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CHAPTER TWO: PHYSICAL ACTIVITY FOR CARDIOVASCULAR DISEASE

Contents

Overview	<i>L</i>
The Cardiovascular System	2
Pathophysiology of Cardiovascular Disease	
Cardiac Rehabilitation	6
Cardiac Exercise Physiology	7
Exercise and Secondary Cardiac Events	12
Psychological Health and Quality of life	13
Physical Activity in Cardiac Rehabilitation	15
Future Research in Cardiac Exercise Rehabilitation	20
Summary	26
References	26

Overview

Cardiovascular disease (CVD) is the greatest cause of morbidity and premature mortality in western society and is an umbrella term for a number of disorders, including coronary artery disease, heart failure, valvular disease, peripheral vascular disease and stroke. The UK has seen a reduction in the mortality of CVD, mainly due to the advancement of medical care and surgical interventions, but also as a result of alteration in lifestyle risk factors of patients following diagnosis through cardiac rehabilitation activities. This chapter will focus on the role of physical activity in the rehabilitation of those diagnosed with a cardiac condition.

The Cardiovascular System

The heart consists of four chambers, the 'upper' right and left atrium and the 'lower' right and left ventricles. Valves between the upper and lower chambers ensure the one directional flow of blood. Both atrium contract at approximately the same time, as do both ventricles, ejecting blood out of the heart ensuring effective blood flow to the pulmonary (right side of the heart) and systemic circulation (left side of the heart). The heart muscle, the myocardium, receives its supply of blood and nutrients via the coronary arteries, which form part of the coronary circulation. The coronary circulation emerges at the root of the aorta, distributing blood and oxygen to the myocardium, with deoxygenated blood returned to the right atrium via coronary veins. The two main coronary arteries

are the left (otherwise known as the left main stem) and right coronary artery, each serving the left and right side of the heart respectively. The left artery further divides into the left anterior descending artery (LAD) and the circumflex artery (Cx), supplying blood to different regions of the myocardium. For a more in depth discussion of cardiovascular physiology consult Levick (2009).

Pathophysiology of Coronary Artery Disease

Atherosclerosis

Atherosclerosis is the term used to describe the changing physiology and structure of the arterial wall which results in endothelial dysfunction and causes the narrowing of the arterial lumen. The complex process of atherosclerosis is slow and progressive and symptoms do not usually present until the artery is more than two-thirds blocked. Two mechanisms can occur that clinically exacerbate the process: either the narrowing (stenosis) is such that blood flow to that area of the myocardium is reduced and the flow cannot meet the demands for oxygen; or the plaque can rupture, leading to platelet aggregation, which subsequently can then either further occlude the artery, or break off (embolus), travel downstream and impede blood supply.

Risk factors that may contribute to the development of atherosclerosis are uncontrolled Type II diabetes, physical inactivity, smoking, stress, hypertension and dyslipidaemia. The initial stages of the process have been found in children and can potentially occur in any of the arteries of the body, but it is commonly found in the coronary arteries (coronary heart disease, CHD), the arteries of the head and neck (cerebrovascular disease or stroke) and the peripheral (leg) arteries (peripheral

vascular disease, PVD), the latter causing leg pain when exercising. It is possible for one artery to have multiple atherosclerotic lesions.

Acute Coronary Syndrome

Angina pectoris is the pain sensation caused by ischaemia to the myocardium due to a partially blocked artery. These symptoms disappear with rest (oxygen demand decreases) or use of a prescribed nitrate spray (inducing dilation of coronary blood vessels). Stable angina refers to symptoms that are predictable, for example during exercise at a known intensity, or after a heavy meal. Unstable angina has no pattern and can occur at any time, even at rest and is an absolute contraindication for exercise.

A myocardial infarction (MI) is caused by the same atherosclerotic process as angina, but refers to the death of the myocardium caused by restriction of oxygen (ischaemia). The term acute MI is given to a sudden episode of complete stenosis that precipitates myocardial damage. MI can be further classified according to which coronary artery has been occluded, for example an Anterior MI (the anterior site of the left ventricle) will result from blockage of the left anterior descending artery (LAD); an occlusion in the right coronary artery will result in an inferior MI (the inferior heart wall).

Symptoms of ischaemia may include pain, shortness of breath, sweating, confusion and nausea, although patients can experience a 'silent MI' where no signs or symptoms are present – common with those with diabetes due to autonomic neuropathy. The range of symptoms differs widely

between individuals. However, with an MI symptoms do not resolve with rest. If an MI is suspected, medical attention should be sought immediately, with the aim of restoring blood flow to the myocardium by removing the blockage with thrombolytic medication or surgical procedure (percutaneous coronary angioplasty [PCI], or re-establishing blood supply with a coronary artery bypass graft [CABG]).

Diagnostic testing following a coronary event may include;

- ➤ Testing of biochemical (enzyme) markers, for example troponin and creatinine kinase.

 Levels of these biomarkers will typically rise following MI and remain raised for several days.
- ECG (electrocardiogram) monitoring. In the days or weeks following MI, some patients may be required to undergo an ECG stress test that usually involves an incremental bout of exercise (e.g. walking on a treadmill) while attached to an electrocardiogram (ECG) monitor. This procedure examines how the heart responds to exertion, and identifies areas of the heart experiencing ischaemia, indicated by changes in the ECG trace (ST elevation or depression).
- ➤ Coronary angiogram, which is an x-ray procedure using intravenous dye into the coronary arteries to determine extent of atherosclerosis and stenosis.
- > CT (computerized tomography) or MRI (magnetic resonance imaging) to determine the extent of myocardial damage.

Chronic Heart Failure

The term chronic heart failure (CHF) refers to the inability of the heart to effectively deliver blood around the body, often due to valvular disease, a large MI or multiple smaller MIs having damaged extensive areas of the myocardium. When the heart is unable to maintain its ability to pump, cardiac output decreases and congestion can develop within the circulatory system. Symptoms of heart failure include peripheral and pulmonary oedema and shortness of breath.

For a more comprehensive discussion of cardiovascular pathophysiology consult Sheppard (2011).

Cardiac Rehabilitation (CR)

CR is a multi-faceted, professionally supervised intervention that aims to improve the health and well-being of cardiac patients. CR usually consists of a 6-12 week programme of exercise, education, psychological support, behavioural change and medical risk factor management. In the UK there are currently over 300 CR programmes that are audited by the National Audit of Cardiac Rehabilitation (NACR).

The multi-disciplinary team may include the following health professionals:

- Cardiologist
- Cardiac specialist nurse
- > Exercise physiologists/specialist
- Dietician
- > Psychologist or other mental health specialist
- > Pharmacist
- > Physiotherapist

Occupational therapist

Benefits of exercise-based cardiac rehabilitation:

- ➤ 13-26% reduction in all-cause mortality
- ➤ 26-46% reduction in cardiac mortality
- ➤ 23-56% reduction in hospital re-admission
- > Cost-effective intervention
- > Improved quality of life
- Improved functional capacity
- > Supports early return to work
- Empowers the development of self-management skills

 (Davies *et al.*, 2010; Heran *et al.*, 2011; Lawler *et al.*, 2011; NICE, 2008; Papadakis *et al.*, 2005; Taylor *et al.*, 2004; Yohannes *et al.*, 2010)

The British Association for Cardiovascular Prevention and Rehabilitation (BACPR) suggest seven core components that should be included within CR in order to ensure a competent, cost effective and clinically-effective service (BACPR, 2012), see figure 2.1.

Figure 2.1

Cardiac Exercise Physiology

Exercise Effects on Physical Fitness

Cardiorespiratory fitness (CRF) is an independent risk factor of cardiac mortality in men and women with CVD. Patients possessing low CRF are 2 to 5 times more likely to die than those patients with higher CRF (Franklin & McCullough, 2009). The research of Martin et al. (2013) found for every 1-MET increase in patient CRF after a 12 week training programme was associated with a 13% point reduction in mortality, but 30% point reduction in those who started with lower CRF. The clinical effectiveness of CR can be clearly reflected by increases in VO_{2peak} , as CRF is not influenced by pharmacological intervention, unlike blood lipid profiles or blood pressure measurements (Hansen et al., 2010). Generally, most studies report increases in VO_{2peak} following training, with increases ranging from 2% - 78% (Hansen et al., 2005). Gender, age or βadrenoceptor antagonist (β-blocker) use do not seem to influence potential increases in VO_{2peak} (Balady et al., 1996; Pavia et al., 1995). However, some patients cannot increase their VO_{2peak} through exercise, with possible explanations including: a high baseline VO_{2peak}, the presence of a hibernating myocardium, or the exercise stimulus was insufficient to stimulate a training response (Hansen et al., 2005). Research evidence suggests that the exercise dose in some UK CR programmes is too limited to significantly influence key patient outcomes, such as physical fitness and mortality, and challenges the efficacy of contemporary exercise CR interventions (Sandercock et al., 2013a). This should provide the stimulus for CR programmes to review their exercise component and ensure it delivers an effective intervention according to recommended guidelines, particularly in terms of exercise intensity. Due to changes in service commissioning, measurable patient outcomes may become necessary to evaluate and provide evidence of measurable patient outcomes; exercise capacity is an outcome with potential global benefit to a range of cardiac patients, and a metric that can be easily captured. CR programmes should also aim to encourage

broader engagement in domestic, occupational and recreational physical activities outside formal delivered CR exercise sessions. This should reinforce the need to engage in a physically active lifestyle, not just one to two structured exercise sessions per week, and avoid sedentary behaviour.

Patients with CVD who were randomised to long-term moderate exercise training (n = 48) significantly increased VO_{2peak} by 18% (P \leq 0.001) and decreased resting heart rate (P \leq 0.01) compared to a sedentary control group (n = 46) (Bellardinelli *et al.*, 1999). Other studies have found 17% (Giannuzzi *et al.*, 2003) and 29% (Gielen *et al.*, 2003) improvement in VO_{2peak} compared to control groups, with either no detrimental effect on left ventricular re-modelling, or attenuating abnormal re-modelling. Physiological adaptations have resulted in improved exercise tolerance, reflected in a 20% increased walking distance in the 6-minute walk test, increased quality of life measures, and fewer hospital re-admissions (Giannuzzi *et al.*, 2003).

More recent studies have also found improvement in VO_{2peak} of 2.06 mL·kg⁻¹·min⁻¹ (Van Tol *et al.*, 2006) and 2.7 mL·kg⁻¹·min⁻¹ (Chien *et al.*, 2008), which are clinically significant since VO_{2peak} decreases by ~0.14 ml·kg·min⁻¹ yearly in patients with heart failure after the age of 40 (Forman *et al.*, 2009). Furthermore, those with a VO_{2peak} <15 mL·kg⁻¹·min⁻¹ are at the greatest risk of mortality but an increase of 1 mL·kg⁻¹·min⁻¹ in an individual's VO_{2peak} was associated with a 15% decrease in the risk of mortality, indicating how important even marginal improvements in CRF can be (Keteyian *et al.*, 2008).

Besides improvements in maximal exercise capacity, favourable adaptations in submaximal measures can be gained following exercise, such as increased exercise time, ventilatory threshold

and quality of life in patients with CHF (Wielenga *et al.*, 1999a). The potential improvements in functional capacity in older adults with CHF can be under-estimated, given the age-related decline in physiological function experienced with advancing age. Although patients with CHF aged >65 years old do not increase their VO_{2peak} to the same extent as those aged <65 years old, clinically significant improvements can still occur (Wielenga *et al.*, 1999b). Older patients with CHF aged 75-90 years significantly improved 6 minute walk test distance (6MWD) by over 40m, representing a 20% increase in distance walked, following a 12 week tailored exercise programme (Owen & Croucher (2000). Whilst many research studies have indicated favourable outcomes following exercise interventions, more work is still needed around interventions across a diverse demographic of the cardiac population. (Lloyd-Williams *et al.*, 2002).

Exercise Effect on Cardiac Function

As exercise capacity should improve following an exercise regime, a number of physiological adaptations occur, especially to cardiac functional capacity, reflected in an increased cardiac output during maximal symptom-limited exercise (Hansen *et al.*, 2010; Hambrecht *et al.*, 1995). Haykowsky *et al.* (2007) found significant improvements in left-ventricular ejection fraction, end diastolic volume and end systolic volume when aerobic training was performed. These cardiac adaptations may contribute to the reduction in secondary cardiac events and mortality rates associated with exercise participation.

Although many arrhythmias of the heart are not life-threatening, some can lead to cardiac arrest. Heart rate variability (HRV), the variation in time between R-R intervals (the time interval between ventricular contractions), can be used as a key predictor of secondary events (Tsuji *et al.*, 1994).

Exercise training within CR has been shown to enhance patients' HRV, thus lowering maximal and resting heart rate (HR). When HR is high, there is an increased risk of arrhythmia (Rennie *et al.*, 2003). A reduction in patients' resting and exercise HR has been associated with arterial remodelling and adaptation in the cardiorespiratory centre, providing cardio-protective mechanisms to reduce sympathetic drive and enhance parasympathetic outflow (Nelson *et al.*, 2005).

Exercise Effects on Vascular Function

A decrease in vasoconstriction of blood vessels, both at rest and during exercise, can reduce hypertension, a key risk factor for CVD (Graham et al., 2007). The endothelium produces numerous vasoactive substances, including nitric oxide (NO), which are crucial anti-atherogenic mediators, but may precipitate CVD when they become dysfunctional (Green et al., 2008). The benefit of exercise-based CR upon endothelial function appears to be a crucial factor in secondary prevention and management of risk factors, as impaired endothelial function inhibits redistribution of blood flow, thus potentially limiting oxygen delivery to the exercising muscles (Maxwell et al., 1998). Improvement in endothelial function increases the ability of the cells to respond to varying vascular conditions and exercise training seems to confer a degree of vascular conditioning, providing a cardioprotective benefit (Green et al., 2004; Green et al., 2008). Exercise-based CR has been shown to directly benefit the coronary vasculature through improved endothelial function to meet MVO₂ more effectively (Green et al., 2004). CR exercise provides the potential to induce a training adaptation in endothelial function and thus preferential redistribution of blood flow to the working muscles during exercise. This may mean the cardiac patient may improve exercise tolerance (Demopoulos et al., 1997; Maxwell et al., 1998).

Exercise-based CR, incorporating both large and small muscle groups (cardiovascular and muscular strength endurance exercises) decreases vasoconstriction in response to a vasoconstrictor stimulus (Hambrecht *et al.*, 2000). This leads to an improvement in NO vasodilator function, increasing blood flow to exercising limbs, which in turn enhances the peak vasodilatory capacity of the vasculature (Green, *et al.*, 1996).

Exercise and Secondary Cardiac Events

Cardiac Mortality

CVD is progressive and there is a strong likelihood of a secondary cardiac event through weakening of the structure and function of the heart (Van Stel *et al.*, 2012; Leon *et al.*, 2005). Vigorous physical activity in individuals unaccustomed to such exertion may disrupt unstable atherosclerotic plaques, causing vasospasm rather than vasodilation, triggering the onset of an MI (Mittleman *et al.* (1993). However, exercise can significantly reduce the occurrence and severity of a secondary cardiac event (Artham *et al.*, 2008; Lavie & Milani, 1997). A Cochrane review of 47 studies determined that exercise reduces the mortality rates of cardiac patients yet found no significant relationship between the overall physical activity dose of the exercise programme (session intensity, frequency and duration of individual sessions), and mortality rates (Heran *et al.*, 2011). Secondary MIs were reduced by 25% in a sample group of 4554 participants (O'Connor *et al.*, 1989) and a 27% reduction in secondary cardiac events in 8440 participants following CR (Jolliffe *et al.*, 2001). Furthermore, after 14 years of follow-up those that attended CR had a 58% lower mortality risk than those who did not attend (Beauchamp *et al.*, 2012). This demonstrates

the value of attending a CR programme and that lifestyle change can potentially contribute to quality of life and survival.

Not only do mortality rates among patients with CVD decrease with exercise training, the number of hospitalisations also reduced (Davies *et al.*, 2010). Following the completion of 16 exercise sessions over the course of 8 weeks, 10.6% of the exercise group was admitted to hospital compared to 20.2% of the non-exercising control group within 24 weeks after completion of training (Austin *et al.*, 2005). Furthermore, those in the non-exercise group had more multiple admissions and remained in hospital longer. A meta-analysis of the effects of the exercise component of CR found significant reductions in hospital admissions when a study with poor adherence was excluded from the analysis (Davies *et al.*, 2010). In a multi-centre trial of 2331 patients with CVD, found that 759 patients in the exercise group were hospitalised or died, compared to 796 patients in the control group (O'Connor *et al.*, 2009). This suggests that involvement in exercise may influence patient survival, however, these findings need to be treated with caution since only 30% of the exercise group completed all of the prescribed exercise, whilst 8% of the control group increased their physical activity levels.

Psychological Health and Quality of life

Health problems associated with CVD are not just physical, as anxiety and depression have a negative inter-relationship with patient cardiovascular health, patient outcomes such as quality of life, and potentially increase mortality (Carney *et al.*, 1999; Rozanski *et al.*, 2005; Stein *et al.*, 1995). Anxiety and/or depression can also adversely affect patient recovery (Lavie *et al.*, 2009). Patients who attended CR had a 40-70% decrease in anxiety and depression along with a 70%

decrease in mortality risk (Lavie *et al.*, 2009). Since CR can potentially provide a supportive social setting for exercise, some of the psychological benefits may accrue from exposure to this environment, not just the physicality element of exercise. Attending CR sessions does place patients within an 'exercise and health-promoting environment' and increases their opportunities to increase physical activity levels. Although patients gain functional improvements through exercise, they often report that the most noticeable benefits of CR are psychosocial in nature. This has implications for CR delivery, as individualised exercise programmes may be insufficient to improve psychological health, and potentially quality of life (Ades, 2001; Chien *et al.*, 2008).

Multidisciplinary CR, including education, individual therapy and group workshops, has been shown to decrease both anxiety and depression, however this is not routinely provided by all CR programmes (Child *et al.*, 2010; British Heart Foundation, 2013). However, exercise can still prevent depression and is therefore valued as an important psychosocial support mechanism compared to other interventions (Rozanski *et al.*, (2005). Exercise for post-MI patients can increase their wellbeing, confidence and happiness, as well as decreasing depression and anxiety (Taylor *et al.*, 1986).

A meta-analysis of 3647 participants from 19 studies of exercise-based CR reported that all studies found an improvement in quality of life (Davies *et al.*, 2010), with one study in particular finding an average improvement of 9.7 points, using the Minnesota Living With Heart Failure questionnaire (MLWHF) (Van Tol *et al.*, 2006). Such improvements are also experienced relatively consistently across sex, age, race and other sub-groups with 54% of those in exercise-based CR demonstrating clinically noticeable improvements in quality of life compared to only

29% of a non-exercise control group (Flynn *et al.*, 2009). Improvements in quality of life scores have been closely correlated with improvements in 6MWD following high intensity training, which may reflect improved endurance capability during active daily living (Nilsson *et al.*, 2008). Physical attributes associated with improved quality of life following CR include improved physical function, energy availability, body pain and exercise tolerance (Lavie & Milani, 1995; Saeidi *et al.*, 2013; Marchionni *et al.*, 2003).

Physical Activity in Cardiac Rehabilitation

Is Exercise in Cardiac Rehabilitation Safe?

There are potential risks with vigorous physical activity. It is known to trigger cardiac complications, as up to a fifth of all MIs are induced after physical exertion (Fletcher et al., 2001). However, in a CR context, these risks are relatively low due to the emphasis on moderate intensity effort. Cardiac mortality has been reported as 0.61 per 100,000 hours of exercise in CR programmes (Fletcher *et al.*, 1996). Similarly low incident rates have been reported elsewhere, with figures ranging from 1 cardiac event in 50,000 patient exercise hours, to 1 in 120,000 hours, with a reported 2 fatalities within 1.5 million hours of exercise (Franklin *et al.*, 1998; Thompson *et al.*, 2003). As the benefits of exercise are widely reported, it is understandable that doctors and health care professionals consider the benefits outweigh the risks. The relatively small numbers of MIs that are experienced during or after vigorous exercise, the majority of these are seen in those who are unaccustomed to this type of activity and whose cardiac profile is undiagnosed (Hambrecht *et al.*, 2000).

Patients with known CVD are initially risk stratified and then supervised during CR exercise sessions. With the 4-stage structure of cardiac rehabilitation in the UK, patients do not graduate to the next phase until it is deemed medically safe. In addition, most cardiac rehabilitation exercise is most likely pitched at a moderate intensity (3 – 6 MET range) to conform to recommended guidelines (Sandercock *et al.*, 2013b); so the risk of a fatal cardiac related event is significantly reduced.

The recommended hierarchy of MET thresholds for risk stratification are: low risk (> 6 METs capacity 3 or more weeks following clinical event), moderate risk (5 - 6 METs 3 or more weeks following clinical event) and high risk patients (< 5 METs) (AACVPR, 2004; ACPICR, 2015).

Establishing appropriate MET thresholds for exercise intensity in CR can be a challenge, especially when there is restricted access to comprehensive cardiovascular testing data. Guidelines for appropriate exercise intensities are usually based upon % VO_{2max}, %HR_{max}, %HRR or %VO_{2reserve} (VO₂R). For the majority of CR patients estimates of exercise intensity have to be made based upon theoretical calculations, such as %HR_{max} or %HRR (Franklin & Fardy, 1998). But these are at best only estimates and there is considerable variability in these methods (Achten & Jeukendrup, 2003; Miller et al. 1993).

Aerobic Exercise Training

The British Association of Cardiovascular Prevention and Rehabilitation (BACPR, 2012) describes the aim of cardiac rehabilitation (CR) as a means to encourage patients to regain full

physical, psychological and social status and ultimately slow, or even reverse the progression of CVD (Fletcher *et al.*, 2001). Structured physical activity is regarded as the cornerstone component of CR, not only to help re-establish function, but also to address low physical fitness as a precursor for CVD (BACPR, 2012; Fletcher *et al.*, 1996; Piepoli, *et al.*, 2010). Physical activity has been known as a therapeutic intervention for disease since ancient times, but neglected until 1772 when William Heberden reported wood sawing as a cure for angina pain. However, the incorporation of exercise rehabilitation into contemporary CR programmes is a more recent phenomenon (Balady *et al.*, 1994). The aim of CR is to encourage exercise independence and to return the patient to occupataional, or recreational activities (Pescatello *et al.*, 2014).

Aerobic exercise forms the primary component of CR and tends to be delivered as a circuit training format (Association of Chartered Physiotherapists in Cardiac Rehabilitation [ACPICR], 2015). This mode of training allows for easy adaptation, the potential for a more social environment (exercise group format) and due to its intermittent nature, facilitates recovery breaks between exercise bouts. This provides a format that suits an older clinical population, allowing them to recover their breath and not over-work one specific part of the body, by alternating cardiovascular (CV) exercise bouts with muscular strength and endurance activities (MSE) as an active recovery. Improvements in aerobic endurance and musculoskeletal strength have been demonstrated following a period of moderate intensity circuit training, without causing any cardiovascular complications (Kelemen *et al.*, 1986).

Interval vs Continuous Aerobic Training

Interval training prescribed in isolation, or combined with MSE training (which is often the typical CR exercise format) has been shown to provide clinically significant adaptations in cardiac patients, and potentially more beneficial than moderate continuous intensity CV training (MCT) (Cornish *et al.*, 2011). Wisloff *et al.* (2007) reported a 46% improvement in peak oxygen uptake (VO_{2peak}) among an interval training group, compared to a substantially smaller 14% increase in a continuous training group, with concomitant less tedium reported. More recently Mohdolt *et al.* (2012) completed a similar study finding a larger improvement in VO_{2peak} in an interval training group against a continuous training group. When comparing 4 interval training protocols, a period of 30 seconds of exercise, followed by a passive recovery, was found to be safest and enabled exercisers to operate above 85% of their VO_{2peak} with no adverse effects reported (Meyer *et al.*, 2012). Normal operating CR procedures encourage active recovery period to reduce the risk of a sudden drop in blood pressure, which could occur due to blood pooling in the legs during inactive periods, and a side-effect of anti-hypertensive medications.

Resistance Training (RT)

Besides the obvious strength gains, the benefits of RT go further by also improving muscular endurance, metabolism and CVD risk factors, such as reduced blood pressure, as well as enhancing cardiovascular function and exercise capacity (Pollock *et al.*, 2000). RT has been shown to increase other aspects of health including: functional independence, self-efficacy and quality of life (Bjarnason-Wehrens *et al.*, 2004; Cornelissen & Fagard, 2005; Fletcher, 2001; McCartney, 1998; Williams *et al.*, 2007). Bjarnason-Wehrens *et al.* (2004) reported no increased risk of cardiovascular events in RT compared to CV. The physical adaptations seem to benefit the heart directly as the rate pressure product (RPP) has been shown to decrease when muscle strength has

improved (Parker *et al.*, 1996). This is important to the cardiac patient as RPP is an indirect measurement of myocardial workload (MVO₂), combining heart rate (HR) and systolic blood pressure (SBP), calculated using the following formula: RPP = HR x SBP. This measurement takes into account not only the rate of myocardial contraction but also force of contraction (afterload). RT adaptations therefore could lead to a decrease in myocardial oxygen demand (MVO₂) during activities of daily life. For example carrying groceries, or completing DIY jobs will be easier and there will be less risk of exceeding the ischaemic threshold of CVD patients (Pollock *et al.*, 2000).

Heavy RT is not advised immediately after cardiac surgery as it may lead to further complications, such as osteomyelitis, and re-opening of surgical wounds, (Williams *et al.*, 2007; Pollock *et al.*, 2000). Consequently, implementation of RT should be delayed until patient's condition permits safe engagement (usually 4-8 weeks post-surgery, or until able to exercise >5 METs), but should be incorporated as a core component of physical conditioning (Williams *et al.* 2007). Bjarnason-Wehrens *et al.*, (2004) did acknowledge the risks of increasing blood pressure during resistance exercise with cardiac patients. Blood pressure increases depend on load intensity, the muscle mass engaged, and the nature of the repetitions performed. Therefore, correct technique and supervision may be necessary, as well as appropriate screening of cardiac patients, their cardiac stress tolerance and clinical status (Bjarnason-Wehrens *et al.*, 2004), to ensure safety during RT exercise. Breath holding, or the Valsalva manoeuvre (attempting to exhale against a closed glottis), should be avoided (Wise & Patrick., 2011).

One of the main concerns with RT is with elevations in blood pressure, which may relate to the nature of the muscle contraction. Dynamic exercises tend to be favoured over static (isometric)

contractions (Bethell, 1999). Isometric exercises are not recommended, due to the potential adverse blood pressure response associated with them (Fletcher *et al.*, 1996; Wenger, 2008). However, performing isometric muscular work is unavoidable when carrying objects or lifting, such as shopping or children, and when performing many active daily living tasks, such as DIY or gardening. Some researchers have found beneficial effects from isometric exercise (McCartney *et al.*, 1991). However, it is safer to teach patients to regulate their breathing if isometric actions cannot be avoided.

Combining CV and RT-based training in exercise programmes appears to be optimum. Smart and Marwick (2004) systematically reviewed studies on patients with CHF. These indicated positive trends of survival rates, along with improved functional capacity and reduced cardiorespiratory symptoms, after a combination of supervised CV and RT. Current guidelines recommend that an exercise regime for cardiac patients incorporate both CV and RT exercises (ACPICR, 2015; Fletcher *et al.*, 2001). This approach has been shown to attenuate the loss of skeletal muscle, which can lead to reductions in basal metabolic rate, and therefore contributing to long term weight management and health - particularly important in an older patient demographic (Bryner *et al.*, 1999). Improvements in muscle strength and overall functional capacity occur due to a combination of these exercise modalities, supporting a more active lifestyle and potential improved quality of life (Hansen *et al.*, 2010).

Future Research in Cardiac Exercise Rehabilitation

High Intensity Training (HIT)

There is a growing interest amongst health professionals in the role of high intensity exercise training (HIT) in CR, both in terms of catering for younger cardiac patients, but also striving to achieve optimal health benefit (Sandercock et al., 2013b). HIT involves exercise bouts of usually < 300 seconds at > 70% VO_{2peak} or > 90% peak heart rate (or RPE > 15), interspersed with bouts of lower intensity exercise, or active recovery. This mixture of work and recovery periods allows more intense exercise to be tolerated before fatigue, and potentially in time, results in better tolerance to fatigue and greater benefit to the patient, due to the higher intensity workloads. The intensity of exercise matters in terms of outcomes and whilst there are many variations of HIT, early research indications suggest it is safe for a CR population with stable CVD to engage in this training, and are performing it under controlled conditions. Rognmo, et al. (2004) found significantly superior improvements in VO_{2peak} following HIT (17.9%) than in the conventional moderate intensity approach (7.9%). There were no significant changes in other health outcomes, for example resting heart rate, blood pressure or body mass. An exercise based CR programme, consisting of repeated 15 second phases of exercise at 100% peak power output, improved health outcomes in stable CVD patients. However, 35% of the group reported exercise-induced ischemia (Guiraud *et al.*, 2009), although it was not prolonged.

It is difficult to compare the relative risk of different forms of exercise training, however the rates of cardiac complications to the number of patient-exercise hours were 1 (fatal cardiac arrest) per 129,456 hours of moderate intensity exercise and 1 (non-fatal) per 23,182 hours of HIT (Rognmo *et al.*, 2012). Both statistics suggest that exercise, at moderate – high intensity presents a small and manageable risk of an adverse event occurring.

Cardiac patients are a heterogenous population (Van Camp *et al.*, 1994), therefore although these patients may 'tolerate' the HIT, other patients may experience difficulties maintaining high workloads, or have poor exercise adherence due to low tolerance of the exercise regime. This highlights the need for further investigation to gain a better understanding into the nature, scope and tolerability of HIT for CVD patients.

Exercise Adherence

The potential benefits of exercise will only be realised through continued participation, so adherence to exercise programmes is fundamental to improved health outcomes. Due to the low uptake of CR both in the UK and the USA (UK ~44% [British Heart Foundation, 2013]; USA <40% [Keteyian et al., 2012]), research needs to focus on increasing the number of eligible patients being referred for CR and promoting long-term exercise adherence. One study found that of the 30% of eligible patients referred to CR only one third still attended CR after 6 months (10% overall) (Daly et al., 2002). This does not necessarily mean these patients are not exercising, just that they are not exercising in a formal CR setting. However, the main factors that were reported for the lack of adherence included a lack of social support, motivation and commitment (Daly et al., 2002). Tracking physical activity levels beyond Phase III CR is not currently catered for in the NACR. This should be considered a priority to determine the longer term impact of CR on physical activity behaviours and patient outcomes. Methods of promoting 'graduation' from phase III to phase IV CR exercise programmes should also be explored, including patient-exercise instructor relationships and effective referral pathways.

Case study of cardiac rehabilitation participant

On presentation at the cardiac rehabilitation programme (6 weeks post cardiac event);

Name: Caroline

Age: 61

Cardiac event: Anterior MI – primary PCI (LAD)

Height (cm): 163

Body mass (kg): 86.4

BMI ($kg \cdot m^2$): 32.5

BP (mmHg): 120/80

Resting pulse (bpm): 66 & regular

Total cholesterol (mmol·L⁻¹): 6.1 /TC/HDL-C ratio 4.4

Past medical history: Hypertension, palpitations

Medication: Aspirin 75mg, Clopidogrel 75mg, Citalopram 20mg, Bisoprolol

2.5mg, Atorvastatin 80mg, Ramipril 5mg, GTN spray

Risk factors present post diagnosis	Yes	No	Risk details, level and
			action plan

Family CHD history (1st degree relatives	✓		Father MI aged 66 years
less than 55 yrs old)			
Personal CHD history		✓	
Diabetes		√	
Current smoker		√	
Ex-smoker	√		Stopped 1 / 12 ago
Cholesterol	✓		Total 6.1, ratio 4.4
Hypertension		✓	119/70
BMI>30 or > waist circumference	√		Height 163cm, weight 86.4kg, BMI 32.5
Exercise		√	Brisk walk 90 mins 4 + per week
Stress	√		Husband recently diagnosed with lymphoma
Alcohol		✓	> 2 units per week

The cardiac rehabilitation intervention;

- 12 week programme of exercise
- 2 x 1 hour sessions per week of interval (circuit) based exercise prescribed according to evidence based guidelines
- Daily walking programme commenced (home)
- Referral to cardiac counsellor
- Goal setting
- 12 weekly lifestyle sessions
- Up titration of medication

Outcome measure	Pre rehabilitation	Post rehabilitation
Weight (kg)	86.4	82.3
BMI	32.5	31
Waist circumference (cm)	101cm	95cm
ISWT score (metres)	260	340
Cholesterol TC	Total 6.1mmols	Total 4.2mmols
TC / HDL ratio	ratio 4.4	ratio 2.9

Summary

Substantial evidence supports the incorporation of exercise within CR programmes to promote the recovery of physical and psychological health. The evidence presented highlights the positive effect of exercise intervention on: secondary cardiac events, mortality rates, cardiac function and physical fitness of CVD patients to supplement contemporary clinical care. However, further research studies are needed on a greater variety of cardiac patient groups to fully verify the effectiveness of different exercise regimes. Many of the studies cited were performed with heart failure patients, who potentially may experience greater improvements in physical function and quality of life, due to the debilitating nature of this condition. Though heart failure patients are incorporated into contemporary CR delivery, they are not representative of the wider patient demographic that access CR. Finally, combined CV and RT provides the greatest potential improvements to physical fitness. However, further research is needed to validate the delivery of contemporary CR services across a heterogenous patient demographic to ensure the exercise component meets an appropriate dose to elicit favourable adaptations that impact positively on patient outcomes.

References

Achten, J. & Jeukendrup, A.E. (2003) Heart rate monitoring: applications and limitations, *Sports Medicine*, 33 (7), pp. 517-538.

Ades, P.A. (2001). Cardiac rehabilitation and secondary prevention of coronary heart disease. *The New England Journal of Medicine*, 345(12), 892-902.

American Association for Cardiovascular and Pulmonary Rehabilitation (2004). *Guidelines for cardiac rehabilitation & secondary prevention programs (Fourth edition)*. Illinois: Human Kinetics.

Artham, S.M., Lavie, C.J., Milani, R.V., Chi, Y., Goldman, C.K. (2008). Benefits of exercise training in secondary prevention of coronary and peripheral arterial disease. *Vascular Disease Prevention*, 5(3), 156-168.

Association of Chartered Physiotherapists in Cardiac Rehabilitation (ACPICR) (2015).

Standards of Physical Activity and Exercise in the Cardiovascular Population (Third edition).

Retrieved from: http://acpicr.com/sites/default/files/ACPICR%20Standards%202015.pdf on 17th

March 2015.

Austin, J., Williams, R., Ross, L., Moseley, L., Hutchison, S. (2005). Randomised controlled trial of cardiac rehabilitation in patients with heart failure. *European Journal of Heart Failure*, 7(3), 411-417.

British Association of Cardiovascular Prevention and Rehabilitation (BACPR) (2012) *BACPR*Standards and Core Components for Cardiovascular Disease Prevention and Rehabilitation (2nd

Edition). London: BACPR

Balady, G. J., Fletcher, B. J., Froelicher, E. S., Hartley, L. H., Krauss, R. M., Oberman, A. Pollock, M.L., Taylor, C.B. (1994). Cardiac rehabilitation programs: A statement for healthcare professionals from the American Heart Association. *Circulation*, 90, 1602-1610.

Balady, G., Jette, D., Scheer, J., Downing, J. (1996) Changes in exercise capacity following cardiac rehabilitation in patients stratified according to age and gender: Results of the Massachusetts Association of Cardiovascular and Pulmonary Rehabilitation Multicenter Database. *Journal of Cardiopulmonary Rehabilitation*, 16(1), 38-46.

Beauchamp, A., Worcester, M., Ng, A., Murphy, B., Tatoulis, J., Grigg, L., Newman, R., Goble, A. (2012). Attendance at cardiac rehabilitation is associated with lower all-cause mortality after 14 years of follow-up. *Heart*, 99(9), 620-625.

Belardinelli, R., Georgiou, D., Cianci, G., Purcaro, A. (1999). Randomized, controlled trial of long-term moderate exercise training in chronic heart failure. *Circulation*, 99, 1173-82.

Bethell, H. J. (1999). Exercise in cardiac rehabilitation, *British Journal of Sports Medicine*, 33(2), 79-86.

Bjarnason-Wehrens, B., Mayer-Berger, W., Meister, E., Baum, K., Hambrecht, R., Gielen, S. (2004). Recommendations for resistance exercise in cardiac rehabilitation. Recommendations of the German Federation for Cardiovascular Prevention and Rehabilitation. *European Journal of Preventive Cardiology*, 11(4), 352-361.

British Heart Foundation (2013) *The national audit of cardiac rehabilitation: annual statistical report 2013*. British Heart Foundation.

Bryner, R.W., Ullrich, I.H., Sauers, J., Donley, D., Hornsby, G, Kolar, M., Yeater, R. (1999). Effect of resistance vs. aerobic training combined with an 800 calorie liquid diet on lean body mass and resting metabolic rate. *Journal of American College of Nutrition*, 18(2), 115-121.

Carney, R.M., Freedland, K.E., Veith, R.C., Jaffe, A.S. (1999). Can treating depression reduce mortality after an acute myocardial infarction? *Psychosomatic Medicine*, 61, 666-675.

Chien, C.L., Lee, C.M., Wu, Y.W., Chen, T.A., Wu, Y.T. (2008). Home-based exercise increases exercise capacity but not quality of life in people with chronic heart failure: a systematic review. *Australian Journal of Physiotherapy*, 54(2), 87-93.

Child, A., Sanders, J., Sigel, P., Hunter, M.S. (2010). Meeting the psychological needs of cardiac patients: an integrated stepped-care approach within a cardiac rehabilitation setting. *The British Journal of Cardiology*, 17(4), 175-9.

Cornelissen, V.A., Fagard, R.H. (2005). Effect of resistance training on resting blood pressure: a meta-analysis of randomized control trials. *Journal of Hypertension*, 23(2), 251-259.

Cornish, A.K., Broadbent, S., Cheema, B.S. (2011). Interval training for patients with coronary artery disease: a systematic review. *European Journal of Applied Physiology*, 111, 579-589.

Daly, J., Sindone, A.P., Thompson, D.R., Hancock, K., & Chang, E. (2002). Barriers to participation in and adherence to cardiac rehabilitation programs: a critical literature review. *Progress in Cardiovascular Nursing*, 17(1), 8-17.

Davies, E.J., Moxham, T., Rees, K., Singh, S., Coats, A.J.S., Ebrahim, S., Lough F., Taylor, R.S. (2010). Exercise Training for Systolic Heart Failure: Cochrane Systematic Review and Meta-analysis. *European Journal of Heart Failure*, 12(7), 706-715.

Demopoulos, L., Bijou, R., Fergus, I., Jones, M., Strom, J., Le Jemtel, T.H. (1997). Exercise training in patients with severe congestive heart failure: enhancing peak aerobic capacity while minimising the increase in ventricular wall stress, *Heart Failure*, *29*, 597-603.

Fletcher, G.F., Balady, G.J., Amsterdam, E.A., Chaitman, B., Eckel, R., Fleg J., Froelicher, V.F., Leon, A.S., Piña, I.L., Rodney, R., Simons-Morton, D.A., Williams, M.A., Bazzarre, T. (2001). Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association. *Circulation*, 104. 1694-1740.

Fletcher, G.F., Balady, G., Blair, S.N., Blumenthal, J., Caspersen, C., Chaitman, B., Epstein, S., Sivarajan Froelicher, E, S., Froelicher, V.F., Pina, I.L., Pollock, M.L. (1996). Statement on exercise: benefits and recommendations for physical activity programs for all Americans. *Circulation*, *94*, 857-862.

Flynn, K.E., Piña, I.L., Whellan, D.J., Lin, L., Blumenthal, J.A., Ellis, S.J., Fine, L.J., Howlett, J.G., Keteyian, S.J., Kitzman, D.W., Kraus, W.E., Miller, N.H., Schulman, K.A., Spertus, J.A., O'Connor, C.M. & Weinfurt, K.P. (2009). Effects of exercise training on health status in patients with chronic heart failure. HF-action randomised controlled trial. *Journal of the American Medical Association*, 301(14), 1451-1459.

Forman, D.E., Cannon, C.P., Hernandez, A.F., Liang, L., Yancy, C. & Fonarow, G.C. (2009). Influence of age on the management of heart failure: findings from Get With the Guidelines-Heart Failure (GWTG-HF). *American Heart Journal*, 157(6), 1010-1017.

Franklin, B.A., Bonzheim, K., Gordon, S. & Timmis, G.C. (1998) Safety of medically supervised cardiac rehabilitation exercise therapy: a 16-year follow-up. *Chest*, *114*, 902–906.

Franklin, B.A. & Fardy, P.S. (1998). Exercise Evaluation, Prescription & Training In: Fardy, P.S., Franklin, B.A., Porcari, J.P. & Verrill, D.E. (ed.) *Training Techniques in Cardiac Rehabilitation*. Illinois: Human Kinetics, 1–40.

Franklin, B.A., McCullough, P.A. (2009). Cardiorespiratory fitness: an independent and additive marker of risk stratification and health outcomes. *Mayo Clinic Proceedings*, 84(9), 776-779.

Giannuzzi, P., Temporelli, P.L., Corrà, U., Tavazzi, L. (2003). Antiremodelling effect of long term exercise training in patients with stable chronic heart failure. *Circulation*, 108, 554-59.

Gielen, S., Adams, V., Möbius-Winkler, S., Linke, A., Erbs, S., Yu, J., Kempf, W., Schubert, A., Schuler, G., Hambrecht, R. (2003). Anti-inflammatory effects of exercise training in the skeletal muscle of patients with chronic heart failure, *Journal of the American College of Cardiology*, 4(5), 861-868.

Graham, I., Atar, D., Borch-Johnsen, K., Boysen, G., Burell, G., Cifkova, R., Dallongeville, J., De Backer, G., Ebrahim, S., Gjelsvik, B., Herrmann-Lingen, C., Hoes, A., Humphries, S., Knapton, M., Perk, J., Priori, S.G., Pyorala, K., Reiner, Z., Ruilope, L., Sans-Menendez, S., Scholte op Reimer, W., Weissberg, P., Wood, D., Yarnell, J., Zamorano, J.L., Walma, E., Fitzgerald, T., Cooney, M.T., Dudina, A.; European Society of Cardiology (ESC) Committee for Practice Guidelines (CPG) (2007). European guidelines on cardiovascular disease prevention in clinical practice. *European Heart Journal*, 28, 2375-2414.

Green, D.J., Fowler, D.T., O'Driscoll, J.G., Blanksby, B.A., Taylor, R.R. (1996). Endothelium-derived nitric oxide activity in forearm vessels of tennis players. *Journal of Applied Physiology*, 81, 943-948.

Green, D.J., Maiorana, A., O'Driscoll, G., Taylor, R. (2004). Effects of exercise training on endothelium-derived nitric oxide function in humans. *Journal of Physiology*, 561, 1-25.

Green, D.J., O'Driscoll, G., Joyner, M.J., Cable, N.T. (2008). Exercise and cardiovascular risk reduction: time to update the rationale for exercise? *Journal of Applied Physiology*, 105, 766-768.

Guiraud, T., Nigam, A., Juneau., Meyer, P., Gayda, M., Bosquet, L. (2009). Acute responses to high-intensity intermittent exercise in CHD patients. *Medicine & Science in Sports & Exercise*, 43, 211-217.

Hambrecht, R., Niebauer, J., Fiehn, E., Kälberer, B., Offner, B., Hauer, K., Riede, U., Schlierf, G., Kübler, W., Schuler, G. (1995). Physical training in patients with stable chronic heart failure: effects on cardiorespiratory fitness and ultrastructural abnormalities of leg muscles. *Journal of American College of Cardiology*, 25(6), 1239-1249.

Hambrecht, R., Wolf, A., Gielen, S., Linke, A., Hofer, J., Erbs, S., Schoene, N., Schuler, G. (2000). Effect Of Exercise On Coronary Endothelial Function In Patients With Coronary Artery Disease. *The New England Journal of Medicine*, *342*, 454 – 460.

Hansen, D., Dendale, P., Berger, J., Meeusen, R. (2005). Rehabilitation in cardiac patients: What do we know about training modalities? *Sports Medicine*, 35(12), 1063-1084.

Hansen, D., Dendale, P., Van Loon, L., Meeusen, R. (2010). The impact of training modalities on the clinical benefits of exercise intervention in patients with cardiovascular disease risk or type 2 diabetes mellitus. *Sports Medicine*, 40(11), 921-940.

Haykowsky, M.J., Liang, Y., Pechter, D., Jones, L.W., McAlister, F.A., Clark, A.M. (2007). A meta-analysis of the effects of exercise training on left ventricular remodeling in heart failure patients. *Journal of the American College of Cardiology*, 49(24), 2329-2336.

Heran, B.S., Chen, J.M.H., Ebrahim, S., Moxham, T., Oldridge, N., Rees, K., Thompson, D.R., Taylor, R.S. (2011). Exercise-based cardiac rehabilitation for coronary heart disease. *Cochrane Database of Systematic Reviews*, 7, CD001800.

Jolliffe, J., Rees, K., Taylor, R.R.S., Thompson, D.R., Oldridge, N., Ebrahim, S. (2001). Exercise-based rehabilitation for coronary heart disease. *Cochrane Database of Systematic Reviews*, 1, CD001800.

Kelemen, M.H., Stewart, K.J., Gillilan, R.E., Ewart, C.K., Valenti, S.A., Manley, J.D, Kelemen, M.D. (1986). Circuit weight training in cardiac patients. *Journal of the American College of Cardiology*, 7(1), 38-42.

Keteyian, S.J., Brawner, C.A., Savage, P.D., Ehrman, J.K., Schairer, J., Divine, G., Aldred, H., Ophaug, K., Ades, P.A. (2008). Peak Aerobic Capacity Predict Prognosis in Patients with Coronary Heart Disease. *American Heart Journal*, 156(2), 292-300.

Keteyian, S.J., Leifer, E.S., Houston-Miller, N., Kraus, W.E., Brawner, C.A., O'Connor, C.M., Whellan, D.J., Cooper, L.S., Fleg, J.L., Kitzman, D.W., Cohen-Solal, A., Blumenthal, J.A., Rendall, D.S. Piña, I.L. (2012). Relation between volume of exercise and clinical outcomes in patients with heart failure. *Journal of the American College of Cardiology*, 60(19), 1899-1905.

Lavie, C.J. Milani, R.V. (1995). Effects of cardiac rehabilitation and exercise training on exercise capacity, coronary risk factors, behavioural characteristics, and quality of life in women. *The American Journal of Cardiology*, 75(5), 340–343.

Lavie, C.J., Milani, R.V. (1997). Effects of cardiac rehabilitation, exercise training, and weight reduction on exercise capacity, coronary risk factors, behavioural characteristics, and quality of life in obese coronary patients. *The American Journal of Cardiology*, 79(4), 397–401.

Lavie, C.J., Thomas, R.J., Squires, R.W., Allison, T.G., Milani, R.V. (2009) Exercise training and cardiac rehabilitation in primary and secondary prevention of coronary heart disease. *Mayo Clinic Proceedings*, 84(4), 373-383.

Lawler, P.R., Filion, K.B., Eisenberg, M.J. (2011). Efficacy of exercise-based cardiac rehabilitation post-myocardial infarction: a systematic review and meta-analysis of randomized controlled trials. *American Heart Journal*, 162, 571-584.

Leon, S., Franklin, B.A., Costa, F, Balady, G.J., Berra, K.A., Stewart, K.J., Thompson, P.D., Williams, M.A., Lauer, M.S. (2005). Cardiac rehabilitation and secondary prevention of coronary heart disease: an American Heart Association scientific statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity), in collaboration with the American Association of Cardiovascular and Pulmonary Rehabilitation. *Circulation*, 111, 369–376.

Levick, R.J (2009). *An Introduction to Cardiovascular Physiology (5th Edition)*. Boca Raton, Florida: CRC Press.

Lloyd-Williams, F., Mair, F.S. Leitner, M. (2002). Exercise training and heart failure: a systematic review of current evidence. *British Journal of General Practice*, 52(474), 47-55.

Marchionni, N., Fattirolli, F., Fumagalli, S., Oldridge, N., Del Lungo F., Morosi L., Burgisser, C., Masotti, G. (2003). Improved exercise tolerance and quality of life with cardiac rehabilitation of older patients after myocardial infarction. *Circulation*, 107, 2201-2206.

Martin, B.J., Arena, R., Haykowsky, M., Hauer, T., Austford, L.D., Knudtson, M., Aggarwal, S., Stone, J.A. (2013). Cardiovascular fitness and mortality after contemporary cardiac rehabilitation. *Mayo Clinic Proceedings*, 88(5), 455-463.

Maxwell, A.J., Schauble, E., Bernstein, D., Cooke, J.P. (1998). Limb blood flow during exercise is dependent on nitric oxide. *Circulation*, 98, 369-374.

McCartney, N. (1998). Role of resistance training in heart disease. *Medicine & Science in Sports & Exercise*, 30(10 Suppl), S396-S402.

McCartney, N., McKelvie, R. S., Haslam, D. R., Jones, N. L. (1991). Usefulness of weightlifting training in improving strength and maximal power output in coronary artery disease. *The American Journal of Cardiology*, 67(11), 939-945.

Meyer P., Normandin, E., Gayda, M., Billon, G., Guiraud, T., Bosquet, L., Fortier, A., Juneau, M., White, M. Nigam, A. (2012). High-intensity interval exercise in chronic heart failure: protocol optimisation. *Journal of Cardiac Failure*, 18(2), 126-133.

Miller, W.C., Wallace, J.P. & Eggert, K.E. (1993) Predicting max HR and the HR-VO₂ relationship for exercise prescription in obesity, *Medicine & Science in Sports & Exercise*, 25 (9), pp. 1077-1081.

Mittleman, M.A., Maclure, M., Tofler, G.H., Sherwood, J.B., Goldberg, R.J., Muller, J.E. (1993) Triggering of acute myocardial infarction by heavy physical exertion – protection against triggering by regular exertion. *The New England Journal of Medicine*, 329, 1677-1683.

Moholdt, T., Aamot, I.L., Granøien, I, Gjerde, L., Myklebust, G., Walderhaug, L., Brattbakk, L., Hole, T., Graven, T., Stølen, T.O., Amundsen, B.H., Mølmen-Hansen, H.E., Støylen, A., Wisløff, U. & Slørdahl, S.A. (2012). Aerobic interval training increases peak oxygen uptake more than usual care exercise training in myocardial infarction patients: a randomised controlled study. *Clinical Rehabilitation*, 26(1), 33-44.

National Institute for Health and Clinical Excellence (NICE) (2008). *Cardiac rehabilitation service*. Commissioning guide: Implementing NICE guidance.

Nelson, A.J., Juraska, J.M., Musch, T.I. & Iwamoto, G.A. (2005). Neuroplastic adaptations to exercise: neuronal remodelling in cardiorespiratory and locomotor areas. *Journal of Applied Physiology*, 99, 2312-2322.

Nilsson, B.B., Westheim, A., Risberg, M.A. (2008). Effects of group-based high-intensity aerobic interval training in patients with chronic heart failure. *American Journal of Cardiology*, 102(10), 1361-1365.

O'Connor, G.T., Buring, J.E., Yusuf, S., Goldhaber, S.Z., Olmstead, E.M., Paffenbarger, R.S. Hennekens, C.H. (1989). An overview of randomized trials of rehabilitation with exercise after myocardial infarction. *Circulation*, 80(2), 234-244.

O'Connor, C.M., Whellan, D.J., Lee, K.L., Keteyian, S.J., Cooper, L.S., Ellis, S.J., Leifer, E.S., Kraus, W.E., Kitzman, D.W., Blumenthal, J.A., Rendall, D.S., Miller, N.H. Fleg, J.L. (2009). Efficacy and Safety of Exercise Training in Patients with Chronic Heart Failure: HF-Action Randomised Controlled Trial. *Journal of the American Medical Association*, 301(14), 1439-1450.

Owen, A. Croucher, I. (2000). Effect of an exercise programme for elderly patients with heart failure. *European Journal of Heart Failure*, 2, 65-70.

Papadakis, S., Oldridge, N. B., Coyle, D., Mayhew, A., Reid, R. D., Beaton, L.: Working Groups on Epidemiology & Prevention and Cardiac Rehabilitation and Exercise Physiology (2005). Economic evaluation of cardiac rehabilitation: a systematic review. *European Journal of Cardiovascular Prevention and Rehabilitation*, 12(6), 513-20.

Parker, N.D., Hunter, G.R., Treuth, M.S., Kekes-Szabo, T., Kell, S.H., Weinsier, R. & White, M. (1996) Effects of strength training on cardiovascular responses during a submaximal walkand a weight-loaded walking test in older females. *Journal of Cardiopulmonary Rehabilitation*, 16(1), 56-62.

Pavia, L, Orlando, G., Myers, J Maestri, M. (1995). The effect of beta-blockade therapy on the response to exercise training in postmyocardial infarction patients. *Clinical Cardiology*, 18, 716-720.

Pescatello, L.S., Arena, R., Riebe, D., Thompson, P. D. (2014). *ACSM's Guide for Exercise Testing and Prescription* (9th Ed). Baltimore, MD: Wolters Kluwer Health/Lippincott, Williams & Wilkins.

Piepoli, M.F., Corrà, U., Benzer, W., Bjarnason-Wehrens, B., Dendale, P., Gaita, D., McGee H., Mendes, M., Niebauer, J., Zwisler, O.A. Schmid J. (2010). Secondary prevention through cardiac rehabilitation: from knowledge to implementation. A position paper from the Cardiac Rehabilitation Section of the European Association of Cardiovascular Prevention and Rehabilitation. *European Journal of Cardiovascular Prevention & Rehabilitation*, 17, 1-17.

Pollock, M.L., Franklin, B.A., Balady, G.J., Chaitman, B.L., Fleg, J.L., Fletcher, B., Limacher, M., Piña, I.L., Stein, R.A., Williams, M. & Bazzarre, T. (2000). Resistance exercise in individuals with and without cardiovascular disease: benefits, rationale, safety, prescription. An advisory from the Committee on Exercise, Rehabilitation, and Prevention, Council on Clinical Cardiology, American Heart Association. *Circulation*, 101, 828-833.

Rennie, K.L., Hemingway, H., Kumari, M., Brunner, E., Malik, M. Marmot, M. (2003). Effects of moderate and vigorous physical activity on heart rate variability in a British study of civil servants. *American Journal of Epidemiology*, 158, 135-143.

Rognmo, Ø., Hetland, E., Helgerud, J., Hoff, J., Slørdahl, S. (2004). High intensity aerobic interval exercise is superior to moderate intensity exercise for increasing aerobic capacity in patients with coronary artery disease. *European Journal of Preventive Cardiology*, 11, 216-222.

Rognmo, Ø., Mohold, T., Bakken, H., Hole, T., Mølstad, P., Myhr, N., Grimsmo, J. Wisløff, U. (2012). Cardiovascular risk of high- versus moderate-intensity aerobic exercise in coronary heart disease patients. *Circulation*, 126, 1436-1440.

Rozanski, A., Blumenthal, J.A., Davidson, K.W., Saab, P.G., Kubzansky, L. (2005). The epidemiology, pathophysiology, and management of psychosocial risk factors in cardiac practice. The emerging field of behavioural cardiology. *Journal of the American College of Cardiology*, 45(5), 637-651.

Saeidi, M. Mostafavi, M. (2013). Effects of a comprehensive cardiac rehabilitation program on quality of life in patients with coronary artery disease. *Heart*, 99(3), A140-A141.

Sandercock, G.R.H., Cardoso, F., Almodhy, M. Pepera, G. (2013a) Cardiorespiratory fitness changes in patients receiving comprehensive outpatient cardiac rehabilitation in the UK: a multicentre study. *Heart*, 99, 785-790.

Sandercock, G., Hurtado, V. Cardoso, F. (2013b). Changes in cardiorespiratory fitness in cardiac rehabilitation patients: A meta-analysis. *International Journal of Cardiology*, 167(3), 894-902.

Sheppard, M. (2011). *Practical cardiovascular pathology (Second edition)*. Boca Raton, Florida: CRC Press.

Smart, N., Marwick, T.H. (2004). Exercise training for patients with heart failure: a systematic review of factors that improve mortality and morbidity. *American Journal of Medicine*, 116, 693-706.

Stein, P.K., Carney, R.M., Freedland, K.E., Skala, J.A., Jaffe, A.S., Kleiger, R.E. Rottman, J.N. (1995). Severe depression is associated with markedly reduced heart rate variability in patients with stable coronary heart disease. *Journal of Psychosomatic Research*, 46(4-5), 493-500.

Taylor, C. B., Houston-Miller, N., Ahn, D. K., Haskell, W., DeBusk, R. F. (1986). The effects of exercise training programs on psychosocial improvement in uncomplicated postmyocardial infarction patients. *Journal of psychosomatic research*, 30(5), 581-587.

Taylor, R.S., Brown, A., Ebrahim, S., Jolliffe, J., Noorani, H., Rees, K., Skidmore, B., Stone, J.A., Thompson, D.R., Oldridge, N. (2004). Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. *The American Journal of Medicine*, 116(10), 682-692.

Thompson, P.D., Buchner, D., Piña, I.L., Balady, G.J., Williams, M.A., Marcus, B.H., Berra, K., Blair, S.N., Costa, F., Franklin, B., Fletcher, G.F., Gordon, N.F., Pate, R.R., Rodriguez, B.L., Yancey, A.K., Wenger, N.K. (2003). Exercise and Physical Activity in the Prevention and

Treatment of Atherosclerotic Cardiovascular Disease: A Statement From the Council on Clinical Cardiology (Subcommittee on Exercise, Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity). *Circulation*, 107, 3109-3116.

Tsuji, H., Venditti, F.J., Manders, E.S., Evans, J.C., Larson, M.G., Feldman, C.L., Levy, D. (1994). Reduced heart rate variability and mortality risk in the elderly cohort. The Framingham Heart Study. *Circulation*, 90, 878-883.

van Stel, H.F., Busschbach, J.J.V., Hunink, M.M.G., Buskens, E. (2012). Impact of secondary cardiovascular events on health status. *Value in Health*, 15(1), 175-182.

Van Tol, B.A.F., Huijsmans, R.J., Kroon, D.W., Schothorst, M., Kwakkel, G. (2006). Effects of exercise training on cardiac performance, exercise capacity and quality of life in patients with heart failure: a meta-analysis. *European Journal of Heart Failure*, 8, 841-850.

Wielenga, R.P., Huisveld, L.A., Bol, E., Dunselman, P.H.J.M., Erdman, R.A.M., Baselier, M.R.P., Mosterd, W.L. (1999a). Safety and effects of physical training in chronic heart failure and graded exercise study (CHANGE). *European Heart Journal*, 20(12), 872-879.

Wielenga, R.P., Huisveld, L.A., Bol, E., Dunselman, P.H.J.M., Erdman, R.A.M., Baselier, M.R.P., Mosterd, W.L. (1999b). Exercise training in elderly patients with chronic heart failure. *Coronary Artery Disease*, 9, 765-770.

Wise, F.M., Patrick, J.M. (2011). Resistance exercise in cardiac rehabilitation. *Clinical Rehabilitation*, 25, 1058.

Wisløff, U., Støylen, A., Loennechen, J.P., Bruvold, M. Rognmo, Ø, Haram, P.M., Tjønna, A.E., Helgerud, J., Slørdahl, S.A., Lee, S.J., Videm, V., Bye, A., Smith, G.L., Najjar, S.M., Ellingsen, Ø. & Skjærpe, T. (2007) Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure. *Circulation*, 115, 3086-3094.

Wenger, N.K. (2008). Current status of cardiac rehabilitation. *Journal of the American College of Cardiology*, 51(17), 1619-1631.

Williams, M.A., Haskell, W.L., Ades, P.A., Amsterdam, E.A., Bittner, V., Franklin, B.A., Gulanick, M., Laing, S.T., Stewart K.J. (2007). Resistance exercise in individuals with and without cardiovascular disease: 2007 Update. A scientific statement from the American Heart Association Council on Clinical Cardiology and Council on Nutrition, Physical Activity and Metabolism. *Circulation*. 116, 572–584.

Yohannes, A.M., Doherty, P., Bundy, C., Yalfani, A. (2010). The long-term benefits of cardiac rehabilitation on depression, anxiety, physical activity and quality of life. *Journal of Clinical Nursing*, 19(19-20), 2806-2813.