Adaptations in cardiac structure and function following high intensity interval training in a physically inactive population

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<u>Acknowledgments</u>

Abstract

Purpose: Physical inactivity is associated with increased risk of cardiovascular disease and myocardial dysfunction. High intensity interval training (HIIT) has been shown to improve cardiovascular health; however, adaptations of cardiac structure and function are uncertain. Therefore, the aim of the present study was to analyse cardiac structural and functional adaptations to a HIIT protocol.

Methods: Forty-one physically inactive individuals (males n=20 and females n=21) were randomised into either a 4-week HIIT intervention or control group. The HIIT consisted of 3 x 30-second maximal cycle ergometer sprints against a resistance of 7.5% body weight, separated by 2-minute active recovery periods. In total, 12-sessions were performed. All cardiac structural and functional parameters were measured by quantitative 2D transthoracic echocardiography, performed using a commercially available, portable ultrasound system (Vivid-q, GE Healthcare, Milwaukee, Wisconsin) with a 1.5–3.6 MHz phased array transducer (M4S-RS Matrix cardiac ultrasound probe).

Results: The HIIT intervention produced significant improvements in resting heart rate (65.59 ± 10.15 to 63.05 ± 13.42 b·min^{-1}, P=0.013), stroke volume (55.48 ± 16.27 to 64.24 ± 20.62ml, P=0.015), left ventricular end diastolic volume (115.59 ± 28.34 to 131.94 ± 33.40ml, P=0.025), E/a ratio (1.98 ± 0.48 to 1.95 ± 0.55; P=0.027), average E/e' ratio (5.41 ± 1.17 to 5.22 ± 0.89; P=0.002) and isovolumetric relaxation time (81.23 ± 12.85 to 77.83 ± 9.81 m·s^{-1}; P=0.022) compared to the control group.

Conclusion: HIIT produced significant improvements in resting haemodynamics and diastolic function. This time efficient exercise intervention produces important improvements in myocardial function in a physically inactive population, which may be of clinical importance in higher risk populations.

1.0: Introduction and Literature Review

1.1: The Cardiovascular System: A Brief Overview

The cardiovascular system is an organ system that is composed of the heart, blood vessels and blood (Silverthorn, 2009). The primary function of the cardiovascular system is the circulation and transport of materials to and from all parts of the body (Tortora, & Derrickson, 2011). The substances transported by the cardiovascular system can be separated into materials that enter the body from an external environment such as oxygen, nutrients and water, materials moved from cell to cell such as wastes, immune cells, antibodies, hormones and stored nutrients, and waste material that cells eliminate from the body such as metabolic waste, heat, carbon dioxide and urea (Willmore, Costill & Kenny, 2008).

The efficiency of the cardiovascular system to function at optimal levels is dependent upon numerous factors (Willmore, Costill & Kenny, 2008). Cardiac output is the volume of blood pumped by one ventricle in a minute, it has been noted that the average total blood volume is approximately 5 litres from the ventricle per minute (Silverthorn, 2009). However, it has been documented that cardiac output is not a fixed value, it continually changes in response to body demands (McArdle, Katch, & Katch, 2010). It has been found that during exercise cardiac output may increase to 30-35 L·min^{-1} (McArdle, Katch, & Katch, 2010). Homeostatic changes in cardiac output is a result of varying heart rate, stroke volume or both (Berne & Levy. 1992). Stroke volume, the volume of blood ejected from the left ventricle per contraction, is directly related to the force generated by the cardiac muscle during systole (Berne & Levy. 1992). The force of ventricular contraction is affected by two parameters, the length of muscle fibres at the beginning of contraction and the contractility of the heart (Silverthorn, 2009). The energy of contraction can be increased by preloading of the myocardium during diastole through raising the end-diastolic pressure, which enhances the contractile energy; this relationship is known as the Frank-Starling law of the heart (McArdle, Katch, & Katch, 2010). However, it has been documented that if an individual has a high risk of cardiovascular disease, the function of the cardiovascular system can become significantly impaired (Kobirumaki-Shimozawa *et al.* 2014).

1.2: Cardiac Cycle

The cardiac cycle refers to the repeating sequence of myocardial contraction and relaxation (Stouffer, Klein & McLaughlin, 2017). The contraction phase is referred to as systole and the

relaxation period is known as diastole (Nishimura & Tajik, 1997). As the human heart has four chambers there is atrial systole, atrial diastole, ventricular systole and ventricular diastole (Levick, 2010). Atrial contraction occurs during ventricular diastole and atrial relaxation occurs during ventricular systole (Nishimura & Tajik, 1997). The heart therefore has a two-step pumping action (Powers & Howley, 2001). The left atrium and right atrium simultaneously contract, emptying atrial blood into the ventricles (Cox *et al.* 1995). Approximately 0.1 seconds after atrial contraction, the ventricles contract and deliver blood into both the systemic and pulmonary circuits (Levick, 2010). The cardiac cycle is divided into four phases based on the positions of the inlet and outlet valves (Levick, 2010). These phases are ventricular filling, isovolumetric contraction, ejection and isovolumetric relaxation (Levick, 2010).

Ventricular filling has two major determinants, ventricular relaxation and effective chamber compliance (Nishimura & Tajik, 1997). At rest, ventricular diastole occupies approximately two-thirds of the cardiac cycle, which provides adequate time for the ventricles to fill (Powers & Howley, 2001). During the initial rapid filling phase, ventricular pressure falls, which is due to the relaxing ventricle recoiling elasticity from its deformed end-systolic shape. Once the pressure in the left ventricle drops to below the pressure in the left atrium, the mitral valve opens, causing accumulated blood from the atrium to be sucked into the ventricle (Nishimura & Tajik, 1997). As ventricular filling begins, the atria is also in diastole, allowing passive blood flow from the great veins through the atria and the open atrioventricular valves into the ventricles (Powers & Howley, 2001). This initial phase is very fast lasting approximately 0.15 seconds (Pocock & Richards, 2006). Further filling is caused by the venous pressure, which distends the ventricle and causes ventricular pressure to rise gradually (Pocock & Richards, 2006). The finally third stage of the filling phase is atrial contraction (Pocock & Richards, 2006). At the end of the filling phase the volume of blood in the ventricle is known as end-diastolic volume (EDV) (Pocock & Richards, 2006). The ventricular filling velocity has two main components; firstly the early (E) diastolic phase which causes ventricular suction, and second, a late phase created by atrial contraction (A) (Keren *et al*. 1988). The E/A ratio is of importance as it can be used as a diagnostic measure, since the ratio is reduced in diastolic dysfunction (Paulus *et al.* 2007).

Ventricular systole follows atrial systole; this is divided into a brief isovolumetric phase and a longer ejection phase which lasts approximately 0.35 seconds (Levick, 2010). As the pressure in the ventricles rises just above atrial pressure the atrioventricular valves are closed by the

reversed pressure gradient (Pocock & Richards, 2006). During atrioventricular valve closure the backflow of blood is minimal due to vortices approximate the valve cusps during the late filling phase (Pocock & Richards, 2006). As the ventricles temporarily become a closed chamber, the tension of its contracting walls causes the pressure of the trapped blood to rise rapidly (Levick, 2010).

As the ventricular pressure exceeds arterial pressure, the outflow valves are pushed open and ejection begins (Levick, 2010). Initially there is a rapid ejection phase which results in three quarters of the stroke volume being ejected, this makes up half of the ejection phase (Levick, 2010). During this rapid ejection phase the blood is ejected faster than it can drain away through the peripheral vessels, therefore, most of the stroke volume is accommodated temporarily in the distended elastic arteries (Nishimura & Tajik, 1997). This causes the arterial pressure to increase to its maximum systolic level (Pocock & Richards, 2006). During ejection, the cusps of the open aortic valve lie close to the entrances to the coronary arteries, but do not block them because vortices behind the cusps cause them to float between midstream and the aorta wall (Pocock & Richards, 2006). During late systole, ejection rate slows down, when the rate at which aortic blood is draining away into the peripheral circulation now exceeds ventricular ejection, pressure begins to fall (Pocock & Richards, 2006). Although ventricular pressure drops to 2-3mmHg below arterial pressure, the outward momentum of the blood prevents immediate closure of the aortic valve (Stouffer, Klein & McLaughlin, 2017). However, the reversed pressure gradient causes the outflow to gradually decelerate, until a brief backflow closes the outflow valve (Levick, 2010). This backflow is typically less than 5% of the stroke volume, although this can increase greatly if the aortic valve is incompetent (Levick, 2010). Valve closure creates a notch in the arterial pressure trace called the incisura (Pocock & Richards, 2006). For the rest of the cycle, the arterial pressure decreases gradually as blood drains away into the periphery (Stouffer, Klein & McLaughlin, 2017). In a resting human, only two thirds of the end diastolic blood volume is ejected (Levick, 2010). Stroke volume is 70-80ml and the end diastolic volume is approximately 50ml (Levick, 2010). Ejection fraction is the stroke volume divided by end diastolic volume, with a normal value of >55% (Pocock & Richards, 2006). The end systolic volume serves as reserve that can be drawn on to raise the stroke volume and ejection fraction during exercise (Levick, 2010).

As the aortic and pulmonary valves close, the ventricles briefly become closed chambers, the elastic recoil of the deformed, relaxing myocardium causes the ventricular blood pressure to

fall rapidly (Levick, 2010). As ventricular blood pressure falls below atrial pressure, the pressure difference pushes open the atrioventricular valves, terminating the isovolumetric relaxation phase (Pocock & Richards, 2006). Blood floods in from the atria which have filled during ventricular systole, starting the next cardiac cycle (Levick, 2010).

1.3: Cardiovascular Disease

Cardiovascular disease (CVD) is the largest contributor to global mortality (Mills et al, 2015), accounting for nearly half of the 36 million annual non-communicable disease deaths, surpassing communicable diseases as the world's major disease burden (Smith *et al*. 2012). CVD is approximately accountable for 17.3 million deaths every year (Townsend et al, 2015) and is responsible for 30.8% of all deaths annually (Uppoor et al, 2015). By 2030, CVD is projected to account for 25 million deaths worldwide (Okwuosa et al, 2016). In 2014, CVD was the second most common cause of death in the United Kingdom (UK), accounting for approximately 155,000 deaths, 27% of all deaths within the UK (Townsend et al, 2015). CVD was responsible for approximately 41,000 premature deaths in the UK, in total 25% of premature deaths in men and 17% of premature deaths in women (Townsend et al, 2014). More than £6.8 billion was spent on treating CVD within the NHS in England in 2012/ 2013 (Townsend et al, 2014). The biggest single cause of death in the UK from CVD is a chronic disease known as coronary artery disease (CAD), which accounts for more than 73,500 deaths each year (Bhatnager et al, 2015). CAD was responsible for 15% of male deaths and 10% of female deaths in the UK in 2014 (Townsend et al. 2015). CAD is a condition where the arteries become hardened, narrowed and less flexible by the build-up of lipids, inflammatory cells, and connective tissue within their intimal layer, the gradual build-up of which stops the delivery of oxygenated blood to the heart (McArdle, Katch & Katch, 2010).

1.4: Hypertension

Chronic high blood pressure, or hypertension, is the most predominant pre-curser of CVD and deaths globally (He & Whelton, 1997). Hypertension has been found to affect approximately 1 billion individuals worldwide (Krum *et al.* 2014), estimated to account for 7.6 million deaths each year attributable to hypertension (Chow *et al.* 2013). It is expected that by 2025 the number of individuals affected with hypertension is expected to rise to 1.6 billion (Krum *et al.* 2014). The National Health Service (NHS) was shown to spend more that £6.8 billion in 2012/2013 on the treatment of CVD (Townsend *et al.* 2014). Hypertension has

been shown to effect one in four adults within the UK and as a result one in five heart attacks is attributed to hypertensive heart disease (Thompson, 2015).

Hypertension has been linked with having an increased risk of developing cardiovascular diseases (Chobanian *et al.* 2003), such as CAD (Stamler, Stamler & Neaton, 1993), stroke (Lee *et al.* 2004), heart failure (Levy *et al.* 1996), myocardial infarction (Uppoor *et al.* 2015), left ventricular hypertrophy (Messerli & Aepfelbacher, 1995), chronic kidney disease (Sarnak *et al.* 2003) and other chronic diseases such as retinopathy (Wong & Mitchell, 2004), cerebral haemorrhage (Qureshi *et al.* 2001) and hypertensive encephalopathy (Schwartz *et al.* 1992). For people suffering with hypertension the risk for cardiac complication has been shown to be greater (Bogousslavsky *et al.* 1996), for example patients who have ischaemic heart disease are 40% more likely to have a fatal myocardial infarction when they have previously suffered with hypertension (Dunn, 1983). The risk of CVD has been shown to double with every 20 and 10 mmHg increase in systolic and diastolic blood pressure respectively after the age of 40 (Kannel, 2009).

Hypertension induces endothelial dysfunction (Chobanian et al, 2003), which is considered the initiating step of atherosclerosis pathogenesis (Huynh et al, 2011). Atherosclerosis is a multifocal, immunoinflammatory disease of medium-sized and large arteries stimulated by lipids (Falk, 2006). Due to inflammation, the smooth muscle cells and endothelial cells proliferate in the intima, creating extracellular matrix molecules which form into atherosclerotic plaques (Ross, 1999). This may result in flow limiting stenosis and cause clinical symptoms such as stable angina (Nabel & Braunwald, 2012). This process has been shown to result in poorer quality of life (Battersby et al, 1995), chronic diseases and possibly a fatal myocardial infarction (Gazmararian et al, 2003; Rakugi et al, 1996).

Blood pressure ranging from 120-139mmHg systolic or from 80-89mmHg diastolic in adults is defined as pre-hypertension (Chobanian *et al*. 2003). Pre-hypertension has increasingly been recognized as a contributing factor to CVD risk (Santos *et al*. 2016). The relative risk of CVD in persons with pre-hypertension has been found to be 2.3-fold higher than for those with optimal blood pressure (Kshirsagar et al. 2006), this risk has been found to be even greater in individuals with other risk factors such as diabetes, low-density lipoprotein 100-129 mg·dl^{-1}, or body mass index greater than 30 kg·m^2 (Kshirsagar et al. 2006). Recent meta-analyses have found that pre-hypertension increases the risk of CAD and stroke independent of other cardiovascular risk factors (Huang *et al*. 2015; Huang *et al*. 2013; Guo *et al*. 2013).

A recent prospective epidemiologic study by Santos *et al*. (2016), designed to investigate atherosclerotic disease in 4871 participants found that pre-hypertension may be associated with preclinical target organ damage. The study categorised the participants into 3 groups: optimal blood pressure (blood pressure <120mmHg systolic and <80mmHg diastolic) (n = 402), pre-hypertension (n = 537) and hypertension (n = 3932) and analysed the alterations in cardiac structure and function between the groups. The study found that individuals with pre-hypertension had higher left ventricular mass index and wall thickness and higher prevalence of abnormal left ventricular geometry compared with those who have optimal blood pressure, however both are lower than individuals with hypertension. Additionally, the participants with pre-hypertension were shown to have impaired diastolic parameters such as E/A ratio, E' and E/E', and had a higher prevalence of mild and moderate-severe diastolic dysfunction compared with those with optimal blood pressure, however no differences in systolic parameters were observed. The results from this study coincide with the generally accepted notion that pre-hypertension is associated with an augmented risk of progression to hypertension (Leitschuh *et al.* 1991), and the linear and continuous relationship between blood pressure levels and cardiovascular events (Lewington *et al.* 2002). They also suggest that even mildly elevated blood pressure within the normal range is associated with cardiac end-organ damage.

1.5: Left Ventricular Hypertrophy

Systemic hypertension has been shown to cause an increase to myocardial workload, which has been found to lead to cardiac enlargement because of increased rate of myocardial and hyperplasia cells or continuation of hyperplasia beyond the normal period of hyperplastic growth (Oparill, Bishop & Clubb, 1984). As an effect to cellular enlargement, structural remodelling of the myocardial cells, which consists of modifications in the relative proportions of cellular organelles and in the ultrastructure of individual organelles, occurs during the development of hypertrophy in the heart (Oparill, Bishop & Clubb, 1984). The materialisation of left ventricular hypertrophy (LVH) is a strong independent risk factor for cardiovascular disease and all-cause mortality (Laine et al, 1999). LVH is the most significant predictor of adverse cardiovascular outcomes in the hypertensive population, and is an independent risk factor for CAD, sudden death, heart failure and stroke (Gradman & Alfayoumi, 2006). Patients who suffer with hypertension and LVH, because of myocardial

workload, are at a 10-fold greater risk of developing cardiovascular disease than those with hypertension and normal LV mass (Vogt et al, 1993).

1.6: Myocardial Dysfunction

CVD such as hypertension, CAD and cardiomyopathies often lead to systolic and diastolic dysfunction (Redfield *et al*. 2003). Diastolic dysfunction is characterised by an increased resistance to filling with increased filling pressures (Federmann & Hess, 1994). There is growing recognition that congestive heart failure caused by a predominant abnormality in diastolic function is both common and causes significant morbidity and mortality (Zile & Brutsaert, 2002). Research has shown that diastolic dysfunction is an independent predictor of mortality in patients with normal left ventricular ejection fraction (AlJaoundi *et al*. 2012). Approximately half of all patients suffering with congestive heart failure have diastolic dysfunction without reduced ejection fraction (Redfield *et al*. 2003). Diastolic dysfunction is graded as either mild (impaired relaxation), moderate (pseudonormal), or severe (restrictive filling) (AlJaoundi *et al*. 2012). The more advanced the stage is, the higher the filling pressures are and the worse the outcomes (AlJaoundi *et al*. 2012).

Diastolic dysfunction develops early in most cardiac diseases and leads to the elevation of LV filling pressures (Nagueh *et al*. 2009). Diastolic dysfunction refers to abnormalities of active myocardial relaxation and passive ventricular filling (Zile & Brutsaert, 2002). It can be attributed to one of four underlying conditions (Kapila & Mahajan, 2009). The most common cause is slow myocardial relaxation, due to myocardial ischaemia, causing a reduced rate of left ventricle pressure decline. In patients with LVH any degree of ischaemia or functional impairment of relaxation is greater, making them more susceptible to diastolic dysfunction (Ix *et al*. 2006). A second condition is impaired peak left ventricle filling rate due to the failure to generate an adequate transmitral pressure gradient, this occurs typically to either elevated left ventricular pressures or the inability to generate left ventricular suction (Kapila & Mahajan, 2009). Another condition is a result of alterations in cytoskeleton properties leading to passive viscoelastic stiffness of the left ventricle. Myocardial fibrosis is initiated by neurohumoral responses that leads to decreased left ventricular compliance (Kapila & Mahajan, 2009). The final underlying condition causing diastolic dysfunction is mechanical obstruction to left ventricular expansion raising left ventricular pressure to transmitral pressure more rapidly, terminating left ventricle filling earlier (Kapila & Mahajan, 2009). The

net effect of all these pathological processes is a higher LV end-diastolic pressure for any given LV end-diastolic volume (Kapila & Mahajan, 2009).

Di Bello *et al*. (2010) study, examining left ventricular mechanics in persons with pre-hypertension, found that there is evidence of abnormalities in early and global diastolic function. Compared to normotensive individuals the peak E wave was found to be progressively lower in pre-hypertension and hypertension patients, however, late diastolic left ventricular functional phase was comparable across the three groups. Analysis of the pulsed wave tissue Doppler imaging at mitral annulus level, showed that there is subtle modification of diastolic longitudinal function (E') and the E/E' ratio (a non-invasive measure of left ventricular filling pressure) showed a progressive and significant increase in pre-hypertension and hypertension patients in comparison with normotensive individuals, confirming that only the early phase of longitudinal diastolic function is impaired. This indicates that mild left ventricular diastolic dysfunction occurs during pre-hypertension. However, it is important to note that the study used a relatively small population, therefore the results cannot be generalised to the pre-hypertensive population, further longitudinal investigations are needed to better clarify these preliminary findings.

Left ventricular failure can be separated into systolic and diastolic dysfunction (Hess, 1993). Systolic dysfunction is determined by an impaired pump function with reduced ejection fraction and an enlarged end-diastolic chamber volume (Federmann & Hess, 1994). The most common cause of heart failure is left ventricular systolic dysfunction (McDonagh *et al*. 1998). Most cases of systolic dysfunction are a result of end stage CAD with either a previous myocardial infarction or with a chronically under-perfused myocardium (Fox *et al*. 2008). Other common causes include hypertensive heart disease, idiopathic dilated cardiomyopathy, valvular heart disease and congenital heart disease (Redfield *et al*. 2003).

Systolic dysfunction can be defined as having a left ventricular ejection fraction less than 40% (Vasan *et al*. 1999). In chronic heart failure this is most likely due to alterations in the transduction mechanisms regulating cardiac excitation-contraction coupling (Federmann & Hess, 1994). This causes a loss of cardiac inotropy causing a downward shift in the Frank-Starling curve, resulting in a decreased stroke volume and a compensatory rise in preload because of incomplete ventricular emptying, causing an increase in ventricular end-diastolic volume and pressure (Hess, 1993). The rise in preload is compensatory because it activates the Frank-Starling mechanism to help maintain stroke volume despite the loss of inotropy

(Hess, 1993). The negative adaptations as a consequence of these compensatory mechanisms is higher wall stress and higher oxygen requirements, these effects are reduced by subsequent myocardial hypertrophy, activation of the baroreceptor reflex and release of atrial natriuretic peptide (Federmann & Hess, 1994). The baroreceptor reflex inhibits sympathetic activation and atrial natriuretic peptide exerts diuretic and vasodilating effects (Federmann & Hess, 1994).

Patients with heart failure as a result of left ventricular systolic dysfunction regularly develop mitral regurgitation due to unfavourable alterations in ventricular geometry (Wu *et al*. 2005). This leads to deformation of the normal mitral valve apparatus and dilation of the ventricle chamber, which in turn leads to incomplete closure of the mitral valve cusps (Kono *et al*. 1992). The presence of mitral regulation in the setting of systolic dysfunction is associated with increased mortality (Robbins *et al*. 2003).

1.6: Physical Activity

In recent decades, major advances have been made in the understating of the pathogenesis of CAD and in the development of diagnostic methods and treatment modalities (Pyörälä *et al*. 1994). Measures aimed at CAD prevention focus on modification of lifestyles and reducing risk factors that are known to be casually linked with the development of atherosclerosis, the underlying disorder for CAD (Thompson *et al*. 2003). Four areas of risk factor modification have received particular attention, specifically cessation of smoking, increase exercise participation, treatment of elevated blood pressure and hypercholesterolaemia, because these risk factors have been considered to be the four major risk factors of CAD (Chobanian *et al*. 2003). There is evidence that indicates that risk factor modification is also effective in reducing the risk of recurrent CAD events in patients with clinically manifest CAD and, more recently, evidence that this can lead to a retardation or even a halt to the progression of coronary atherosclerosis. It has also been shown that risk factor modification reduces CAD risk in asymptomatic high risk subjects (Pyörälä *et al*. 1994).

Elevated blood pressure was the first risk factor to become a subject of specific recommendations (Pyörälä *et al*. 1994). It has been well reported that hypertension is a modifiable risk factor that when treated can reduce the risk of mortality (Sacco et al, 1997). Changes in life style such as participating in regular exercise (Ebrahim & Smith, 1998), reducing salt intake (Meneton *et al*. 2005), and reducing alcohol intake (Puddey, Beilin &

Vandongen, 1987) have been shown to positively affect the treatment of hypertension (Chobanian *et al*. 2003). Prospective epidemiological studies give strong support to the view that a sedentary lifestyle is associated with an increased risk of hypertension and CAD (Pyörälä *et al*. 1994).

Physical inactivity can be used as a term to identify individuals who do not meet the recommended level of physical activity (Townsend et al. 2015). It has been estimated that physical inactivity contributes to approximately 10% of all deaths worldwide from non-transmissible diseases (Lee *et al*. 2012). Although progress has been made in the prevention, detection, control and treatment of hypertension, it has been established that the adoption and adherence to long term exercise and fitness programs are much lower than expected. It has been reported that 31% of the global population are not currently meeting the recommendations for exercise (Hallal *et al*. 2012). Approximately only 50% of all individuals who begin participating in an exercise program will continue the habit for a period longer than 6 months (Bartlett *et al*. 2011). The issue of non-adherence is vital as the beneficial health effects of exercise are only maintained if exercise is maintained for extended periods of time (Fletcher *et al*. 1996). If the issue of non-adherence to exercise was addressed by developing strategies to improve exercise initiation, then the cardiovascular risks associated with hypertension could be reduced (King et al, 1992). Additionally, it has been noted that approximately 240,000 newly diagnosed chronic diseases each year have been attributed to physical inactivity (Martin *et al.* 2009). The national cost of medical bills attributed to physical inactivity within the UK has been estimated to amount to £1.06 billion (Allender *et al.* 2007).

Physical activity can be defined as any bodily movement produced by skeletal muscles that results in energy expenditure beyond resting expenditure (Thompson *et al*. 2003). The recommended amount of physical activity performed on a weekly basis is currently 30 minutes of tradition aerobic exercise 5-7 days a week (Townsend et al. 2015) or 20 minutes vigorous intensity exercise 3 days per week (Haskell *et al.* 2007). Regular physical activity has been shown to produce cardiovascular adaptations that increase exercise capacity, endurance and skeletal muscle strength (Thompson *et al*. 2003). Maximal aerobic capacity increases due to the cardiovascular systems increased capacity to deliver oxygen to the muscles, via an increased cardiac output, and the capability of the muscles to extract and utilise oxygen, which is reflected by the greater arteriovenous oxygen difference (Thompson,

2005). This process is demonstrated by the Fick equation, which is calculated as maximal aerobic capacity = cardiac output x arteriovenous oxygen difference (Albouaini *et al.* 2007).

It is also evident that regular physical activity can be a low cost non-pharmacological intervention in the prevention and management of chronic diseases (Thompson *et al*. 2003). Lee & Skerrett (2001) found that there is a transparent inverse relationship between the capacity of physical activity and all-cause mortality rates in men and women, of all ages, and that adherence to the recommended guidelines for physical activity resulted in approximately 20-30% reduction in all-cause mortality. It has been hypothesised that if worldwide participation in physical activity increased by approximately 10%, then almost 500,000 deaths each year as a consequence of physical inactivity could be averted (Lee *et al.* 2012).

Research shows that habitual physical activity prevents the development of CAD and reduces symptoms in patients with established cardiovascular disease (Durstine *et al*. 2000). Regular physical activity has been shown to cause adaptations in vascular function as a result of arterial sheer stress being used as a stimulus to trigger anti-atherosclerotic adaptations and vascular remodelling within the vascular system, helping to prevent the onset of age-related decline in indices of vascular function (Green, 2009). These adaptations are supported by Haskell et al. (1993), who found that physically active males have an increased coronary artery size and dilation capacity when compared to sedentary individuals. It has been documented that physically active individuals have endothelial adaptations in conduit arteries as a result of increased shear stress rate as a result of exercise (Green *et al.* 2011). The possible mechanisms prompting vasodilatory adaptations include increases in endothelial nitric oxide synthase and prostaglandin release as well as declines in free-radical-mediated nitric oxide degradation and sympathetic vasoconstrictor tone (Heydari, Boutcher & Boutcher, 2013). This increases the number of circulating endothelial progenitor cells, which results in greater endothelial regeneration and improved endothelial function (Hambrecht *et al.* 1998), reducing the risk of hypertension, the greatest precursor to cardiovascular disease (He & Whelton, 1997). The reduced risk of hypertension is supported by Fagard (2006), who found that physically active individuals have lower levels of plasma renin activity and less plasma noradrenaline compared to sedentary individuals. Following regular bouts of physical activity, heart rate variability and stroke volume have been shown to increase (Fletcher *et al*. 2013). This is due to increased arterial baroreflex sensitivity because of inhibition of the sympathetic nervous system and activation of the parasympathetic nervous system (Lanfranchi & Somers, 2002).

Further research by Barlow et al. (2012) support the notion that it is beneficial to have a more physically active lifestyle compared to sedentary individuals. Over a 27 ± 2 year period, it was shown that it was significantly (P=0.001) more beneficial to be physically active, as these individuals had greater survival rates and were less likely to suffer from cardiovascular diseases compared to physically inactive individuals. Delaying and preventing the onset of hypertension may therefore have a large impact on public health, especially in individuals who are at a high risk for cardiovascular events (Mosca *et al.* 2004), such as established CAD patients (De Backer *et al.* 2003), asymptomatic individuals (Greenland, Smith & Grundy, 2001) and obese individuals (Mosca *et al.* 2004). It has also been documented that regular physical activity reduces the risk of other chronic diseases, including type 2 diabetes (Knowler *et al*. 2002), osteoporosis (Vuori, 2001), obesity (Wing & Hill, 2001), depression (Pollock, 2001) and cancer of the breast (Breslow *et al*. 2001) and colon (Slattery & Potter, 2002).

1.7: Traditional Aerobic Training

In accordance with current guidelines, adults are advised to participate in at least 150 minutes of moderate intensity exercise each week (Townsend et al. 2015). It has been documented that partaking in this amount of exercise, working at an intensity of 40-59% HR_{max}, is beneficial to cardiovascular health by reducing cardiovascular risk factors (Thompson *et al.* 2003). This is demonstrated by the Cornelisson & Fargard (2005) meta-analysis, which included 72 trials of traditional aerobic training programmes, 105 study groups and 3936 participants consisting of normotensive, pre-hypertensive and hypertensive participants. The reported findings indicated that a variety of variables associated with being beneficial to cardiovascular health improved. It is reported that VO_{2peak} significantly increased (P < 0.001), which is an indicator of improved cardiovascular health (Keteyian *et al.* 2008). Significant reductions in systolic blood pressure (P < 0.001) and diastolic blood pressure (P < 0.001) were also reported, as well as a significant reduction in resting heart rate (P < 0.001). The impact on cardiac structure and function was not reported.

Empirical research surrounding traditional aerobic training has also shown that it may lead to improvements in cardiac structure and function (Andrea *et al*. 2002). A relationship between athletic participation and specific cardiac morphology has been well established. Increased left atrial size and left ventricular mass, wall thickness, and chamber size have been documented among trained athletes, and some recent reports have also noted similar characteristics in the right ventricle (Andrea *et al*. 2002; Baggish *et al*. 2007). An early study

by Fagard *et al*. (1983) assessing the effects of traditional aerobic training versus a physically inactive control group, showed that 12 male cyclists aged between 17-35 years old in competitive season compared with the 12 control subjects, matched for age, height and weight, have significantly greater left ventricular internal dimensions ($P < 0.05$) and increased wall thickness ($P < 0.05$), with similar left ventricular function.

A more recent study by Baggish *et al*. (2007) reported that 40 recreational athletes, had significant training-specific changes in cardiac structure and function following a 90-day aerobic training programme. Following the aerobic training programme, the participants experienced significant increases in left ventricular mass ($P < 0.05$) and end-diastolic volume ($P < 0.001$) and a non-significant trend toward increased wall thickness. It was also reported that stroke volume was increased following the training protocol, however, resting cardiac output (due to a marked reduction in resting heart rate) was significantly reduced. These findings correlate with the previous study in that by following an aerobic training programme the participants experienced left ventricular hypertrophy and biatrial enlargement. In contrast the participants Bassigh's study experienced significant increases in LV diastolic tissue velocities, which were positively correlated with the magnitude of LV mass increase. In aggregate, this data demonstrates direct evidence that traditional aerobic training produces left ventricular hypertrophy with associated augmentation of left ventricular function.

It has been suggested that due to the time commitment and the physical challenges of performing aerobic training, many population groups find it challenging to adhere to an aerobic training programme (Gillen & Gibala, 2013). Therefore, it could be postulated that current physical activity guidelines could be a factor influencing non-adherence to exercise programmes and further research is needed to explore the adoption of vigorous intensity exercise.

1.8: High Intensity Interval Training

More recently, research has focused on the intensity of exercise, with high intensity interval training (HIIT) fast becoming a popular alternative to more traditional aerobic training programmes (Gibala et al. 2012). HIIT is a time-efficient exercise strategy that has been documented to elicit beneficial adaptations in cardiorespiratory function as well as enhancements in metabolic health (Schoenfeld & Dawes, 2009). Compared to more traditional aerobic training programmes, HIIT has been shown to produce significantly

greater improvements in 24-hour ambulatory systolic blood pressure and diastolic blood pressure, VO_{2max}, total peripheral resistance, and left ventricular systolic and diastolic function in patients with hypertension and pre-hypertension (Sharman, La Gerche & Coombes, 2015). It has also been reported that sessions of HIIT (4 four minute intervals at 95% HR_{max}) is more efficient than aerobic exercise (45 minutes at 70% HR_{max}) as it allows for greater improvements in cardiac output and stroke volume which can reduce strain upon the cardiac muscle, reducing the risk of metabolic disorders (Helgerud *et al.* 2007).

HIIT refers to brief intervals of vigorous activity combined with periods of low activity or rest, and produces a strong cardiac response compared with aerobic exercise (Gibala et al. 2012). It has been recognised that HIIT using a 30-secind Wingate protocol is sufficiently long enough to allow for developing the maximal glycolytic power and short enough for maximal effort to be exerted until the end of the bout (MacInnis & Gibala, 2017). The recovery period performed at a reduced intensity is designed so that the cardiopulmonary system does not fully recover to near resting levels, whilst allowing the individual enough recovery to be able to repeat the next bout of high intensity exercise (MacInnis & Gibala, 2017). Research indicates that HIIT performed 3 times per week is adequate to decrease markers of chronic disease in both healthy individuals and people with cardio metabolic disorders (Shiraev & Barclay, 2012). As lack of time remains one of the main cited barriers to regular exercise participation, HIIT is a time-efficient exercise strategy that could be used to encourage exercise participation by fitness professionals and health practitioners (Gillen & Gibala, 2013).

The adaptions observed after HIIT is said to be due to the metabolic rate being raised for a brief period that is considerably higher than that of traditional aerobic training, this permits a longer duration of a training period spent at a higher percentage of $V0_{2max}$ (MacInnis & Gibala, 2017). Research suggests that the relative intensity of cycling is more important than the duration in relation to all-cause mortality in healthy subjects (MacInnis & Gibala, 2017).

There is increasing evidence that supports HIIT as a well-tolerated and safe training method, even amongst populations with high risk of cardiometabolic disease, the protocol can be adapted to the specific needs of the individual, with the work periods and recovery periods simply being adjusted to create a variety of different HIIT protocols (Arena *et al.* 2013). A meta-analysis on patients with lifestyle induced chronic diseases from Weston, Wisloff & Coombes (2014) support the potential cardiovascular health benefits of performing HIIT over

aerobic training programmes. Ten studies were included in the meta-analysis, all of which followed a randomised control trial protocol, assessing a cardio-metabolic chronic disease population, where physical inactivity was the main contributor. It can be noted that the meta-analysis showed greater increases in Vo_{2max} in the HIIT programme by 19.4% compared against a 10.9% increase in the aerobic training programme. The increase in Vo_{2max} because of exercise training could be explained due to a higher maximum cardiac output and greater extraction of oxygen from the systemic circulation demonstrated in the participants, reflecting both central and peripheral adaptations (Fletcher *et al*. 1990). Greater central adaptations demonstrated in the meta-analysis include improved left ventricular ejection fraction in the HIIT group with no change in the aerobic training group, highlighting the potential for further left ventricular remodelling with HIIT (Wisloff *et al*. 2007). It was also found that cardiac function was improved with HIIT, in terms of stroke volume, mitral annular excursion, ejection velocity and systolic mitral annular velocity, demonstrating improvements in systolic and diastolic function that were not found with the aerobic training group. Increased maximal rate of calcium ions (Ca^{2+}) uptake and greater reductions in resting blood pressure were also reported in the HIIT group.

The effects of HIIT and the subsequent clinical benefits in both healthy and high-risk populations have been well documented within empirical literature (Gilbala *et al.* 2012). Evidence based research has investigated the effects of acute and chronic HIIT protocols on cardiac structure and function in healthy populations and chronic disease patients. A study by Cote *et al*. (2013) demonstrated that an acute bout of HIIT can cause alterations in cardiac mechanics in healthy individuals. Thirty-nine normally active and endurance trained men and women completed an echocardiographic evaluation of left ventricular function before and after an acute bout of HIIT. It was reported that following the HIIT session fractional shortening, wall stress, septal and lateral wall tissue velocities, and isovolumetric relaxation time were reduced ($P < 0.05$). It was also found that males demonstrated greater reductions in cardiac contractility compared to females, which may reflect differential intrinsic myocardial relaxation properties, the mechanisms of which require further research. The findings demonstrate that a single session of HIIT can alter cardiac function, leading to significant improvements in diastolic function, an independent predictor of cardiovascular morbidity and mortality (AlJaoundi *et al*. 2012).

In addition, a chronic study of 12 weeks with a total of twenty-eight physically inactive participants investigated the effects of HIIT on cardiac structure and function in patients with

type 2 diabetes (Cassidy *et al*. 2015). The participants were randomised into either a HIIT (n=14) or control group (n=14). It was reported that left ventricular mass was significantly improved (HIIT: 104±17 g to 116±20 g vs Con: 107±25 g to 105±25 g, p<0.05) and systolic function through stroke volume was significantly improved (HIIT: 76±16 ml to 87±19 ml vs Con: 79±14 ml to 75±15 ml, p<0.01) following the HIIT programme. It was also reported that in the HIIT group early diastolic filling rates significantly increased (HIIT: 241±84 ml/s to 299±89 ml/s vs Con: 250±44 ml/s to 251±47 ml/s, p<0.05) and peak torsion significantly decreased (HIIT: 8.1±1.8° to 6.9±1.6° vs Con: 7.1±2.2° to 7.6±1.9°, p<0.05). The increase in early diastolic filling demonstrates improve diastolic function, suggesting that the myocardium has become more compliant and quicker to relax following HIIT. This is clinically significant as diastolic dysfunction is an independent predictor of cardiovascular morbidity and mortality (AlJaoundi *et al*. 2012).

A study by Molmen-Hansen *et al*. (2012) investigated the effects of moderate aerobic training and HIIT on cardiac function and blood pressure in patients with hypertension. The participants were randomised into three groups, either the HIIT group (n=31), aerobic training group (n=28) or the control group (n=29). The results show that HIIT was superior to aerobic training in terms of improved cardiac function, aerobic capacity and reducing mean heart rate. It was reported that only the HIIT group had an improvement in left ventricular ejection fraction, stroke volume, systolic flow velocity, end-diastolic volume (11%, p < 0.01), and early diastolic mitral annulus tissue velocity, E' (14%, p < 0.001). It was also found that systolic mitral annulus tissue velocity, S' increased by 15% (p < 0.001) after HIIT and 8% (p < 0.04) after aerobic training. The isovolumetic relaxation rate decreased significantly in the HIIT group only, by 16% (p < 0.01). However, it could be argued that despite positive results, the long duration on the HIIT sessions (38 mins) may be too long and participants may not adhere to sessions of this duration in the long term.

The results from this study coincide with Weston, Wisloff & Coombes (2014) meta-analysis who found that there was a greater improvement in in heart rate, systolic and diastolic function in patients with hypertension following HIIT when compared to aerobic training. However, it can be noted that the results differ in terms of changes in myocardial structure, therefore it can be suggested that more research is needed to further understand the relationship between HIIT and hypertension and to clarify the physiological adaptations that take place.

Furthermore, a 12-week study including twenty-seven chronic heart failure patients (Wisloff *et al*. 2007), investigated the effects of HIIT compared against traditional aerobic training and a control group on cardiac structure and function. The study demonstrated significant improvements in cardiac, vascular and autonomic function after adherence to a long-term HIIT programme compared to aerobic training or a control group. There was a significantly greater increase in VO_{2max} following HIIT compared to aerobic training (46% compared to 14%, $P<0.001$) which was associated with reverse left ventricular remodelling. The HIIT group was more effective in improving systolic function, with left ventricular ejection fraction significantly improving by 35% ($P<0.01$), accompanied by increases in systolic mitral annulus excursion and stroke volume by 30% and 17% ($P<0.01$) respectively. In addition, peak systolic mitral annulus velocity, an indicator of global contractility increased by 22% ($P<0.01$), whereas there were no significant changes in systolic function in the aerobic or control groups. It was also shown that HIIT was more effective in improving diastolic function, with HIIT but not aerobic training significantly improving E/E' and E/A ratio by 49% and 15% ($P<0.01$, $P<0.05$) respectively. Isovolumetric relaxation time significantly decreased by 22% ($P<0.05$) only in the HIIT group. HIIT and aerobic training reduced E/E' by 26% ($P<0.001$) and 15% ($P<0.043$) respectively. The results from this study give insight into the benefits of prescribing HIIT as a rehabilitative intervention in stable chronic heart failure patients.

The literature reviewed demonstrates how HIIT programmes can induce physiological adaptations that are beneficial to cardiovascular health in different populations. Empirical literature shows how acute and chronic sessions of HIIT can alter cardiac structure and function. However there has been no research to examine the effects of a short-term HIIT intervention over a 4-week period on cardiac structure and function in a young, physically inactive population.

1.9: Rationale

It is well recognised that taking part in a HIIT programme offers cardiovascular protective adaptations that can reduce risk factors of CVD, like that of traditional aerobic training programmes, but with less time commitment. However, literature supporting HIIT and the effect on cardiac structure and function in physically inactive populations is limited and can be considered equivocal in regard to the amount, mode, frequency and intensity of what is the best intervention for improvements. The reported benefits in cardiac structure and function can be seen in hypertensive patients, physically inactive older men, patients with type 2

diabetes, patients with chronic heart failure as well as patients with other cardio-metabolic chronic diseases. Current research supports HIIT as an effective intervention which can improve traditional and novel risk factors for CVD in healthy and high-risk populations. Therefore, the aim of this study is to investigate the effects upon cardiac structure and function in a physically inactive population following a 4-week HIIT intervention.

1.10: Hypothesis

Considering empirical research, the following hypothesis can be theorised;

Experimental hypothesis (H_a) - There will be a statistically significant difference in cardiac structure and function measured via a transthoracic echocardiogram in participants completing a HIIT intervention compared to a control group.

Null hypothesis (H_0) - There will not be a statistically significant difference in cardiac structure and function measured via a transthoracic echocardiogram in participants completing a HIIT intervention compared to a control group.

2.0: Method

2.1: Ethical approval and study population

All procedures for the current investigation conformed to Canterbury Christ Church Universities Research Governance Handbook, and the Canterbury Christ Church Universities Faculty of Social and Applied Sciences Research Ethics Committee approved the study. Signed informed written consent and a completed physical activity readiness questionnaire was obtained from all participants.

Forty-five participants including a mix of male and females who were physically inactive from Canterbury Christ Church University volunteered to participate in the study. The participant's demographics (see table 2.1), including age (Control = 22 ± 3.5 years, HIIT = 21 ± 1.7 years) and height (Control = 172.4 ± 8.8 cm, HIIT = 173.7 ± 9.5 cm) were recorded prior to each phase of the study. Height was measured using a stadiometer (Seca model 220, Seca Gmbh & co.kg, Hamburg, Germany) and weight was measured using balance scales (Seca Model 710, Seca Gmbh & co.kg, Hamburg, Germany).

Table 2.1: Participants demographic information pre-intervention.

	Control (n=20) Mean ± SD	HIIT (n=21) Mean ± SD
	Pre	Pre
Weight (kg)	74.3 ± 15.9	73.9 ± 14.4
BMI (kg.m^2)	24.9 ± 4.5	23.4 ± 3.2
BSA (m^2)	1.87 ± 0.22	1.84 ± 022
Resting sBP (mmHg)	120.9 ± 9.6	121.2 ± 10.3
Resting mBP (mmHg)	88.6 ± 7.6	87.8 ± 8.4
Resting dBP (mmHg)	69.9 ± 7.4	69.5 ± 10.8
Resting PP (mmHg)	51.2 ± 8.6	51.7 ± 12.3

Although forty-five participants were recruited for the study, it must be documented that due to undisclosed reasons only forty-one participants completed the investigation.

2.2: Apparatus

All cardiac structural and functional parameters were measured by Quantitative 2-D transthoracic echocardiography, a method which enables characterization of left ventricular remodelling in normal subjects and in a variety of heart diseases (Lang *et al*. 2006). Transthoracic echocardiography was performed using a commercially available, portable ultrasound system (Vivid-q, GE Healthcare, Milwaukee, Wisconsin) with a 1.5–3.6 MHz phased array transducer (M4S-RS Matrix cardiac ultrasound probe), pre-and post the 4-week intervention. All image acquisitions and measurements were performed as recommended by the American Society of Echocardiography (Lang *et al*. 2015). Three consecutive cardiac cycles were recorded and stored for offline analysis using commercial software on a proprietary workstation (EchoPAC; V.113.0.x, GE Healthcare), with the results averaged. Images were obtained in parasternal long axis and short axis level to mitral valve and apex, and apical 2-, 3-, and 4-chamber views at baseline following 15 min of supine rest. Left ventricular mass was calculated according to Devereux *et al*. (1986). Left ventricular ejection fraction was determined by the modified biplane Simpson's rule. Pulsed wave Doppler was

used to record transmitral flow in the apical four chamber view. Tissue Doppler velocities were acquired at the lateral mitral annulus. LV filling pressure was estimated from the mitral E/E' ratios (Ommen *et al.* 2000). Doppler-echocardiography has emerged as important clinical tool providing reliable and useful data on cardiac performance (Mandinov *et al.* 2000).

Resting blood pressure was measured using a Dinamap blood pressure monitor (Dinamap, PRO 200, GE Medical Systems Information Technologies GmbH, Munzinger Strasse 3, 79111, Freiburg, Germany) to confirm blood pressure status. The Dinamap PRO 200 has been shown to be a valid tool for measuring resting blood pressure and is approved by the American National Standards Institute (Lai *et al.* 2013).

A Wattbike cycle ergometer (Wattbike Ltd, Nottingham, UK) programmed using Wattbike expert software (V2.50.42, Wattbike Ltd, Nottingham, UK) was used for a Wingate test protocol in the HIIT intervention. It has been reported that the measurements produced from the Wattbike are valid and reproducible (Driller, Argus, & Shing, 2013). Hopker et al. (2010) demonstrated that the Wattbike is sufficiently accurate to track performance changes over time and thus would serve as an acceptable training tool for both trained and untrained populations. The Wingate protocol developed in the 1970s is documented as being the most common HIIT intervention used in studies (Shiraev & Barclay, 2012). The participant's Wattbike resistance during the 30 second maximal sprints were prepared to 7.5% of the participant's bodyweight.

2.3: Experimental Procedure

Volunteered for study

(n=45)

Excluded

- Declined to participate (n=2)

Randomised (n=43)

Allocation

Allocated to control

Received allocated intervention (n=21)

Allocated to HIIT

Received allocated intervention (n=22)

Intervention

Completed intervention (n=20)

Discontinued intervention (could not commit time, n=1)

Completed intervention (n=21)

Discontinued intervention (did not re-contact, n=1)

Analysis

Analysed (n=20)

Excluded from analysis (n=0)

Analysed (n=21)
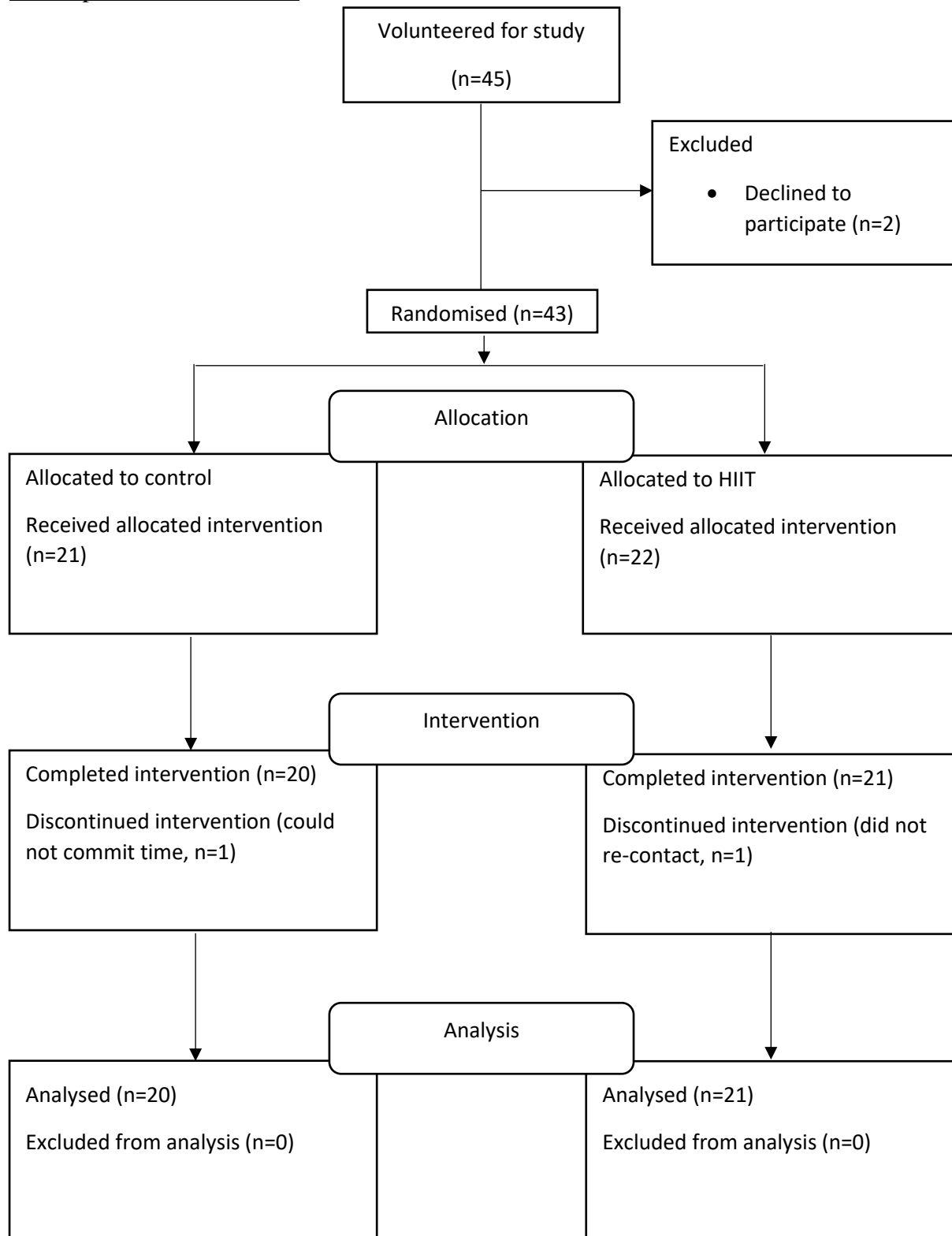
Excluded from analysis (n=0)

Figure 2.1. Flow diagram depicting the flow of participants at each stage of the study.

Prior to testing the participants were required to abstain from caffeine and alcohol for 24 hours. All participants were required to maintain their normal lifestyle and dietary patterns throughout the 4-week investigation. Prior to testing the participants were randomised, using stratified randomisation for gender into either the HIIT group or control group, to ensure an equal number of male and female participants in each condition, in addition to reducing any bias with pre-test variables (Blüher *et al*. 2017). The participants were then required to have 15 minutes seated rest while they had their seated resting BP and HR recorded. A reading was taken every 5 minutes in order to calculate an average. Following blood pressure assessment, A transthoracic echocardiogram was performed on each participant by using a portable ultrasound system (Vivid-q, GE Healthcare, Milwaukee, Wisconsin) with a 1.5–3.6 MHz phased array transducer (M4S-RS Matrix cardiac ultrasound probe) to measure cardiac structural and functional parameters. The same sonographer acquired all images, with the participant examined in the left lateral decubitus position. This was performed pre-and post HIIT and Control phases. Upon completion of the 4- week intervention participants were asked to come into the lab 48 hours after the last HIIT session to monitor any potential changes. The rationale behind participants coming in 48 hours prior to the last HIIT session is to ensure that sufficient time had been left for any post exercise hypotension to subside (Forjaz *et al.* 2000).

2.3.1. HIIT Group

The HIIT intervention consisted of supervised sessions 3 times a week for 4 weeks. Each HIIT session consisted of a 5-minute warm up, followed by 3x 30 second maximal sprints at a resistance of 7.5% body weight separated by a 2-minute active recovery period, similar to the HIIT protocol reported by Shiraev & Barclay (2012), to improve cardiovascular and metabolic health. Each session lasted approximately 12 minutes. HIIT sessions were performed in groups with verbal encouragement given throughout to maximise beneficial effects from the intervention (Burke *et al.* 2006). Upon completion of the 4-week intervention the participants underwent the same procedure as pre-testing, 48 hours after the final HIIT session, in order to assess the influence HIIT had upon cardiac variables.

2.3.2. Control Group

The participants were instructed to maintain their lifestyle and dietary habits for a 4-week period. Once completed the participants underwent the same procedure as pre-testing to assess any influence upon cardiac structural and functional variables.

2.4: Power Calculation

Based on operator coefficient of variation for diastolic function and estimated filling pressure (primary outcome variables) using transthoracic echocardiography, a sample size of 14 to 17 participants in each group has 80% power to detect a significant difference in diastolic function and estimated filling pressure, respectively, with a 2-sided $p<0.05$. It was estimated a drop-out rate of between 10-30% leading to an overall sample size of 44 participants (22 in each group).

2.5: Data Analysis

All data was analysed using statistical package for social sciences (SPSS V22.0, release version for Windows; SPSS Inc., Chicago IL, USA). Unless specified otherwise, continuous variables are presented as mean ± SD. Change in cardiac parameters in control and HIIT groups were analysed using an analysis of covariance (ANCOVA), as the data was normally distributed. Statistically significant data was report as $P< 0.05$.

3.0: Results

Forty-five participants were recruited for the study. Forty-one participants completed the intervention, 21 in the HIIT group and 20 in the control group. Two participants declined to participate before being allocated to a group, due to lack of time. One participate removed themselves from the control group due to an inability to complete post testing. One participant removed themselves from the HIIT intervention due to unknown reasons. There were no adverse effects following the HIIT sessions. There was no significant change in the participants pre and post demographic data between groups following the intervention (see table 3.1).

Table 3.1: Participants demographic data pre and post intervention.

	Control (n=20)	HIIT (n=20)

	Mean ± SD		Mean ± SD	
	Pre	Post	Pre	Post
Weight (kg)	74.3 ± 15.9	74.2 ± 15.7	73.9 ± 14.4	74.3 ± 15
BMI (kg.m^2)	24.9 ± 4.5	24.8 ± 4.4	23.4 ± 3.2	23.5 ± 3.4
BSA (m^2)	1.87 ± 0.22	1.87 ± 0.23	1.84 ± 022	1.84 ± 0.23
Resting sBP (mmHg)	120.9 ± 9.6	119.7 ± 10.9	121.2 ± 10.3	114.6 ± 8.8*
Resting mBP (mmHg)	88.6 ± 7.6	88.8 ± 9.3	87.8 ± 8.4	85 ± 6.3
Resting dBP (mmHg)	69.9 ± 7.4	69.9 ± 8.8	69.5 ± 10.8	66.1 ± 5.9
Resting PP (mmHg)	51.2 ± 8.6	49.7 ± 7.9	51.7 ± 12.3	48.5 ± 8.34

Values are presented as mean ± SD. sBP, systolic blood pressure; dBP, diastolic blood pressure; mBP, mean blood pressure; PP, pulse pressure. * indicates significant ($P < 0.05$) difference in the pre- to post-change value between control and HIIT intervention group.

<u>3.1: Haemodynamic Parameters</u>

Following 4 weeks of HIIT there was a significant reduction in resting SBP (-6.86 ± 8.76 mmHg) compared against the control group (-1.15 ± 9.4 mmHg, $P = 0.041$). There were no significant differences found in resting DBP or MBP in either the HIIT group or control group (see table 3.1). As shown in figure 3.1A, there was a significant reduction in resting heart rate (65.59±10.15 to 63.05±13.42 b·min^{-1}) in the HIIT intervention and no significant change (60.7±8.19 to 61.3±7.32 b·min^{-1}; P=0.013) during the control period. As shown in figure 3.1B, there was a significant increase in SV (55.48±16.27 to 64.24±20.62ml) in the HIIT intervention and no significant change (56.8±11.94 to 59.4±14.81ml; P=0.015) during the control period. As illustrated in figure 3.1C, there was no significant change in either group in cardiac output.
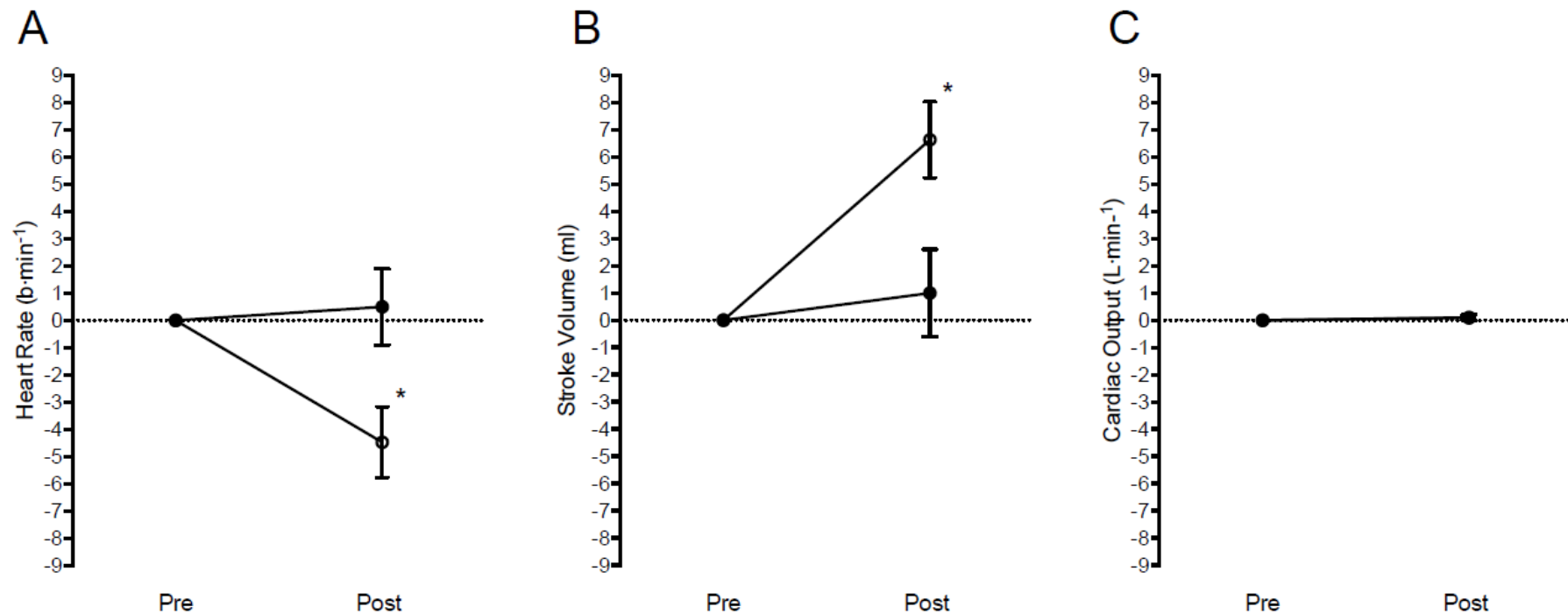

Figure. 3.1. Mean heart rate (A), stroke volume (B), cardiac output (C) change values at rest for the control (filled circles) and HIIT (open circles) conditions. *Error bars* indicate standard error of the mean. * Significant (P<0.05) difference in the control and HIIT change value.

3.2: Cardiac Structural Parameters

As displayed in table 3.2 there was no significant change in either group in cardiac structural parameters.

Table 3.2 displays changes in cardiac structural parameters following HIIT and control period

Parameter	Control		HIIT	
	Pre [b]	Post	Pre [b]	Post
IVSd (cm)	0.7 ± 0.1	0.6 ± 0.1	0.71 ± 0.14	0.68 ± 0.12
LVIDd (cm)	4.6 ± 0.42	4.6 ± 0.39	4.63 ± 0.42	4.64 ± 0.46
LVPWd (cm)	0.8 ± 0.11	0.8 ± 0.11	0.86 ± 0.16	0.82 ± 0.14
LVIDs (cm)	3.7 ± 0.4	3.7 ± 0.36	3.47 ± 0.36	3.52 ± 0.38
FS (%)	20.4 ± 7.81	19.7 ± 5.65	24.76 ± 7.12	23.79 ± 7.47
LA (cm)	3 ± 0.22	3 ± 0.27	3.07 ± 0.36	3.05 ± 0.38
LVLd (cm)	8 ± 0.71	8.1 ± 0.71	8.06 ± 0.66	8.16 ± 0.73
LVLS (cm)	6.5 ± 0.58	6.3 ± 1.02	6.45 ± 0.62	6.43 ± 0.64
LVEF (%)	50.1 ± 5.61	48.3 ± 5.88	49.61 ± 6.01	49.18 ± 6.05
LVM (g)	110.88 ± 29.62	106.21 ± 26.45	119 ± 37.27	112.4 ± 29.6
RWT (cm)	0.35 ± 0.04	0.35 ± 0.05	0.37 ± 0.07	0.35 ± 0.06

Note: *IVSd,* interventricular septum thickness at diastole*; LVIDd,* Left Ventricular Internal Dimension -Diastole; *LVPWd, Left Ventricular Posterior Wall Dimensions; LVIDs,* Left Ventricular Internal Dimension - Systole*; FS,* Fractional Shortening; *LA,* Left Atrium*; LVLd,* Left Ventricle Length Diastole*; LVLs,* Left Ventricle Length Systole*; LVEF,* Left ventricular ejection fraction*; LVM,* Left Ventricular Mass*; RWT, Relative wall thickness.* Values are presented as mean ± standard deviation. [b] Adjusted for baseline value for ANCOVA. * Indicates significant (P < 0.05) difference in the pre- to post-delta value between control and HIIT intervention.

3.3: Cardiac Function Parameters

As illustrated in table 3.3, it can be noted that there was a significant increase in LVEDV
(115.59 ± 28.34 to 131.94 ± 33.40ml) in the HIIT intervention and no significant change
(117.1 ± 27.93 to 121.4 ± 24.5; P=0.025) during the control period. There was a significant
reduction in E/A ratio (1.98 ± 0.48 to 1.95 ± 0.55) in the HIIT intervention and no significant
change (2.02 ± 0.34 to 2.05 ± 0.29; P=0.027). There was a significant reduction in lateral
E/E' ratio (4.67 ± 1.28 to 4.20 ± 0.87) in the HIIT intervention and no significant change
(4.23 ± 1.16 to 4.57 ± 1.27; P=0.04) in the control group. There was a significant reduction in
septal E/E' ratio (6.74 ± 1.41 to 6.23 ± 1.06) in the HIIT intervention and no significant
change (6.35 ± 1.98 to 6.67 ± 1.9; P=0.01) in the control group. There was a significant
reduction in average E/E' ratio (5.41 ± 1.17 to 5.22 ± 0.89) in the HIIT intervention and no
significant change (5 ± 1.83 to 5.37 ± 1.38; P=0.002) in the control group.

Table 3.3 displays changes in cardiac function parameters following HIIT and control period

Parameter	Control		HIIT	
	Pre [b]	Post	Pre [b]	Post
LVEDV (ml)	117.1 ± 27.93	121.4 ± 24.5	115.59 ± 28.34	131.94 ± 33.40*
LVESV (ml)	62.6 ± 17.71	63.7 ± 17.23	56.21 ± 14.94	66.64 ± 16.29
MV E Vel(m/s)	0.79 ± 0.17	0.82 ± 0.17	0.79 ± 0.15	0.8 ± 0.13
MV DecT (m/s)	181.5 ± 21.51	176.3 ± 16.66	186.33 ± 40.88	166.26 ± 26.99
MV Dec Slope (m/s^2)	4.5 ± 1.08	4.6 ± 0.99	4.57 ± 1.37	4.99 ± 1.06
MV A Vel (m/s)	0.48 ± 0.11	0.4 ± 0.08	0.41 ± 0.06	0.44 ± 0.11
MV E/A Ratio	2.02 ± 0.34	2.05 ± 0.29	1.98 ± 0.48	1.95 ± 0.55*
E' Lateral (m/s)	0.18 ± 0.03	0.18 ± 0.03	0.19 ± 0.04	0.19 ± 0.03
E/E' Lateral	4.23 ± 1.16	4.57 ± 1.27	4.67 ± 1.28	4.20 ± 0.87*
A' Lateral (m/s)	0.07 ± 0.02	0.07 ± 0.02	0.06 ± 0.02	0.07 ± 0.02
S' Lateral (m/s)	0.11 ± 0.02	0.11 ± 0.03	0.1 ± 0.02	0.11 ± 0.02
E' Septal (m/s)	013 ± 0.02	0.13 ± 0.02	0.13 ± 0.02	0.13 ± 0.02
E/E' Septal	6.35 ± 1.98	6.67 ± 1.9	6.74 ± 1.41	6.23 ± 1.06*
Avg E/E'	5 ± 1.83	5.37 ± 1.38	5.41 ± 1.17	5.22 ± 0.89*
A' Septal (m/s)	0.08 ± 0.03	0.08 ± 0.01	0.09 ± 0.04	0.08 ± 0.01
S' Septal (m/s)	0.09 ± 0.02	0.08 ± 0.01	0.1 ± 0.01	0.09 ± 0.01
RV E'(m/s)	0.14 ± 0.03	0.14 ± 0.02	0.14 ± 0.02	0.15 ± 0.03
RV A' (m/s)	0.1 ± 0.03	0.09 ± 0.03	0.1 ± 0.02	0.1 ± 0.02
RV S' (m/s)	0.13 ± 0.02	0.13 ± 0.02	0.14 ± 0.02	0.16 ±0.11
TAPSE (cm)	1.94 ± 0.18	1.95 ± 0.21	2.02 ± 0.21	2.06 ± 0.18

Note: *LVDEV,* left ventricular end-diastolic volume*; LVESV,* left ventricular end-systolic volume*; LVEF, E,* peak mitral inflow velocity during early filling*; DecT,* deceleration time*; A,* peak mitral inflow during atrial systole*; E',* peak annulus tissue velocity during early filling*; A',* peak annulus tissue velocity during atrial systole*; S',* systolic peak flow velocity in left ventricular outlet tract*; TAPSE,* Tricuspid annular plane systolic excursion. Values are presented as mean ± standard deviation. [b] Adjusted for baseline value for ANCOVA. * Indicates significant ($P < 0.05$) difference in the pre- to post- delta value between control and HIIT intervention.

<u>3.4: Cardiac Time Intervals</u>

As illustrated in figure 3.2, it can be noted that there was a significant reduction in isovolumetric relaxation time (81.23 ± 12.85 to 77.83 ± 9.81 m/s) in the HIIT intervention and no significant change (83.45 ± 10.36 to 85.71 ± 8.24 m/s; P=0.022) in the control group. It can also be noted that there was no significant change in either group in isovolumetric contraction and ejection time.
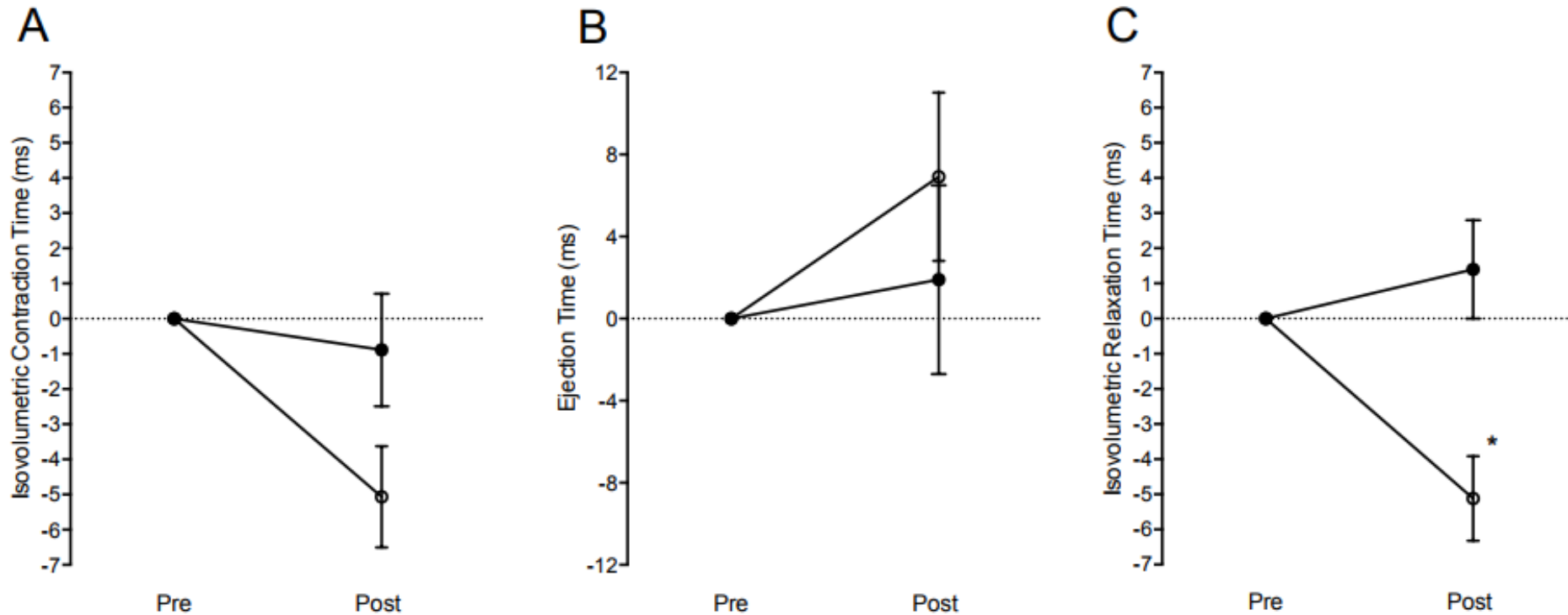

Figure. 3.2. Isovolumetric contraction (A), ejection time (B), isovolumetric relaxation (C) change values at rest for the control (filled circles) and HIIT (open circles) conditions. *Error bars* indicate standard error of the mean. * Significant (P<0.05) difference in the control and HIIT change value.

4.0: Discussion

Empirical literature indicates that participation in regular physical activity can reduce the risk of chronic diseases related to unhealthy lifestyles. Findings from the present study offer new and consistent research which demonstrate the response of HIIT on health markers in a physically inactive population. These findings offer insight of the role of HIIT and the potential it could have on primary health care and physical activity guidelines.

4.1: HIIT and Myocardial Compliance

Subsequent to the 4-week HIIT intervention, it can be noted that resting heart rate was significantly reduced by -4.47 ± 5.68 b·min^{-1} (P=0.013). It can also be observed that SV (6.56 $\pm$ 8.04 ml; P=0.015) and LVEDV (16.35 $\pm$ 20.44 ml; P=0.025) significantly increased. These findings indicate that myocardial compliance can be improved following a short term HIIT intervention compared against a control group, which could be beneficial to individuals who cite lack of time as their main barrier to regular exercise.

Findings from the present study coincide with those by Molmen-Hansen *et al*. (2012) as they reported improvements in resting heart rate, stroke volume and end diastolic volume following a 12-week HIIT intervention. Molmen-Hansen's study used a similar HIIT protocol to the present study and compared it to an aerobic training group, in individuals with hypertension. Molmen-Hansen *et al*. (2012) reported reductions of 3.8 b·min^{-1} following the HIIT intervention, as well as increases of 8ml in SV and 12ml in LVEDV, opposed to no significant changes in the aerobic group, further reinforcing the benefits of HIIT. Heydari, Boutcher & Boutcher's (2013) investigation also found reductions in resting heart rate of 6.2 b·min^{-1} following a 12-week HIIT intervention. In comparison to these findings it could be theorised that if the present study was longer, further improvements in myocardial compliance could be observed. It can also be noted that the participants in the present study had greater improvements compared to Molmen-Hansen in a shorter time-period. The present study had shorter work periods and shorter recovery periods which may have allowed the participants to perform at a higher intensity compared to the participants in Molmen-Hansen's study. This would suggest that the exercise protocol in the present study permits a longer duration of the training period to be spent at a higher percentage of VO$_{2max}$. Which could possibly explain the greater adaptations in the present study.

Empirical literature frequently acknowledges the improvements in myocardial compliance following HIIT interventions, however, the mechanisms underlying these improvements are complex and are yet to be completely understood. However, it has been suggested that the underlying mechanisms that potentially could explain improvements in myocardial compliance following HIIT interventions are similar to those of aerobic exercise, findings that have been reported in many longitudinal studies surrounding HIIT and aerobic exercise training (Lavie *et al.* 2015).

A possible mechanism explaining a reduction in resting HR following HIIT, which coincides with the result of the present study is the increase in SV. It has been reported that increased LVEDV is associated with increased ventricular preload. Higher LVEDV has previously been found to be a consequence of increased venous return, which stretches the sarcomeres, thereby increasing their preload. Changes in ventricular preload have been shown to dramatically effect stroke volume due to the Frank-Starling mechanism. According to the Frank-Starling law, the increase in blood volume causes a direct increase in myocardial contractility and to maintain cardiac output, resting HR can decrease as a response to the higher SV. This response influences a reduction in myocardial workload, which has been reported to be beneficial in the prevention of CVD (Heydari, Boutcher & Boutcher, 2013).

Another possible mechanism explaining a reduction in resting HR following the HIIT intervention could be improvements in cardiac autonomic parameters. Research has shown that short-term HIIT intervention increases parasympathetic activity and decreases sympathetic activity to the heart at rest (Besnier *et al.* 2017). This has been shown to improve cardiovascular health by increasing stroke volume, heart rate variability whilst reducing resting HR, peripheral resistance and blood pressure parameters (Lanfranchi & Somers, 2002). An improvement in cardiac autonomic function would indicate a greater sympathovagel balance (Goldstein *et al.* 2011). This response would offer a cardio-protective effect as well as reducing the incidence of CVD (Heydari, Boutcher & Boutcher, 2013).

Alternatively, the reductions in resting HR could possibly be linked with a training-induced increase in vagal activity (Hautala, Kiviniemi & Tulppo, 2009). It has been reported that HIIT interventions can increase parasympathetic activity whilst also decreasing sympathetic activity over the sinus node autorhythmicity when at rest (McCorry, 2007). This improvement in sympathovagal balance after the interval exercise session, could represent a greater cardio protective effect (Borresen & Lambert, 2008). The research that explains the

possible mechanisms responsible for improving cardiac vagal modulation is limited, however, angiotensin II and nitric oxide are potential mediators (Routledge *et al*. 2010). Further research is required to clarify the role of nitric oxide and its potential influence on cardiac vagal tone.

The improvements in resting HR could also be attributed to exercise-induced sinus bradycardia (D'Souza *et al*. 2014). A case study by D'Souza *et al.* (2014) investigating the effects of exercise on sedentary mice found electrophysiological adaptations in the sinus node. The study observed training induced remodelling of pacemaker ion channels, most notable was the downregulation of HCN4, mRNA and protein, possibly due to a decrease in density of I_f. However, it was also noted that there was widespread remodelling of the sinus node and it is possible that other aspects of the remodelling may have had an impact on pacemaker mechanisms.

4.2: Cardiac Function

HIIT improved diastolic function significantly when compared against the control group. The changes in tissue Doppler measurements were significant, while it can be noted the control group suffered further impairment. The positive effect of HIIT on myocardial function in other CVD has been well documented in previous literature (Cassidy *et al*. 2015; Molmen-Hansen *et al*. 2012).

The findings from the present study suggest that the improved SV with enhanced ventricular preload and recruitment of the Frank-Starling mechanism, are associated with enhanced diastolic filling indices. In the HIIT group, favourable trends were observed for improvements in E/E' (5.41 ± 1.17 to 5.22 ± 0.89; P=0.002) and E/A ratio (1.98 ± 0.48 to 1.95 ± 0.55; P=0.027). Even though these changes were modest, all participants had normal diastolic function. However, these findings may have important clinical implications in patients with borderline and established diastolic dysfunction, due to diastolic function being a strong independent predictor of all-cause mortality (Ha *et al.* 2004).

The significant reduction in E/A ratio suggests that the myocardium is more compliant and quicker to relax following HIIT. This enables greater filling and emptying of the ventricle, demonstrated from the increase in SV and LVEDV. Improved diastolic filling is also consistent with the decrease in the isovolumetric relaxation rate following the HIIT intervention (Thomas & Weyman, 1991). A reduced isovolumetric relaxation time might be

indicative of an enhanced atrioventricular pressure gradient and may be the precursor to the enhanced left ventricular early filling, observed by the improvement in E/A ratio (Lalande & Johnson, 2008). Diastolic dysfunction is a common finding of the hypertensive heart and an independent predictor of mortality (Redfiled *et al.* 2003), thus emphasising the clinical relevance of these findings.

Further mechanisms explaining the improvements in diastolic function could be associated with factors effecting myocardial twist and deformation. Previous literature has identified reductions in cardiac torsion following a HIIT protocol (Cassidy *et al.* 2015). Research has identified that cardiac torsion describes the twisting motion of the myocardium during contraction and reflects the dominance of epicardial fibres over endocardial fibres, therefore, improvements in cardiac torsion suggest a reduction in endocardial damage following HIIT (Buckberg *et al.* 2008). It is plausible to suggest that improvements in myocardial torsion could be a mechanism for generating stored energy during systole, which is released during early diastole to produce ventricular recoil, upward annular motion and suction, enabling greater rapid filling of the ventricle (Tan *et al.* 2009).

E/E' ratio has been shown to be a non-invasive marker of left ventricular filling pressure at rest (Sato *et al.* 2017). The significant reduction in E/E' following the HIIT intervention suggests lower myocardial workload at rest. A possible mechanism explaining this adaptation is an improvement in exercise capacity. E/E' ratio has been shown to have a significant correlation with exercise capacity, namely VO_{2max} (Edelmann *et al.* 2011).

Existing research has identified significant improvements in VO_{2max} following a 2 week HIIT intervention (Astorino *et al.* 2012). This evidence could suggest significant cardiorespiratory adaptations following a short term HIIT intervention. It is therefore plausible to suggest that if VO_{2peak} had been measured in the present study, improvements alongside E/E' could have been discovered. An increase in peak aerobic capacity apparent by the significant reduction in E/E' ratio is associated with a lower risk of all-cause mortality and major cardiovascular events (Hillis *et al.* 2005). However, future research is needed to clarify these findings, as generalisation cannot be made in the present population.

Further mechanisms explaining the significant reduction in left ventricular filling pressure could be adaptations in the pulmonary, vascular or peripheral systems. Research suggests that a significant reduction in HR combined with improvements in blood pressure parameters, could indicate a significantly reduced myocardial oxygen demand (Fletcher *et al.* 2013). These

significant reductions could result in an anti-ischaemic effect which is beneficial to cardiovascular health (Fletcher *et al.* 2013).

Reductions in E/E' ratio because of improved blood pressure parameters would suggest improvements in endothelial function and sympathetic tone. Previous research has shown HIIT to be superior to traditional aerobic training programmes for improving flow mediated dilation (Ramos *et al.* 2015). It has been suggested that the sheer stress experienced during HIIT, increases the stimuli for increasing NO availability in the endothelium. As a consequence of improved flow mediated dilation, there would be greater perfusion and oxygen supply to peripheral tissue. This vasodilation because of enhanced endothelial function would indicate a reduction in systemic vascular resistance, this could potentially explain the reduction in left ventricular filling pressures and improvement in diastolic function.

Research indicates that adherence to an aerobic or HIIT program can lead to physiological adaptations in the vasculature and trigger anti-atherosclerotic adaptations (Green, 2009). A case study investigating the effect an exercise intervention had on the internal mammary artery (Hambrecht *et al.* 2003) reported an improvement in acetylcholine and adenosine-mediated blood flow, indicating enhanced function of both the conduit and resistance artery endothelium-dependant vasodilator. It was also found that there was an increase in endothelial nitic oxide synthase and shear stress-related endothelial nitric oxide synthase phosphorylation. This infers that a shear stress-dependant mechanism may result in increased nitric oxide bioactivity as a result of exercise training (Green, 2009). These findings coincide with that of Fletcher *et al.* (2013) who found that adherence to an exercise programme increases arterial wall stress, which over a prolonged period can increase dilation capacity and lumen size. This could result in enhanced myocardial compliance as a result of reduced total peripheral resistance as well as contribute to the blood pressure reductions reported.

The management and control of blood pressure is crucial for improving public health. Hypertension, is the most predominant pre-curser of cardiovascular disease and deaths globally (He & Whelton, 1997). Reductions in blood pressure lead to reduced myocardial workload and decrease the risk of major cardiovascular events. However, it can be noted that the mechanisms responsible remain unclear. It has been suggested that improvements in endothelial function, reductions in plasma renin activity and lower plasma noradrenaline are possible explanations to improvements observed at rest following exercise interventions. Further research is needed

to help understand the physiological adaptations on haemodynamic parameters following HIIT interventions.

Following the 4-week HIIT intervention, it can be noted that isovolumetric relaxation time was significantly reduced (81.23 ± 12.85 to 77.83 ± 9.81 m/s; P=0.022), compared to no significant change in the control group. Myocardial time intervals are sensitive markers of cardiac dysfunction and can identify miniscule cardiac impairments which are unrecognised by conventional echocardiography (Biering-Sørensen *et al.* 2016). Improvements in isovolumetric relaxation time indicates improved myocardial performance, as a measure of active ventricular relaxation, which further supports the notion that HIIT is beneficial to diastolic function. A reduction in isovolumetric relaxation time is associated with a lower risk of all-cause mortality and major cardiovascular events (Biering-Sørensen *et al.* 2015).

Following the HIIT intervention, adaptations at the cellular level could potentially explain reductions in isovolumetric relaxation time. Increased Ca^{2+} uptake into the sarcoplasmic reticulum results in faster relaxation rates in the myocardial cells due to improved diastolic Ca^{2+} handling in trained cardiomyocytes (Kemi *et al.* 2005; Kemi *et al.* 2008). This could potentially be recognised as an adaptation following the HIIT intervention due to the longer periods of diastole resulting in increased preload which due to the Frank-Starling mechanism increases SV, which has been shown to influence greater cardiovascular protective adaptations (Shephard & Balady, 1999).

Relative to current physical activity guidelines, the findings observed from the present study found significant improvements in resting HR, SV and diastolic function can be accomplished when completing exercise training of a shorter duration, which have been previously associated with reduced CVD risk. The 4-week HIIT intervention was a time efficient strategy to induce myocardial functional adaptations in a group exercise setting compared to a control group. This study provides evidence that individuals who cite lack of time and motivation could benefit from a training programme similar to the present study. In relation to health, the clinical importance of these findings is significant as HR (Aune *et al.* 2017) and diastolic function (Sato *et al.* 2017) are independent predictors of CVD and as little as 4 weeks of HIIT observed in this study produce significant improvements in these markers.

The findings from the present study highlight the possibility for short-term HIIT programmes as effective strategies for improving health. However, as the present study was only a short term HIIT intervention and had 4 drop outs, it is unknown whether adherence to long-term

HIIT interventions is sustainable. However, previous research has found that drop-out rates in a HIIT programme tend to be lower compared to traditional aerobic training programmes (Heydari, Boutcher & Boutcher, 2013). The findings from the present study demonstrate important clinical evidence in regards to HIIT frequency (3 days per week), low volume per session (3 x 30 seconds), low active recovery (2 minutes) and short-term duration (4-weeks) in a young population with pre-hypertension. It can be concluded that the significant improvements found from the present study identify a need for the current physical activity guidelines to adapt to allow for a potentially greater exercise adoption and adherence from the wider population.

4.3: Limitations

This study is not without limitation. In regards to the study population, it could be suggested that stress and anxiety from the student lifestyle and university assessments may have had an influence on a variety of variables measured throughout. In addition, there were no dietary recommendations, measurements of alcohol consumption or measurements of physical activity outside of testing throughout the duration of the study which could possibly affect the results. Participants were instructed to abstain from any structured exercise outside of the study and to maintain their normal daily living, however, this was not measure or recorded just confirmed verbally.

Previous research investigating HIIT and cardiac structure and function in a young, physically inactive population is limited and can be considered equivocal, making the results difficult to generalise to a larger population. In the present study HIIT produced significant changes in myocardial compliance and diastolic function. Therefore, future research in young, physically inactive populations should consider utilising this protocol in order to make comparisons and decisions on its clinical effect.

It is also possible that due to the HIIT being performed in a group environment, this may have influenced the engagement, enjoyment, improved adherence and maximal effort produced from the participants within the study. HIIT performed in isolation may have affected adherence and training intensity, which may affect physiological adaptations.

Due to the control group receiving no treatment it may be suggested that there is a potential for nocebo effects to take place. Future research may benefit from developing strategies to mitigate its impact on research findings and clinical practice.

The mechanisms responsible for the changes observed following the HIIT intervention are complex and likely multifaceted. It is possible that the use of blood tests to measure blood plasma volume and other important biomarkers could be used to ascertain potential mechanisms supporting physiological adaptation. The use of VO_{2peak} testing could have also been useful for measuring cardiorespiratory adaptations. The use of blood tests was unavailable for the present study due to lack of training and VO_{2peak} was not measured due to lack of research time. In addition, methods used to assess vascular function may have supported the observed improvements in myocardial function.

4.4: Conclusion

The findings of the present study demonstrate that a 4-week HIIT programme can significantly improve diastolic function and reduce resting blood pressure when compared against a control group. These findings support HIIT as a time-efficient strategy to induce significant adaptations in cardiovascular health. Therefore, the null hypothesis is rejected. Continued engagement in regular physical activity is required to maintain and/or produce chronic adaptations from exercise, as well as limiting cardiovascular risk factors and all cause morality. As such, future research is required to ascertain the long-term physiological responses and adaptations to HIIT compared to alternative exercise training interventions. Longer-term HIIT interventions may provide evidence to support this method of exercise training in future guidelines for the prevention of numerous chronic diseases.

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6.0: Appendix.
6.1: Appendix 3- Physical Activity Readiness Questionnaire (PARQ)

Department of Sport Science, Tourism and Leisure

Sport Science Informed Consent & Health and Fitness Questionnaire

Name: ………………………………………………….

Date of Birth: ………………   **Age: ………**   **Sex: ….……**

Please answer the following questions by *circling* the appropriate response and if necessary providing extra information in the spaces provided.

ANY INFORMATION CONTAINED HEREIN WILL BE TREATED AS CONFIDENTIAL

1. How would you describe your present level of fitness?

Untrained / Moderately trained / Trained / Highly trained

2. Average number of hours spent exercising   **………….…………per wk**

3. How would you describe your present bodyweight?

Underweight / Ideal / Slightly overweight / Very overweight

4. How would you describe your smoking habits?

Non smoker / Previous smoker / Currently smoking

5. How would you describe your alcohol intake?

Never Drink / An occasional drink / A drink every day / More than one drink a day

  (Note 1 drink = 1 unit)

6. Have you had to consult your doctor within the last six months?   **Yes**

  / No

If you have answered **yes**, please give details:**………………………………………….**

7. Are you presently taking any form of medication? **Yes / No**

   If you have answered **yes**, please give details:

   …………………………………………

8. Do you suffer or have you ever suffered from any of the following?

   a. Diabetes   **Yes / No**   b. Asthma   **Yes / No**

   c. Epilepsy   **Yes / No**   d. Bronchitis   **Yes / No**

   e. Any form of heart complaint **Yes / No**   f. Serious Back or Neck Injury **Yes / No**

   g. High blood pressure   **Yes / No**   h. Aneurysm [1] or Embolism[2] **Yes / No**

   1: Arterial wall weakness causing dilation.   2: Obstruction in the Artery.

9. Is there a history of heart complaint in your family?

   Yes / No

   If you have answered **yes**, please give details:

   …………………………………………

10. Do you have any allergies?

    Yes / No

    If you have answered **yes**, please give details:

    …………………………………………

11. Do you currently have any form of muscle or joint injury?

Yes / No

If you have answered **yes**, please give details:

……………………………………………………

12. Have you had to suspend your normal training/physical activity in the last two weeks?

Yes / No

If you have answered **yes**, please give details:

……………………………………………………

6.2: Informed Consent

The full details of the tests have been explained to me. I am clear about what will be involved and I am aware of the purpose of the tests.

I know that I am not obliged to complete the tests. I am free to stop the test at any point and for any reason.

The test results are confidential and will only be communicated to others such as my coach if agreed in advance.

As far as I am aware, there is nothing that might prevent me from successfully completing the tests that have been outlined to me.

Signature of Participant: …………………………………………..

Signature of Sport Scientist: …………………………………..

Date: …………………