied systematically in order to develop a better understanding of this phenomenon [16]. With these considerations in mind, the purpose of this literature review is to address the effects of aging on the cardiovascular system. In addition, HIIT interventions aimed at improving cardiovascular health in older adults will be related to the structural and functional changes that occur with aging.

Review of Literature

Normal Cardiovascular Physiology

The cardiovascular system is a physiological system of vital importance in the human body. Consisting of the heart and blood vessels, the cardiovascular system is the body's main transport system of oxygenated blood, nutrients, and hormones [17]. In addition, the cardiovascular system helps transport waste products to the kidneys for excretion, delivers carbon dioxide to the lungs in exchange for new oxygen, and assists with thermoregulation of the body [17]. Arteries, large blood vessels, contain elastic and flexible properties, which reduce the resistance to blood flow during the heart's contractions [17]. Arteries are made up of several layers, including the tunica externa, tunica media, and tunica intima. The lumen of the artery, the space where blood flows through, is wider in healthy arteries [17]. Furthermore, the tunica media, made up of smooth muscle cells, is typically thinner in healthy arteries [17]. The combination of a wide lumen and thin tunica media allows less resistance to blood flow, which impacts blood pressure. Thus, the ability of a blood vessel to vasoconstrict and vasodilate is related to blood pressure regulation. The endothelium lines the interior surface of blood vessels and is in direct contact with circulating blood [17]. This endothelium layer is smooth in young adults, which reduces overall resistance to blood flow [17]. Endothelial cells also release chemicals, such as nitric oxide, which causes vasodilation and expands the blood vessels [17].

While blood vessels are responsible for transporting various materials throughout the body, the heart is responsible for pumping blood through these vessels. The heart is comprised of four inner chambers, two atria and two ventricles. Blood flows through the atria into the ventricles through valves in the heart. Cardiac muscle, referred to as myocardium, is responsible for contraction of the heart and located in the middle layer of the heart wall.18 The heart contracts with enough force to transport blood throughout the body, maintaining tissue and organ perfusion [18]. An electrical conduction system maintains the heart's contraction rhythm. The sinus node, located in the right atrium, generates electrical impulses which determine a person's heart rate. Depolarization of the heart contributes to contraction of the myocardium [18]. The amount of calcium released from the sarcoplasmic reticulum in cardiac muscle cells is related to actin-myosin binding and cross-bridge cycling, which correlates with contractile force of the heart.18 Next, general age-related changes in the cardiovascular system will be discussed.

Age-Related Changes in the Cardiovascular System

Aging is associated with a number of changes in the structure and function of the cardiovascular system [1]. Macroscopic and microscopic arterial structural changes occur with age [19]. For example, large arteries, such as the aorta, dilate and become thicker with age [19]. A longitudinal study tracked aortic root diameter among 4,542 participants over a period of 16 years.20 Researchers discovered age was a significant correlate of aortic remodeling ($p \leq 0.01$). Every 10-year increase in age was associated with an increase in aortic root diameter of 0.89mm (0.79-0.9876) in men and 0.68mm (0.5844-0.78) in women. Aortic root dilation stimulates left ventricular hypertrophy because the heart must pump against a larger volume of blood in the aorta [19]. When the left ventricle becomes enlarged, the heart may not be able to pump blood with enough force, which increases the risk of developing heart failure [19,20].

Blood vessels become stiffer and thicker with age [21]. In particular, the tunica intima and tunica media gradually thicken, which is associated with increases in the density of collagen fibers in vessel walls [21]. The endothelium can also become thicker with aging, which decreases arterial compliance and elasticity.21 These changes reduce the size of the lumen, thereby increasing blood flow resistance [21]. Arterial stiffness causes increases in systolic blood pressure, left ventricular hypertrophy, and afterload on the left ventricle [22]. Increases in arterial stiffness are associated with myocardium compensatory mechanisms, such as left ventricular hypertrophy and fibroblast proliferation, which decrease cardiac output and increase fibrotic tissue [3]. The increases in fibrotic tissue and calcification on the heart's valves can lead to stenosis, a condition in which the valve is narrowed and blood supply is reduced [1]. Finally, arterial stiffness is linked to increased aortic PWV and pulse pressure [23]. Increased aortic PWV contributes to decreased diastolic pressure, which ultimately decreases coronary artery blood flow to the heart [23].

Aging is also associated with changes in the heart's conductive system [21]. A sharp decrease in the number of sinoatrial node cells occurs after age 60 [21]. In addition, fat can accumulate around the sinoatrial node, which increases the risk of atrioventricular conduction block [21]. Fibrosis and calcification can cause damage to the bundle of His, which transmits impulses from the atrioventricular node to the ventricles [22]. These age-related changes in the heart's conduction system increase the risk of developing arrhythmias, such as atrial fibrillation and ventricular tachycardia [21]. Certain arrhythmias, such as atrial fibrillation, are believed to be strong predictive risk factors of cardiac morbidity and mortality in older adults [21].

Biochemical changes in the cardiovascular system occur during the aging process as well. Age-related damage to the endothelium results in decreased nitric oxide production, which reduces blood flow [21]. The increase in vasoconstrictor synthesis, and decrease in vasodilator release, is associated with increased arterial stiffness [21]. Furthermore, arteries become less responsive to vasodilators, which contributes to increases in blood pressure [19]. Oxidative stress increases with aging, which reduces the number of cardiomyocytes, cells that make up cardiac muscle [3]. Necrotic death of cardiomyocytes contributes to a proinflammatory and profibrotic environment in the heart [3]. Ultimately, these conditions increase the risk of multiple types of CVD in elderly populations.

These structural and functional changes are apparent in multiple parameters of the cardiovascular system. Systolic blood pressure, impacted by arterial stiffness, peripheral vascular resistance, and cardiac function, typically increases with age [21]. Diastolic blood pressure typically rises with increased peripheral vascular resistance but lowers with increased arterial stiffness [21]. Thus, diastolic blood pressure typically declines after the age 60 [24]. A progressive decline in maximal heart rate is evident with aging, due to reduced activity of the sinoatrial node, electrical remodeling of pacemaker cells, structural remodeling of cardiac tissue, and reduced beta-adrenergic response [25]. Aerobic capacity, measured by VO2-Max, also declines with age [19]. Maximal oxygen consumption is a product of cardiac output and arteriovenous oxygen difference [19]. Essentially, this value represents how well the body can utilize oxygen during exercise. Increased vascular afterload, reduced myocardial contractility, and impaired autonomic regulation are various age-related factors that impact cardiac reserve, an index of cardiac function [21]. Left ventricular contractility and ejection fraction also decrease with age [3]. The myocardium compensates for a reduction in cardiac output by stimulating cardiac hypertrophy, which increases the risk of CVD and cardiac dysfunction among the elderly [3]. Next, previous studies investigating specific age-related changes in the cardiovascular system will be examined in greater detail.

Cardiac Power Output

Cardiac power output, the product of cardiac output and mean arterial blood pressure, is a commonly used measure of cardiac functioning [26-29]. Augmentation index, a measurement of vascular function, can be used in conjunction with cardiac power output as a means of predicting mortality in patients with heart failure [27]. Houghton, et al. [27] investigated cardiac power output and augmentation index among 20 young adults (aged 20-30 years) and 10 older adults (aged 60-71 years). Researchers discovered augmentation index, measured at rest, was significantly higher ($p < 0.01$) in older adults (27.7% ± 10.1) compared with younger adults (2.5% ± 10.1). During a graded exercise test until volitional exhaustion, older adults had significantly ($p < 0.05$) higher mean arterial blood pressure (133 mmHg ± 12 vs. 122 mmHg ± 9) compared with young adults. However, older adults had a significantly ($p < 0.01$) lower heart rate (145 beats/min ± 13 vs. 172 beats/min ± 10) and peak oxygen consumption (22.5 ml/kg/min ± 5.2 vs. 41.2 ml/kg/min ± 8.4) compared with young adults during the graded exercise test. There was no significant difference found in cardiac power output at rest ($p = 0.082$, 1.5 watts ± 0.3 vs. 1.3 watts ± 0.3) or during peak exercise ($p = 0.855$, 4.9 watts ± 0.9 vs. 5.0 watts ± 1.7) between old and young adults, respectively. Reductions in cardiac output, as well as increases in augmentation index, indicate declines in vascular function with age [27]. However, the hemodynamic variables were obtained non-invasively in this study, which may impact accuracy. In addition, the older adult sample size was relatively small, which limits the generalizability of the findings [27]. Finally, researchers did not compare differences in cardiac functioning between genders. In order to address this concern, the results of a study conducted by Goldspink, et al. [26] will be discussed next.

Researchers conducted a cross-sectional study investigating left ventricular mass and cardiac power output in 122 women

and 93 men ranging from 20-75 years of age [26]. Left ventricular mass significantly ($p < 0.001$) decreased by 21% in men, but non-significantly ($p = 0.19$) increased by 13% in women between 20 and 75 years. Cardiac power output declined 1.6W in men and 0.06W in women over 55 years ($p = 0.8$). These findings indicate women's hearts may be more resilient to age-related pathologies. Gender differences may exist due to a greater amount of myocyte necrosis in men; however, additional research specifically investigating cardiovascular pathologies in women is warranted.26 This research highlights the importance of understanding potential gender differences in cardiovascular morphology that occur with aging.

With the understanding that gender differences in age-related cardiac functioning exist, Jakovljevic, et al. [30]. and Nathania et al.29 specifically investigated these changes in women. Jakovljevic, et al. [30]. grouped 63 healthy women into three age groups: Young (20-30 years), middle (40-50 years), and older (65-81 years). Statistical analysis indicated age was associated with declines in cardiac functioning, as indicated by peak exercise cardiac power output ($r = -0.37$; $p < 0.01$), cardiac output ($r = -0.48$; $p < 0.01$), and oxygen consumption ($r = -0.54$; $p < 0.01$). When stratified by physical activity level (highly active > 12,500 steps/day vs. low active < 7,500 steps/day), older highly active women had a similar phosphocreatine/ATP ratio (1.9 ± 0.2 vs. 1.4 ± 0.1, $p < 0.05$) and relative peak O2 consumption (24.1 mL/kg/min ± 3.8 vs. 17.8 mL/kg/min ± 2.0, $p < 0.01$) compared with young low active women, respectively. However, physical activity had no effect on peak cardiac power output in older women (3.4 W ± 0.7 vs. 3.4 W ± 0.8, $p = 0.91$).

These findings were supported by Nathania, et al. [29]. who tested 35 healthy women grouped by age (young ≤ 50 years; old ≥ 60 years)? Phosphocreatine/ATP ratio was significantly ($p = 0.03$) lower in the old group compared with the young group (1.92 ± 0.48 vs. 2.29 ± 0.55), as well as cardiac power output (3.35 W ± 0.73 vs. 4.14 W ± 0.81, $p = 0.01$). In addition, peak exercise oxygen consumption during a maximal graded exercise test was significantly ($p < 0.01$) lower in the old group compared with the young group (1,382.9 mL/min ± 255.0 vs. 1,940.3 mL/min ± 434.4). These findings indicate the heart's pumping ability and functionality decrease with age among women [29,30]. The declines observed in the phosphocreatine/ATP ratio suggest disruptions in cardiac contractility, which could impede cardiovascular function. Although physical activity appears to be a mediator by preserving cardiac metabolism and aerobic capacity in older women, regular activity may not prevent age-related changes in cardiac structure and pumping ability [30]. Further research investigating the specific linkages between cardiac metabolism and cardiac function in men and women is warranted in order to prevent CVD.

The previous studies examined in this section have included healthy participants; however, aging is associated with a number of co-morbidities, including chronic heart failure [28]. Thus, researchers investigated cardiac power output, cardiac output, and oxygen consumption among patients with heart failure, implanted left ventricular assist devices (LVAD), and explanted LVADs due to myocardial recovery [28]. During a peak graded exercise test, cardiac power output was significantly ($p < 0.01$) higher in the explanted LVAD group (3.39 W ± 0.61) compared with implanted LVAD (2.37 W ± 0.55) and heart failure (1.90 W ± 0.45). In addition, peak cardiac output was significantly ($p < 0.01$) higher in the explanted LVAD group (14.6 L/min ± 2.9) compared with implanted LVAD (12.4 L/min ± 2.2) and heart failure (9.1 L/min ± 2.1). Finally, peak oxygen consumption was significantly ($p < 0.05$) higher in the explanted LVAD group (28.2 ml/kg/min ± 5.0) compared with implanted LVAD (19.8 ml/kg/min ± 5.8) and heart failure (15.8 ml/kg/min ± 4.1). These findings are significant because additional research indicates implanted LVADs may contribute to reverse remodeling of the heart, thereby improving cardiac functioning [31]. Results of the Jakovljevic, et al. [28]. study indicate differences in cardiac power output at various stages in cardiac function restoration. Therefore, cardiac power output is a critical physiological marker of cardiac function and heart failure severity among older adults. Many of the previous studies utilized a cross-sectional design studying participants at one point in time [26, 28-30]. Thus, future longitudinal studies are required in order to address any potential long-term cardiovascular changes that occur with age. In addition to cardiac power output, vascular pathologies, such as arterial stiffness, can be used as a predictor of cardiac pumping ability in older populations.

Arterial stiffness

Arterial stiffness has been utilized as a prognostic indicator of cardiovascular health in older adults [13, 32-34]. The mechanisms that contribute to arterial stiffness with aging appear to be varied; however, research has provided evidence linking arterial stiffness to CVD [34]. In fact, a meta-analysis conducted by Vlachopoulos, et al. [34]. indicated an increase in aortic PWV by 1 m/s corresponded to a 14% increase in total cardiovascular events and 15% increase in cardiovascular mortality ($p < 0.001$). Additional research conducted by Mitchell, et al. [33]. supports the findings of Vlachopoulos, et al. [34]. Researchers studied arterial stiffness among 2,232 participants (average age 63 years ± 12) in the Framingham Heart Study [33]. Statistical analysis revealed greater aortic PWV was associated with a 48% increase in CVD risk (1.16 to 1.91 per SD; $p = 0.002$). Increased arterial stiffness induces a myriad of physiological and functional conditions that impact the human body. In particular, increased arterial stiffness has a direct impact on systolic blood pressure. Thus, it is important to study the interactions between blood pressure and arterial stiffness.

Several researchers have investigated the effects of aging on PWV and the role of blood pressure during these changes [32,35]. Diaz, et al. [32]. studied arterial stiffness among 1,079 normotensive

and hypertensive patients. Researchers discovered PWV was significantly ($p < 0.001$) higher in older patients compared with younger patients (8.35 m/s ± 1.5 vs. 5.92 m/s ± 1.2, respectively). When specifically analyzing the hypertensive group, the average PWV value was 8.04 m/s ± 1.8 and increased with age ($R2 = 0.243$; $p < 0.05$). Furthermore, the PWV increase in the hypertensive patients was significantly ($p < 0.001$) higher compared with the normotensive patients (0.93 m/s per decade vs. 0.44 m/s per decade, respectively). Additional research conducted by AlGhatrif, et al. [35] supports the findings of Diaz, et al. [32] AlGhatrif, et al. [35] conducted a longitudinal study involving 777 participants and discovered higher systolic blood pressure was associated with a greater rate of PWV increase over time in men ($\beta = 0.17$; $p = 0.004$) and women ($\beta = 0.13$; $p = 0.0167$). These findings support the claim that age and systolic blood pressure are two primary determinants of arterial stiffness. Hypertension increases artery wall stress and elastin degradation.36 In addition, arterial stiffness contributes to a higher pulse pressure in older adults, which indicates increases in systolic blood pressure and decreases in diastolic blood pressure.36 It is important to establish reference values in order to use PWV as an indicator of arterial stiffness and CVD risk across populations.

The Reference Values for Arterial Stiffness Collaboration37 gathered data from 1,455 patients with optimal/normal blood pressure in order to establish reference values for PWV. Researchers found PWV increased with age from 6.2 m/s (4.7-7.6) at < 30 years to 10.9 m/s (5.5-16.3) at ≥ 70 years. PWV also increased with each rise in blood pressure category. For example, in the ≥ 70 years age group, PWV increased from 10.4 m/s (5.2–15.6) in the optimal blood pressure group to 14.0 m/s (7.4–20.6) in the grade II/III hypertension group. It is important to note the authors simply listed reference values for each age group and did not test for statistical differences in these reference values with age. An additional study was conducted by Díaz, et al. [38] in order to establish PWV reference values. Díaz, et al. [38] used a smaller sample size of 780 participants and discovered PWV increases linearly with aging ($r2 = 0.61$; $p < 0.05$). PWV values were significantly ($p < 0.05$) higher in participants over 50 years for males (8.52 m/s ± 1.39 vs. 5.86 m/s ± 1.17) and females (8.20 m/s ± 1.13 vs. 6.03 m/s ± 1). Compared with the reference values reported by the Reference Values for Arterial Stiffness Collaboration37, Díaz, et al. [38] reported slightly smaller reference values of 5.86 m/s (3.92-8.14) for the 20-29 years age group and 9.01 m/s (5.52-13.4) for the > 70 years age group. Reference values were obtained from different populations, so slight variances could be expected. Díaz, et al. [38] collected data from an Argentinean population, while the Reference Values for Arterial Stiffness Collaboration37 collected data from a European population. Despite these small differences, both studies provide evidence of the rise in PWV with aging, which indicates increased arterial stiffness. Additional data is needed in order to track changes in PWV over time and assess the future risk of CVD among older adults.

Some researchers have speculated physical activity can help decrease the age-related increase in arterial stiffness.13 When Deiseroth, et al. [13] stratified older adults by activity level, they found PWV was significantly ($p < 0.001$) higher in sedentary at-risk older adults (8.2 m/s ± 1.4) compared with healthy sedentary (7.5 m/s ± 1.6) and healthy active older adults (7.0 m/s ± 1.1). As a follow up, the sedentary at-risk participants completed a 12-week HIIT intervention; however, PWV did not change (8.2 m/s ± 1.2 pre vs. 8.1 m/s ± 1.1 post). These results indicate 12 weeks of HIIT may not improve arterial stiffness in sedentary older adults at risk of CVD; however, greater cardiorespiratory fitness, measured by VO2-Max, was associated with lower PWV ($p < 0.001$). A meta-analysis conducted by Huang, et al. [39] confirmed aerobic endurance exercise significantly reduced PWV (-0.67, 95% CI -0.97, -0.38; $I2 = 89\%$; heterogeneity, $p < 0.0001$). A short-term exercise intervention does not appear to be enough to reduce the long-term wear and tear damage that occurs in the arteries due to aging. However, improvements in cardiorespiratory fitness, stimulated by regular exercise, may help reduce the risk of cardiovascular pathologies contributing to CVD.39 VO2-Max, often considered to be the gold-standard measurement of cardiorespiratory fitness, can be a valuable assessment in elderly populations.

VO2-Max

The age-related decline in maximum oxygen uptake is extensively documented in previous literature. 40-43 Loe, et al. [41] conducted a large study investigating VO2-Max among 3,810 participants (age 20-90 years) during a treadmill exercise test. The greatest VO2-Max values were observed in the youngest age group (20-29 years), and these values were significantly ($p < 0.001$) different between men (54.4 ml/kg/min ± 8.4) and women (43.0 ml/kg/min ± 7.7). There was a reduction in VO2-Max of 3.5 ml/kg/min per decade, with an 8% reduction per decade in both genders after the age 50. These findings were supported by Edvardsen, et al. [40], who found a linear decline in VO2-Max of 8% per decade after the age of 30 years in both genders. A third study conducted by Pandey, et al. [42] found a 40% decrease in peak VO2 over a 5.5 decade range, which was comparable to previous findings. In addition, Pandey, et al. [42] reported older age was significantly associated with reduced peak VO2 ($r = -0.57$; $p < 0.001$). A significant ($p < 0.001$) difference in peak VO2 was observed during peak exercise between the > 60 years age group (792 ml/m2/min ± 179) and the < 40 years age group (1,226 ml/m2/min ± 252). Based on these findings, it is apparent VO2-Max declines with age. This decline in VO2-Max is also associated with an increased burden of heart failure in older adults [42].

Based on observed gender differences in age-related cardiovascular changes, researchers have investigated these differences in oxygen consumption as well.43, 44 In a study conducted by Ridout, et al. [43], participants were grouped by age: 20-32 years and 61-79 years for men; 20-30 years and 61-73 years

for women. Participants completed a graded treadmill exercise test until peak effort. Researchers discovered a significant ($p < 0.05$) difference in VO2-Max between the younger men (45.8 ml/kg/min ± 4.1) and older men (30.2 ml/kg/min ± 4.1), as well as between younger women (38.1 ml/kg/min ± 5.4) and older women (23.5 ml/kg/min ± 2.9). Furthermore, researchers found significant ($p < 0.05$) gender differences within the same age groups. Stensvold, et al. [44] discovered similar results among 1,537 older adults aged 70-77 years who completed a cardiopulmonary exercise test. Men had significantly ($p < 0.05$) higher VO2 peak values (31.3 mL/min/kg ± 6.7) compared with women (26.2 mL/min/kg ± 5.0). In addition, healthy men and women had significantly ($p < 0.05$) higher VO2 peak values compared with men and women with CVD (35.0 mL/min/kg ± 6.6 vs. 29.3 mL/min/kg ± 6.9; 27.8 mL/min/kg ± 5.5 vs. 24.4 mL/min/kg ± 4.1, respectively). This research indicates gender differences in age-related cardiovascular changes may become more pronounced as age further increases.

Some researchers hypothesize gender differences may exist due to differences in cardiac output in response to vascular resistance and other age-related changes [43]. For example, decreased cardiac output is related to decreases in heart rate, stroke volume, and ejection fraction that commonly occur with aging [42]. Age-related reduced diastolic compliance also plays a role in reducing maximal oxygen uptake.42 Additional research is needed to investigate specific cardiovascular regulatory mechanisms that occur with aging in both males and females. Previous studies used different exercise tests, such as cycle and treadmill tests. Therefore, future studies can compare differences in VO2-Max depending on exercise modality. Regular exercise has demonstrated vasoprotective effects during aging [23]. In addition, aerobic exercise may contribute to improvements in oxygen consumption.21 The next section of this literature review will explore the use of HIIT interventions among older adults in order to offset the impact of age-related changes in cardiovascular functioning.

HIIT in Older Adults

HIIT appears to be a novel approach used to improve age-related pathologies in cardiovascular functioning [9, 45, 46]. HIIT typically consists of intermittent bouts of vigorous exercise (≤ four minutes at 70-90% VO2-Max) combined with active rest periods.45 As cardiovascular functioning decreases with age, individuals may begin to notice significant physical impairments linked to reductions in maximal oxygen uptake [9]. In addition, cardiovascular disorders are associated with increased mortality and morbidity, particularly in older populations [47]. HIIT appears to modulate the age-related impacts on the cardiovascular system through a variety of mechanisms, including autonomic, cardiac, vascular, respiratory, and metabolic pathways [45].

Systolic blood pressure, one of the primary mechanisms involved in the increase of arterial stiffness with age, appears to be influenced with HIIT [8, 48]. In the Adamson, et al. [48] study, 17 older adults participated in a 10-week sprint interval training program in which they completed six bouts of sprinting for six seconds twice per week. Systolic blood pressure significantly ($p < 0.05$) decreased in males (136 mmHg ± 13 to 122 mmHg ± 9) and females (141 mmHg ± 13 to 131 mmHg ± 6). An additional study conducted by Molmen, et al. [8] confirmed decreases in systolic blood pressure with participation in HIIT. Participants completed four bouts of four-minute high intensity (85%-90% VO2-Max) treadmill running on three days per week for 12 weeks. Researchers discovered systolic blood pressure significantly ($p < 0.05$) decreased after the 12-week intervention (143 mmHg ± 15.0 to 126 mmHg ± 8.5). Researchers speculated the decreases in systolic blood pressure were attributed to exercise-induced changes in arterial stiffness, indicating improved endothelial function [8, 48]. The Molmen, et al. [8] study provided more details regarding the specific exercise protocol participants followed, whereas the Adamson, et al. [48] study only included information pertaining to the sprint protocol and active rest period. Both studies had relatively smaller sample sizes ranging from 16-17 participants, with interventions lasting only 10-12 weeks. Thus, future interventional studies can focus on recruiting larger sample sizes and studying blood pressure responses over a longer duration. Finally, future studies should investigate the specific intensity level required to elicit beneficial blood pressure adaptations in older adults.

Additional research has investigated the effects of HIIT on cardiac functioning in older adults [6,7]. Coswig, et al. [6] recruited 46 participants who performed treadmill exercise (four bouts of four-minute exercise at 85-95% max heart rate) twice per week for eight weeks. Participants significantly ($p < 0.001$) reduced resting heart rate (76.9 bpm ± 5.7 to 69.5 bpm ± 4.5), as well as improved chair stand test results (8.4 reps ± 1.4 to 11.8 reps ± 2.1) and six-minute walking test results (406 m ± 73.5 to 454 m ± 72.2). In the Hwang, et al. [7] study, participants also completed four bouts of four-minute exercise at 90% peak heart rate; however, these individuals exercised four days per week for eight weeks. With the understanding that weight-bearing exercise may be difficult for older adults, researchers decided to use a cycle ergometer protocol instead of treadmill exercise.7 Researchers found systolic function, indicated by ejection fraction percentage, significantly ($p = 0.001$) improved from 56.2% ± 0.8 to 58.4% ± 0.7. In addition, VO2-peak significantly ($p < 0.0001$) increased from 23.1 mL/kg/min ± 0.7 to 25.7 mL/kg/min ± 0.8. These findings indicate cardiac functioning improvements in cycle ergometer HIIT are consistent with treadmill-based HIIT. Thus, HIIT-related improvements in ejection fraction appear to support improvements in overall cardiac functioning among older adults, regardless of exercise modality. Improvements in systolic function appear to be associated with improvements in VO2-peak; however, additional research is warranted investigating this association [7].

Conclusion

In summary, the cardiovascular system undergoes several structural and functional changes with aging [1, 19, 21]. Some of the most significant changes involve blood pressure,14 arterial stiffness [13,32,33], cardiac power output [27-29], and VO2-Max [40-42]. Although these changes have a strong impact on CVD risk and overall mortality in older adults, exercise appears to be a non-pharmacological approach to reduce the impact of age-related cardiovascular pathologies [9,45,46]. Despite this knowledge, data indicates only one third of older adults ≥ 65 years of age in the United States meet physical activity guidelines [49].

While research has advanced knowledge regarding age-related changes in the cardiovascular system, there are multiple gaps left unanswered. For example, many studies have utilized relatively smaller sample sizes, which impacts the generalizability of the findings to larger populations. Furthermore, many studies did not track cardiovascular changes over a long duration; thus, future studies can obtain additional insight regarding the long-term impact of age-related changes. Research also indicates there may be gender differences in age-related cardiovascular changes [29,30]. Therefore, future research studies can make comparisons of significant physiological changes between older males and females. Finally, additional research is needed to identify the optimal dose, and intensity, of exercise required to attenuate the age-related changes in cardiovascular function. This research has the ability to support evidence-based physical activity interventions for elderly populations, as well as improve CVD risk factors and overall mortality.

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Conflict of Interest

No conflict of interest.

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