European Journal of Human Movement, 2018: **41**, 49-72

# INFLUENCE OF THE EXERCISE FREQUENCY, INTENSITY, TIME AND TYPE ACCORDING TO DIFFERENT TRAINING MODALITIES ON THE CARDIAC REHABILITATION PROGRAMS

José Manuel Sarabia [1,2]; Agustín Manresa-Rocamora [1]; José Oliveira [3]; Manuel Moya-Ramón [1,2]

1. Department of Sport Science, Sport Research Centre, Miguel Hernandez University of Elche, Spain.
2. Department of Health Psychology, Miguel Hernandez University of Elche, Elche, Institute for Health and Biomedical Re-search (ISABIAL-FISABIO Foundation), Spain.
3. Research Center in Physical Activity, Health and Leisure, Faculty of Sport, University of Porto, Portugal.

ABSTRACT

Exercise-based cardiac rehabilitation is considered as a cornerstone of non-pharmacological treatments in cardiac patients and several previous studies have been performed with this population to know the effects of this treatment. The main goal of these researches has been to analyse the influence of different training modalities, such as endurance training, resistance training or combined endurance and resistance training. Within endurance training, the principal topic is the efficacy of moderate continuous training and high-intensity interval training. However, the findings of these previous studies are controversial and a very high heterogeneity has been reported in previous meta-analyses. Despite the fact that the influence of the training variables, such as frequency, intensity, time and type (FITT variables) has been widely reported, none of the previous studies have considered these variables globally in order to explain the controversial results. Therefore, the aim of this review was to interpret previous studies to explain this heterogeneity and set out proposals to manage exercise-based cardiac rehabilitation properly. The review helped to show the lack of control of FITT variables and their influence in the effect of exercise-based cardiac rehabilitation, highlighting the need to control these variables properly to reach higher adaptations in cardiac rehabilitation.

**Keywords**: coronary heart disease, chronic heart failure, resistance training, high-intensity interval training, combined training

# INFLUENCIA DE LA FRECUENCIA, INTENSIDAD, TIEMPO Y TIPO DE EJERCICIO, EN FUNCIÓN DE LAS DIFERENTES MODALIDADES DE ENTRENAMIENTO, EN LOS PROGRAMAS DE REHABILITACIÓN CARDIACA

RESUMEN

La rehabilitación cardíaca basada en el ejercicio se considera la piedra angular de los tratamientos no farmacológicos en pacientes cardíacos y, por ello, se han llevado a cabo varios estudios con esta población, para conocer los efectos de este tratamiento. El objetivo principal de estas investigaciones ha sido analizar la influencia de diferentes modalidades de entrenamiento, como el entrenamiento de resistencia, el entrenamiento de fuerza o el entrenamiento combinado de resistencia y fuerza. Dentro del entrenamiento de resistencia, el tema principal de debate es la eficacia del entrenamiento continúo moderado y el entrenamiento de intervalos de alta intensidad. Sin embargo, los resultados de estos estudios son controvertidos y se ha encontrado una heterogeneidad muy alta en los meta-análisis realizados. A pesar de que la influencia de las variables de entrenamiento, como la frecuencia, la intensidad, el tiempo y el tipo (variables FITT) ha sido ampliamente demostrada, ninguno de los estudios anteriores ha considerado estas variables de forma global para explicar sus resultados. Por lo tanto, el objetivo de esta revisión fue

interpretar los estudios previos, para explicar esta heterogeneidad y presentar una propuesta para manejar adecuadamente la rehabilitación cardíaca basada en el ejercicio. La revisión permitió mostrar la falta de control de las variables FITT y su influencia en el efecto de la rehabilitación cardíaca, siendo necesario controlar y gestionar adecuadamente estas variables para alcanzar mayores adaptaciones en estos programas.
**Palabras clave:** cardiopatía isquémica, insuficiencia cardiaca, entrenamiento de fuerza, entrenamiento interválico de alta intensidad, entrenamiento combinado

---

*Correspondence:*
Manuel Moya-Ramón
mmoya@umh.es
Sport Research Centre, Miguel Hernandez University.
Avenida de la Universidad s/n, 03202, Elche, Spain.
*Submitted:* 09/10/2018 *Accepted:* 09/12/2018

## INTRODUCTION

In the last few years the number of deaths caused by cardiovascular disease has fallen due to the improvements in the diagnosis and treatment of this pathology (Nichols, Townsend, Scarborough, & Rayner, 2013). The increase in the surviving population makes it necessary to develop integral treatments, with cost-effective improvements in the prognosis and quality of life (QoL) of these patients. Previous evidence has shown that exercise-based cardiac rehabilitation (CR) is an effective strategy for the reduction of cardiovascular mortality and the improvement of the QoL in cardiac patients (Anderson et al., 2016). CR was also shown to be safe in individuals with either coronary heart disease (CHD) and/or chronic heart failure (CHF) (Beauchamp et al., 2013; Hammill, Curtis, Schulman, & Whellan, 2010).

Cardiac patients usually have a reduced capacity to perform exercise, which seems to be related to central and peripheral limitations, and therefore, researches have focused their aims on both of these limitations. At the central level, the global parameter to assess the capacity to perform exercise is cardiorespiratory fitness (CRF), which is directly measured by oxygen uptake peak (VO2peak). VO2peak has been deemed as a strong predictor of mortality in cardiac patients (Kodama et al., 2009). Several previous studies have reported that CR is suitable to increase VO2peak (Conraads et al., 2015; Santos et al., 2018) and exercise capacity in cardiac patients (Yamamoto, Hotta, Ota, Mori, & Matsunaga, 2016). There is ample evidence that shows the importance of exercise training in cardiac patients, highlighting CR as a cornerstone of non-pharmacological treatments in this population. This is so to such an extent that most cardiac rehabilitation guidelines recommend timely and early access to the program. Early mobilization of the patients has shown greater benefits in different aspects related to the mortality risk as CRF (Valkeinen, Aaltonen, & Kujala, 2010), distance in *6-minutes walk test* or left ventricular remodelling (Haykowsky, 2011). However, the effects of CR on other aspects related to the pathology are not so clear, as will be indicated further on.

In response to a variety of forms of myocardial injury and increased wall stress, cardiac patients could suffer alterations in their ventricular architecture, with associated increased volume and altered chamber configuration. These changes in the ventricular architecture frequently produce a reduction in the cardiac function (Konstam, Kramer, Patel, Maron, & Udelson, 2011), which is measured by left ventricular ejection fraction (LVEF). Besides, endothelial dysfunction could be found in cardiac patients due to the activation of the sympathetic nervous system and the renin-angiotensin system, and also because of the impairment of the endothelial cells in the release of nitric oxide, an important physiological vasodilator (Miche et al., 2006). Endothelial dysfunction brings about the progression of the pathology and it is associated with an increased risk of mortality. Flow-mediated dilation and endothelial progenitor cells are used to evaluate endothelial function (Pearson & Smart, 2017). These patients also suffer chronically elevated levels of inflammatory markers which could produce structural damages, such as endothelial and left ventricular dysfunction, cardiac hypertrophy, apoptosis and fibrosis (Shirazi, Bissett, Romeo, & Mehta, 2017), as well as functional consequences (Briasoulis, Androulakis, Christophides, & Tousoulis, 2016). Thus, elevated concentrations of inflammatory markers, such as tumour necrosis factor-alpha (TNF-$\alpha$), interleukin 6 (IL-6), C-reactive protein (CRP) and fibrinogen are also associated with the disease severity and prognosis (Van Linthout & Tschöpe, 2017). Previous studies have reported contradictory results related to the effectiveness of CR, showing improvements in cardiac function (Cornelis, Beckers, Taeymans, Vrints, & Vissers, 2016), endothelial function (Dean, Libonati, Madonna, Ratcliffe, & Margulies, 2011; Sandri et al., 2016) or serum levels of inflammatory markers in cardiac patients (Gielen et al., 2003; Pearson, Mungovan, & Smart, 2018). Nevertheless, there are also opposite results that do not show improvements in these functions (Munch et al., 2018; Santos et al., 2018).

At the peripheral level, skeletal muscle atrophy, abnormalities of muscle blood flow, alterations in skeletal muscle metabolism and biochemical abnormalities are common in cardiac patients, as well as changes in muscle fibre types and down-regulation of the skeletal muscle enzyme systems (King, 2001). These changes are related to a drop of strength levels and cardiovascular impairment (Garber et al., 2011), as well as to a shift to anaerobic metabolism (Caminiti et al., 2009), which could help to explain the exercise intolerance found in cardiac patients. CR has also been shown adequate to improve these changes and increase strength levels (Marzolini, Oh, & Brooks, 2012; Yamamoto et al., 2016), lipidic profile, blood pressure and body composition in cardiac patients (Gayda, Ribeiro, Juneau, & Nigam, 2016), but there are also studies which again show contradictory results (Levinger, Bronks, Cody, Linton, & Davie, 2005; Salehi, Salehi, Moeini, Kargarfard, & Sadeghi, 2017).

Previous meta-analyses have reported that CR is proper to improve endothelial function (Pearson & Smart, 2017) or inflammatory activity (Swardfager et al., 2012). However, these meta-analyses showed high heterogeneity in the included studies and they did not consider the training modality or the training method used to carry out CR. This aspect limits the scope of their findings and does not help to interpret the heterogeneity of previous empirical studies. Another aspect that could explain this heterogeneity is the effect of modifying the components of exercise prescription like frequency, intensity, time (duration) and type (modality)

(Vanhees et al., 2012) that is, the FITT variables. Besides the controversial findings of the previous studies, another aspect that shows the importance to manage FITT variables properly is the variability in the response of the patients to the same treatment and the effect dose-dependent of the exercise. A study by de Schutter et al. (2018), which performed 36 sessions of CR with 1,171 patients, found that 23% of the patients did not improve or decrease their VO2peak, while 39% and 38% of patients improved less or more than 2.5 $ml \cdot kg^{-1} \cdot min^{-1}$, respectively. On the other hand, the exercise has a dose-dependent relationship with a reduction in cardiovascular disease risk (Mora, Cook, Buring, Ridker, & Lee, 2007). However, this relationship is not lineal but a U-shaped association (Leggio et al., 2018; Schnohr, Marott, & O'Keefe, 2015), which makes the correct control of the response of the patients and the management of the training load to prevent maladaptation necessary (Leggio et al., 2018).

All the above-mentioned evidence shows the importance of improving the exercise prescription in CR to maximize the effects of exercise training in each patient. Most of the previous reviews and meta-analyses performed have focused their aim in comparing the effect of endurance training (ET), resistance training (RT) or combined resistance and endurance training (CT) without taking into account FITT variables to analyse their results. Therefore, the purposes of this paper are: a) to review the effect of different programs of CR (ET, RT or CT); b) to find differences between the studies regarding the prescription of FITT variables to explain their controversial results and to try to optimise the prescription methods in CR.

## ENDURANCE TRAINING

According to the Churchill Livingstone's Dictionary of Sport and Exercise Science and Medicine (2008), "endurance" is the ability to perform physical work for a long time; quantitatively, the maximum duration for which an individual can sustain a specific activity, preferably also at a specific intensity. Used in isolation, the word usually implies whole-body endurance consideration in terms of minutes or hours which is principally limited by cardiovascular fitness and muscle glycogen storage.

### *Intensity*

To refer to the intensity of exercise, it can be found in absolute values, indicating a rate of energy expenditure usually expressed in metabolic equivalents (METs), or in kcal/min. However, in CR programs, the intensity usually is individualized to each patient and it is expressed as a percentage of maximal oxygen uptake (VO2max), maximal heart rate, heart rate reserve or maximal aerobic power output, all of them calculated through a gradual exercise test. However, with these methods of individualization, the metabolic response of each patient can be different, showing different lactate concentrations and time duration at the same percentage of maximum intensity (Scharhag-Rosenberger, Meyer, Gäßler, Faude, & Kindermann, 2010). For this reason, the best option to individualize the intensity in this heterogeneous population could be to use ventilatory thresholds, making sure that the requirements of training are similar for each patient (Mann, Beedie, & Jimenez, 2014; Wolpern, Burgos, Janot, & Dalleck, 2015). In this case the exercise intensity below the first threshold is defined as a low intensity, the exercise between the first and second threshold is defined as a moderate intensity, and intensity above the second threshold to VO2max is defined as a high intensity (Wolpern et al., 2015).

One of the most significant current discussions in CR focuses on the different changes reached through moderate continuous training (MCT) or high-intensity interval training (HIIT). MCT is characterized by long-term training periods (for 30 – 60 min) at 60 – 85% VO2peak (Fletcher et al., 2001). On the other hand, the main principle of HIIT is to perform brief periods of high-intensity exercise (> 85% VO2peak) interspersed by periods of low-intensity exercise (typically, below aerobic threshold) or rest (Gayda et al., 2016). Original studies and meta-analyses reported similar effects, which improve some risk factors (like circulating cholesterol and triglycerides) (Pattyn, Beulque, & Cornelissen, 2018) independent of the cardiovascular disease (coronary or heart failure with or without preserved ejection fraction), with similar reductions in resting blood pressure (Cornelissen, Verheyden, Aubert, & Fagard, 2010) and both were well tolerated and safe for patients with CHF (Nilsson, Westheim, & Risberg, 2008). However, the improvement of CRF is a controversial issue in the literature, as while studies and meta-analyses found better improvements for HIIT (Elliott, Rajopadhyaya, Bentley, Beltrame, & Aromataris, 2015; Ismail, McFarlane, Nojoumian, Dieberg, & Smart, 2013; Liou, Ho, Fildes, & Ooi, 2016), some randomized control trials did not show superiority for any intensity (Conraads et al., 2015; Ellingsen et al., 2017). Besides, empirical studies always report the prescribed exercise program. However, the performed exercise program during CR often diverts from the prescribed exercise program (Kraal, Vromen, Spee, Kemps, & Peek, 2017). Conraads et al. (2015), in a multicentre study, reported that MCT and HIIT equally improve VO2peak in CHD patients. However, some patients in the HIIT group did not reach the prescribed intensity during the program and the continuous moderate training group in some cases trained above target intensity. The difference between a prescribed and a performed exercise program could explain this contradictory conclusion regarding other studies and could show the relevance of intensity training.

This improvement associated to HIIT seems to be related among other things with the major activation of 5’-AMP-activated protein kinase, p38 mitogen-activated protein kinase (Gibala, Little, Macdonald, & Hawley, 2012) and the upregulation of vascular endothelial growth factor (Hoier & Hellsten, 2014). Two of these three are implicated in the direct phosphorylation and activation of PGC-1α and they co-activate transcription factors to increase mitochondrial gene transcription. These improvements in CRF can be reflected in a better mechanical efficiency (Villelabeitia-Jaureguizar et al., 2018).

However, to prescribe ET at different intensities was related with greater reductions in inflammatory markers like high-sensitivity CRP in patients with CHD (Milani, Lavie, & Mehra, 2004; Munk, Staal, Butt, Isaksen, & Larsen, 2009; Parrinello et al., 2010; Walther et al., 2008). In addition, reduced circulating levels of pro-inflammatory cytokines (TNF- α and IL-6), CRP and fibrinogen has been observed in patients with CHF (Pearson et al., 2018). Different treatment lengths (from 6 weeks to 24 months) and training methods (continuous moderate training and HIIT) were used in these studies showing a probable low effect of these variables as moderator of inflammatory effect, but nevertheless no previous meta-analysis studied this.

*Volume*

As previously described, physical exercise regulates biomarkers as IL-1, IL-6, CRP and endothelial progenitor cells. Again, as with the intensity, these inflammatory biomarkers seem to respond to small stimulus like only two-week interventions, while no changes were described in endothelial progenitor cells in that short-term period (Cesari et al., 2009). At least an intervention longer than 8 weeks, is necessary to increase endothelial progenitor cells (Paul et al., 2007).

The most common way to measure volume is to quantify the time spent in the exercise. Currently, a widely used parameter to adjust this time is the total energy expenditure during the training session. Some previous meta-analyses have analysed if total energy expenditure was a potential moderator of ET effect, showing a direct relationship between this variable and VO2peak improvement (Kraal et al., 2017), even diluting differences found between MCT and HIIT when isocaloric exercise training protocols were pooled to perform the analyses (Gomes-Neto et al., 2017; Neto et al., 2018). Based on these findings, Cornelissen, Buys, and Pattyn (2017) reported that “not the intensity nor the method but the total energy expenditure of the exercise programmes determines the improvement in exercise capacity after training”. Nevertheless, only four articles which used isocaloric exercise training protocols were pooled to perform this analysis.

Regarding treatment length, a recent meta-analysis reported an indirect relationship between the program duration and the increase of VO2peak when HIIT is performed (García, Arias, Campo, González-Moro, & Poyatos, 2018). However, Taylor et al. (2017) indicated in their study that long-term adherence to supervised exercise (> 36 months) produced a higher reduction of long-term mortality risk. These results could highlight the importance of supervised exercise and the necessity of a well-established progression of the training load.

*Frequency*

Regarding the number of training days per week (d/w), most clinical guides recommend a frequency of 3 d/w (Piepoli et al., 2010; Steg et al., 2012) and most of the experimental research used this frequency of training in their training prescription. However, there is little knowledge (Dressendorfer et al., 1995) about the comparison among different training frequencies during a second phase of CR on CHD patients. This study did not show significant differences between training frequencies of 2 or 3 d/w (patients were divided in 0, 1, 2 and 3 d/w). The rest of the evidence was through prospective studies of cohorts highlighting that a frequency of 2 – 4 d/w points to a higher cardiovascular mortality reduction (Moholdt, Wisløff, Nilsen, & Slørdahl, 2008).

## RESISTANCE TRAINING

Although ET is the most used training modality in CR, other training modes like RT are effective for improving aspects related to the pathology and QoL in these patients. RT was defined by the American Heart Association as "an exercise modality in which skeletal muscle groups of upper and/or lower limbs are trained by the repetitive lifting of weights to increase muscle strength or endurance". Maximal muscle strength is the maximum force or tension generated by a muscle or group of muscles and it is usually measured by the maximum load that can be lifted in one repetition maximum (1RM) (King, 2001), and muscular endurance is the ability to do work over time (King, 2001) and it is usually determined by the number of dynamic repetitions that can be correctly completed using a fixed load (Foldvari et al., 2000).

RT is considered a safe method for cardiac patients (Dean et al., 2011; Giuliano, Karahalios, Neil, Allen, & Levinger, 2017; McCartney & McKelvie, 1996), and recent evidence has shown that RT produces important adaptations without worsening cardiac function (Santos et al., 2018). Besides this, RT has been accepted as the best method for developing or maintaining muscle mass, strength, power, and endurance (Feiereisen, Delagardelle, Vaillant, Lasar, & Beissel, 2007). Nevertheless, this training method might elicit other important adaptations that could improve the prognosis of these patients. There is evidence that shows that some cardiac patients could have skeletal muscle alterations with a lower proportion of slow twitch and a higher proportion of fast twitch (Schulze, Gielen, Schuler, & Hambrecht, 2002). Besides increases in muscular strength and endurance, RT seems to favourably alter muscle fibre type distribution and up-regulate the expression of oxidative enzymes, increasing the tolerance to exercise in cardiac patients (King, 2001). Previous studies have also reported that RT is suitable to increase CRF (Giuliano et al., 2017; Jewiss, Ostman, & Smart, 2016; Santos et al., 2018), LVEF (Bartlo, 2007; Feiereisen et al., 2007; Palevo, Keteyian, Kang, & Caputo, 2009) or endothelial function (Maiorana et al., 2011). Despite the relevance of this modality to improve the QoL and prognosis in cardiac patients, previous studies have not directly analysed the influence of the FITT variables on the effect of RT.

*Intensity*

There are different ways to prescribe RT intensity, such as a percentage of maximal dynamic strength (% of 1RM), a rating of perceived exertion (RPE) or velocity. The most used method to prescribe RT intensity in CR is as a percentage of maximal strength. The influence of the intensity on the adaptations produced by RT has been widely described and a proper management of this variable should be applied throughout the exercise training.

Previous studies, in which patients trained at intensities greater than 50% of 1RM, have shown the effectiveness of RT to produce myofibrillar shifts (Braith et al., 2005), to increase the activity of synthase and the area of fibre type I (Pu et al., 2001), LVEF (Feiereisen et al., 2007; Palevo et al., 2009) and endothelial function (Dean et al., 2011) or to reduce serum levels of inflammatory markers (Feiereisen, Vaillant, Gilson, & Delagardelle, 2013). Nevertheless, studies in which the intensity was lower did not find that RT was adequate to improve the prognosis and QoL in cardiac patients. For instance, patients who took part in the studies by Munch et al. (2018) trained at an intensity lower than 50% of 1RM and no significant changes were found in LVEF or inflammatory markers. Despite the fact that other variables could be related with the above-mentioned adaptations, future studies should analyse the role of RT intensity in this population, taking into account that a minimum level of intensity is necessary to reach important adaptations when RT is carried out in CR.

An RT program should be initiated under the supervision of an exercise science professional specialist in CR and the intensity should be low for maximum safety. In this first phase, the aim is to teach patients to perform the correct movements. Another goal in this phase to control the subjective perception of intensity along the exercise training should be to teach patients to use the RPE scale properly. To finish, an increase of intensity will allow to help to improve the prognosis in cardiac patients.

*Volume and frequency*

The volume of RT is related to the number of sets and repetitions within each set. None of previous empirical studies have analysed the influence of these variables on the effects of RT in cardiac patients. In a recent meta-analysis, Hollings, Mavros, Freeston, and Fiatarone Singh (2017) showed a direct association between sets and weekly volume with the improvement in VO2peak. This study also found that sets were also directly associated with increased workload.

None of the previous studies have analysed the effect of applying different frequency training when RT is performed in CR. The majority of these studies have used 3 sessions per week in their protocols (Jankowska et al., 2008; Munch et al., 2018; Palevo et al., 2009), complying with the current guidelines.

*Future approaches*

Previous studies have shown that the improvement of power strength is important in elderly people since it helps to increase strength and it reduces the number of falls in this population (Pamukoff et al., 2014; Tschopp, Sattelmayer, & Hilfiker, 2011). Since most cardiac patients are elderly, we think that power strength should be carried out in advanced stages of RT. To carry out power training, patients must perform the concentric phase of the movement at maximum speed and the eccentric phase at low speed.

### COMBINED RESISTANCE AND ENDURANCE TRAINING

Due to the benefit of both RT and ET, most recent guidelines recommend that RT should be performed in combination with ET (Gayda et al., 2016). In this case, the interaction effect of FITT variables makes exercise prescription and the interpretation of results more complicated. However, none of the previous reviews and meta-analyses have analysed the influence of the variables that allow to reach conclusive findings and improve the training prescription methods in CR when CT is performed. Therefore, it is necessary to know the effect to manage FITT variables to design the exercise program of CR properly and, in addition, to be able to ensure that CT has greater effects than ET or RT programs separately.

*FITT effects of CT*

In recent meta-analyses carried out with CHD (Hollings et al., 2017; Marzolini et al., 2012; Yang, He, Guo, Wang, & Zhu, 2015) and CHF (Santos et al., 2018) patients did not show differences between CT and ET when their aim was to increase VO2peak. The main problem has been to include HIIT and MCT in the meta-analysis studies as a single training variable without differentiating them. This fact has favoured that there have not been differences in VO2peak improvements between ET and CT. But even when the studies have dealt with HIIT or MCT in ET separately the results are contradictory. Yang et al. (2015) found that in studies in which a HIIT was applied a tendency in favour ET was found, while the tendency was favourable to CT when an MCT was performed. According to these results, the benefits of adding an RT to ET in order to increase VO2peak arise when an MCT is applied. However, Cornelis et al. (2016), who performed their meta-analysis considering the training method to carry out ET, reported that ET alone was more effective than CT to improve VO2peak, regardless of the training method applied. Likely, as we can see, the training method may not be the single variable to reach conclusive findings, and other variables should also be considered when direct comparisons of the training modalities on CRF are performed.

Regarding body strength levels, Hollings et al. (2017) reported that CT was more effective than ET to improve lower and upper body strength. However, the benefits could be dependent of the intensity of RT. Moghadam, Tavakol, Hadian, Bagheri, and Jalaei (2009) reported that as the intensity of RT increases, it also boosts the difference of both training modalities on the effects of body strength levels in favour of CT. In this study, they did not find differences between CT and ET when the intensity of RT was fixed at 40% of 1RM. Nevertheless, when the intensity was set at 60% or 80% of 1RM, they reported that CT is better than ET to improve body strength levels. Thus, a minimum level of intensity should be used to increase the benefits of adding an RT on body strength levels when CT is applied.

Findings are also controversial about the effect of CT on left ventricular remodelling. Previous meta-analyses have reported that CT is not suitable to improve variables related to cardiac function, such as LVEF, end-diastolic volume or end-systolic volume (Chen, Li, Zhu, & Cao, 2012; Haykowsky et al., 2007; Santos et al., 2018). However, the findings of the empirical studies included are likewise controversial. When the studies take the prescription exercise variables into account (Delagardelle et al., 2002; Feiereisen et al., 2007), especially a minimal volume (3 d/w throughout 3 months) and ET (50 – 75% of VO2peak) and RT (60% of 1RM) intensities, the authors found that CT is proper to increase LVEF and decrease end-diastolic volume and end-systolic volume. In contrast, even if the CT is longer (> 3 months), minor weekly training frequencies (< 2 d/w) and RT intensities (40% of 1RM) did not reach a significant improvement in cardiac function (Jónsdóttir, Andersen, Sigurðsson, & Sigurðsson, 2006; McKelvie et al., 2002).

In the same line, the anti-inflammatory effect of CT programmes in patients with CHF depends on a good fit of the exercise variables. When ET and RT intensities reach the minimal stimulation levels (60 – 75% VO2peak and 60 –

75% of 1RM) and a weekly frequency of 3 d/w, the effects reported were reductions in serum levels of IL-6 and TNF-α (Feiereisen et al., 2013), TNF-α, CRP and fibrinogen (de Meirelles et al., 2014); although both studies had a different duration, 3 and 6 months, respectively. Based on this finding, it seems that a larger volume is not necessary to reach an anti-inflammatory effect if you use a minimal intensity on RT and ET. In this line, longer studies (12 months) did not report a significantly decrease of plasma IL-6 and TNF-α in patients with CHF (Trippel et al., 2017). Probably, the lower inflammatory biomarker levels of the patients, and also of the CT duration, could influence these results.

## Conclusions

The individualization of ET intensity in CR programs is an important part to adjust the training load and a revaluation to recalculate intensity zones is necessary. Whenever possible, an ergoespirometry should be performed to establish the ventilatory threshold. Regarding the method used (MCT or HIIT), both of them are necessary to shape a good progression on training load. In those cases that are able to tolerate the MCT well, our proposal is to start with moderate intensity (between thresholds) and progress first increasing frequency (if it is possible) and then volume. The second step is to change some session to high aerobic intensity (between the second ventilatory threshold and VO2peak). In those patients who may not be able to tolerate MCT well, HIIT performed over the maximal aerobic power at very short intervals (30 – 60 s) may be an effective strategy (Kondamudi, Haykowsky, Forman, Berry, & Pandey, 2017). It is important to collect data to know if the patient is tolerating this training and progression well. Some variables were used to monitoring the training adaptation. The heart rate variability is one of these emerging variables, favoured by the technological advance and allowing the control of the fatigue produced by the exercise in a simple way (Javaloyes, Sarabia, Lamberts, & Moya-Ramon, 2018).

An RT program should start with a phase of familiarization to teach patients the movements and manage the RPE scale. During this phase, the exercise training should be prescribed at low intensity (< 30% of 1RM), paying special attention to the correct execution of the movement. The exercise should finish when the patient can no longer to do it correctly. The second phase should be oriented to the improvement of the endurance and coordination. For that, the intensity should be fixed at 30 – 50% of 1RM, with a high number of repetitions (15 – 25 repetitions) and little time to recover (60 – 90 s). The third phase goal is to improve muscle mass, muscle strength and other variables related to the prognosis of cardiac patients. For these aims, the intensity should be higher than 50% of 1RM.

Throughout the training period, estimations of the maximal dynamic strength should be regularly carried out to adjust the intensity properly. For this purpose, indirect methods always should be used with cardiac patients. RPE values in each exercise could help the supervisor of the session to know when it could be necessary to re-evaluate maximal dynamic strength or to increase the intensity in each exercise.

It seems that to include the CT in the CR programs could be effective as long as we make sure to reach minimal exercise intensities in ET and RT (above 60% VO2peak and 60% of 1RM) as well as a minimum of 3 exercise sessions per week. This fact, combined with at least 3 months of CT duration, would produce improvements in the prognosis and QoL in cardiac patients. Besides, all aspects related to both training modalities (ET and RT) above commented must be considered to carry out CT in CR.

Another important aspect to design CT sessions is the first training mode performed in each session or training period. We think that at the beginning of the session, in order to increase the security of the movements and to avoid the fatigue effect, RT must be performed first and later ET. However, when a patient performs each exercise properly, the design of the session should depend on the period goal.

Despite the close approaches described above, we think that the most important thing is to find the stimulation threshold in each patient to produce adaptations and manage the FITT variables properly to produce continuous improvements with each training modality in cardiac patients. The increase of the training load must be individualized for each patient and a progression must be performed when the previous training load is not enough stimulus. As we have commented at the beginning of this review, there is much heterogeneity in the findings of the previous studies, which may be due to the lack of individualization of the training protocols.

Another aspect which should be considered is that CR must be the first contact with the exercise and that patients should remain physically active throughout their life. From this point of view, the aim throughout the exercise training should perform the minimum level of exercise to reach the highest benefit, thus fulfilling one of the principles of training. This approach will also allow to manage training load properly in the future.

In order to apply the principles of individualization and progression of the training load, and supervise the correct execution of strength exercises suitably, the design of the training protocols in CR and their supervision must be carried out by personal who have an adequate formation in the correct manage of the FITT variables and other variables related to the training, like exercise science professionals or exercise physiologists.

## References

Anderson, L., Oldridge, N., Thompson, D. R., Zwisler, A. D., Rees, K., Martin, N., & Taylor, R. S. (2016). Exercise-based cardiac rehabilitation for coronary heart disease: Cochrane systematic review and meta-analysis. *Journal of the American College of Cardiology, 67*(1), 1–12. https://doi.org/10.1016/j.jacc.2015.10.044.

Bartlo, P. (2007). Evidence-based application of aerobic and resistance training in patients with congestive heart failure. *Journal Of Cardiopulmonary Rehabilitation and Prevention, 27*(6), 368–375. https://doi.org/10.1097/01.hcr.0000300263.07764.4a.

Beauchamp, A., Worcester, M., Ng, A., Murphy, B., Tatoulis, J., Grigg, L., & Goble, A. (2013). Attendance at cardiac rehabilitation is associated with lower all-cause mortality after 14 years of follow-up. *Heart, 99*(9), 620–625. http://dx.doi.org/10.1136/heartjnl-2012-303022.

Braith, R. W., Magyari, P. M., Pierce, G. L., Edwards, D. G., Hill, J. A., White, L. J., & Aranda Jr, J. M. (2005). Effect of resistance exercise on skeletal muscle myopathy in heart transplant recipients. *The American Journal of Cardiology, 95*(10), 1192–1198. https://doi.org/10.1016/j.amjcard.2005.01.048.

Briasoulis, A., Androulakis, E., Christophides, T., & Tousoulis, D. (2016). The role of inflammation and cell death in the pathogenesis, progression and treatment of heart failure. *Heart Failure Reviews, 21*(2), 169–176. https://doi.org/10.1007/s10741-016-9533-z.

Caminiti, G., Volterrani, M., Iellamo, F., Marazzi, G., Massaro, R., Miceli, M., & Rosano, G. M. (2009). Effect of long-acting testosterone treatment on functional exercise capacity, skeletal muscle performance, insulin resistance, and baroreflex sensitivity in elderly patients with chronic heart failure: a double-blind, placebo-controlled, randomized study. *Journal of the American College of Cardiology, 54*(10), 919–927. https://doi.org/10.1016/j.jacc.2009.04.078.

Cesari, F., Sofi, F., Caporale, R., Capalbo, A., Marcucci, R., Macchi, C., & Gori, A. M. (2009). Relationship between exercise capacity, endothelial progenitor cells and cytochemokines in patients undergoing cardiac rehabilitation. *Thrombosis and Haemostasis, 101*(3), 521–526.

Conraads, V. M., Pattyn, N., De Maeyer, C., Beckers, P. J., Coeckelberghs, E., Cornelissen, V. A., & Hoymans, V. Y. (2015). Aerobic interval training and continuous training equally improve aerobic exercise capacity in patients with coronary artery disease: the SAINTEX-CAD study. *International Journal of Cardiology, 179*, 203-210. https://doi.org/10.1016/j.ijcard.2014.10.155.

Cornelis, J., Beckers, P., Taeymans, J., Vrints, C., & Vissers, D. (2016). Comparing exercise training modalities in heart failure: a systematic review and meta-analysis. *International Journal of Cardiology, 221*, 867–876. https://doi.org/10.1016/j.ijcard.2016.07.105.

Cornelissen, V. A., Buys, R., & Pattyn, N. (2017). High intensity interval training in coronary artery disease patients, is it worth the effort? *European Journal of Preventive Cardiolog,. 24*(16), 1692–1695. https://doi.org/10.1177/2047487317734051.

Cornelissen, V. A., Verheyden, B., Aubert, A. E., & Fagard, R. H. (2010). Effects of aerobic training intensity on resting, exercise and post-exercise blood pressure, heart rate and heart-rate variability. *Journal of Human Hypertension, 24*(3), 175–182. https://doi.org/10.1038/jhh.2009.51.

Chen, Y., Li, Z., Zhu, M., & Cao, Y. (2012). Effects of exercise training on left ventricular remodelling in heart failure patients: an updated meta-analysis of randomised controlled trials. *International Journal of Clinical Practice, 66*(8), 782–791. https://doi.org/10.1111/j.1742-1241.2012.02942.x.

De Meirelles, L. R., Matsuura, C., Castro Resende, A. de, Antunes Salgado, Â., Rodrigues Pereira, N., Coscarelli, P. G., ... & Brunini, T. M. (2014). Chronic exercise leads to antiaggregant, antioxidant and anti-inflammatory effects in heart failure patients. *European Journal of Preventive Cardiology*, 21(10), 1225–1232. https://doi.org/10.1177/2047487313491662.

De Schutter, A., Kachur, S., Lavie, C. J., Menezes, A., Shum, K. K., Bangalore, S., & Milani, R. V. (2018). Cardiac rehabilitation fitness changes and subsequent survival. *European Heart Journal Quality of Care and Clinical Outcomes, 4*(3), 173–179. https://doi.org/10.1093/ehjqcco/qcy018.

Dean, A. S., Libonati, J. R., Madonna, D., Ratcliffe, S. J., & Margulies, K. B. (2011). Resistance training improves vasoreactivity in end-stage heart failure patients on inotropic support. *Journal of Cardiovascular Nursing, 26*(3), 218–223. https://doi.org/10.1097/jcn.0b013e3181f29a46.

Delagardelle, C., Feiereisen, P., Autier, P., Shita, R., Krecke, R., & Beissel, J. (2002). Strength/endurance training versus endurance training in congestive heart failure. *Medicine and Science in Sports and Exercise, 34*(12), 1868–1872. https://doi.org/10.1249/01.mss.0000040997.94707.6F.

Dressendorfer, R. H., Franklin, B. A., Cameron, J. L., Trahan, K. J., Gordon, S., & Timmis, G. C. (1995). Exercise training frequency in early post-infarction cardiac rehabilitation. Influence on aerobic conditioning. *Journal of Cardiopulmonary Rehabilitation, 15*(4), 269–276.

Ellingsen, Ø., Halle, M., Conraads, V., Støylen, A., Dalen, H., Delagardelle, C., & Van Craenenbroeck, E. M. (2017). High-Intensity interval training in patients with heart failure with reduced ejection fraction clinical perspective. *Circulation, 135*(9), 839–849. https://doi.org/10.1161/circulationaha.116.022924.

Elliott, A. D., Rajopadhyaya, K., Bentley, D. J., Beltrame, J. F., & Aromataris, E. C. (2015). Interval training versus continuous exercise in patients with coronary artery disease: a meta-analysis. *Heart, Lung and Circulation, 24*(2), 149–157. https://doi.org/10.1016/j.hlc.2014.09.001.

Feiereisen, P., Delagardelle, C., Vaillant, M., Lasar, Y., & Beissel, J. (2007). Is strength training the more efficient training modality in chronic heart failure? *Medicine and Science in Sports and Exercise, 39*(11), 1910–1917. https://doi.org/10.1249/mss.0b013e31814fb545.

Feiereisen, P., Vaillant, M., Gilson, G., & Delagardelle, C. (2013). Effects of different training modalities on circulating anabolic/catabolic markers in chronic heart failure. *Journal of Cardiopulmonary Rehabilitation and Prevention, 33*(5), 303–308. https://doi.org/10.1097/hcr.0b013e3182a1e4e5.

Fletcher, G. F., Balady, G. J., Amsterdam, E. A., Chaitman, B., Eckel, R., Fleg, J., & Rodney, R. (2001). Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association. *Circulation, 104*(14), 1694–1740.

Foldvari, M., Clark, M., Laviolette, L. C., Bernstein, M. A., Kaliton, D., Castaneda, C., & Singh, M. A. F. (2000). Association of muscle power with functional status in community-dwelling elderly women. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 55*(4), M192–M199.

Garber, C. E., Blissmer, B., Deschenes, M. R., Franklin, B. A., Lamonte, M. J., Lee, I.-M., & Swain, D. P. (2011). American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Medicine and Science in Sports and Exercise, 43*(7), 1334–1359. https://doi.org/10.1249/mss.0b013e318213fefb.

García, I. B., Arias, J. Á. R., Campo, D. J. R., González-Moro, I. M., & Poyatos, M. C. (2018). High-intensity Interval Training Dosage for Heart Failure and Coronary Artery Disease Cardiac Rehabilitation. A Systematic Review and Meta-analysis. *Revista Española de Cardiología (English Edition), Apr 9*. https://doi.org/10.1016/j.rec.2018.02.015.

Gayda, M., Ribeiro, P. A., Juneau, M., & Nigam, A. (2016). Comparison of different forms of exercise training in patients with cardiac disease: where does high-intensity interval training fit? *Canadian Journal of Cardiology, 32*(4), 485–494. https://doi.org/10.1016/j.cjca.2016.01.017.

Gibala, M. J., Little, J. P., Macdonald, M. J., & Hawley, J. A. (2012). Physiological adaptations to low-volume, high-intensity interval training in health and disease. *Journal of Physiology, 590*(5), 1077–1084. https://doi.org/10.1113/jphysiol.2011.224725.

Gielen, S., Adams, V., Möbius-Winkler, S., Linke, A., Erbs, S., Yu, J., & 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, 42*(5), 861–868.

Giuliano, C., Karahalios, A., Neil, C., Allen, J., & Levinger, I. (2017). The effects of resistance training on muscle strength, quality of life and aerobic capacity in patients with chronic heart failure—A meta-analysis. *International Journal of Cardiology, 227*, 413–423. https://doi.org/10.1016/j.ijcard.2016.11.023.

Gomes-Neto, M., Durães, A. R., Reis, H. F. C. d., Neves, V. R., Martinez, B. P., & Carvalho, V. O. (2017). High-intensity interval training versus moderate-intensity continuous training on exercise capacity and quality of life in patients with coronary artery disease: a systematic review and meta-analysis. *European Journal of Preventive Cardiology, 24*(16), 1696–1707. https://doi.org/10.1177/2047487317728370.

Hammill, B. G., Curtis, L. H., Schulman, K. A., & Whellan, D. J. (2010). Relationship between cardiac rehabilitation and long-term risks of death and myocardial infarction among elderly Medicare beneficiaries. *Circulation, 121*(1), 63–70. https://doi.org/10.1161/circulationaha.109.876383.

Haykowsky, M. J. (2011). Left ventricular remodelling and the athlete's heart: time to revisit the Morganroth hypothesis. *Journal of Physiology, 589*(Pt 24), 5915. https://doi.org/10.1113/jphysiol.2011.221903.

Haykowsky, M. J., Liang, Y., Pechter, D., Jones, L. W., McAlister, F. A., & Clark, A. M. (2007). A meta-analysis of the effect of exercise training on left ventricular remodeling in heart failure patients: the benefit depends on the type of training performed. *Journal of the American College of Cardiology, 49*(24), 2329–2336. https://doi.org/10.1016/j.jacc.2007.02.055.

Hoier, B., & Hellsten, Y. (2014). Exercise-induced capillary growth in human skeletal muscle and the dynamics of VEGF. *Microcirculation, 21*(4), 301–314. https://doi.org/10.1111/micc.12117.

Hollings, M., Mavros, Y., Freeston, J., & Fiatarone Singh, M. (2017). The effect of progressive resistance training on aerobic fitness and strength in adults with coronary heart disease: a systematic review and meta-analysis of randomised controlled trials. *European Journal of Preventive Cardiology, 24*(12), 1242–1259. https://doi.org/10.1177/2047487317713329.

Ismail, H., McFarlane, J. R., Nojoumian, A. H., Dieberg, G., & Smart, N. A. (2013). Clinical outcomes and cardiovascular responses to different exercise training intensities in patients with heart failure: a systematic review and meta-analysis. *JACC: Heart Failure, 1*(6), 514–522. https://doi.org/10.1016/j.jchf.2013.08.006.

Jankowska, E. A., Wegrzynowska, K., Superlak, M., Nowakowska, K., Lazorczyk, M., Biel, B., & Wozniewski, M. (2008). The 12-week progressive quadriceps resistance training improves muscle strength, exercise capacity and quality of life in patients with stable chronic heart failure. *International Journal of Cardiology, 130*(1), 36–43. https://doi.org/10.1016/j.ijcard.2007.07.158.

Javaloyes, A., Sarabia, J. M., Lamberts, R. P., & Moya-Ramon, M. (2018). Training Prescription Guided by Heart Rate Variability in Cycling. *International Journal of Sports Physiology and Performance*, 1–28. https://doi.org/10.1123/ijspp.2018-0122.

Jennett, S. (2008). *Churchill Livingstone's Dictionary of Sport and Exercise Science and Medicine E-Book*: Elsevier Health Sciences.

Jewiss, D., Ostman, C., & Smart, N. (2016). The effect of resistance training on clinical outcomes in heart failure: a systematic review and meta-analysis. *International Journal of Cardiology, 221*, 674–681. https://doi.org/10.1016/j.ijcard.2016.07.046.

Jónsdóttir, S., Andersen, K. K., Sigurðsson, A. F., & Sigurðsson, S. B. (2006). The effect of physical training in chronic heart failure. *European Journal of Heart Failure, 8*(1), 97–101. https://doi.org/10.1016/j.ejheart.2005.05.002.

King, L. (2001). The effects of resistance exercise on skeletal muscle abnormalities in patients with advanced heart failure. *Progress in Cardiovascular Nursing, 16*(4), 142–151.

Kodama, S., Saito, K., Tanaka, S., Maki, M., Yachi, Y., Asumi, M., & Sone, H. (2009). Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. *Jama, 301*(19), 2024–2035. https://doi.org/10.1001/jama.2009.681.

Kondamudi, N., Haykowsky, M., Forman, D. E., Berry, J. D., & Pandey, A. (2017). Exercise Training for Prevention and Treatment of Heart Failure. *Progress in Cardiovascular Disease, 60*(1), 115–120. https://doi.org/10.1016/j.pcad.2017.07.001.

Konstam, M. A., Kramer, D. G., Patel, A. R., Maron, M. S., & Udelson, J. E. (2011). Left ventricular remodeling in heart failure: current concepts in clinical significance and assessment. *JACC: Cardiovascular Imaging, 4*(1), 98–108. https://doi.org/10.1016/j.jcmg.2010.10.008.

Kraal, J. J., Vromen, T., Spee, R., Kemps, H. M., & Peek, N. (2017). The influence of training characteristics on the effect of exercise training in patients with coronary artery disease: systematic review and meta-regression analysis. *International Journal of Cardiology, 245*, 52–58. https://doi.org/10.1016/j.ijcard.2017.07.051.

Leggio, M., Bendini, M. G., D'Emidio, S., Caldarone, E., Lombardi, M., Severi, P., & Mazza, A. (2018). Exercise dose in clinical practice: Right is better than more. *Cardiology Journal, 25*(2), 287–288. https://doi.org/10.5603/cj.2018.0040.

Levinger, I., Bronks, R., Cody, D. V., Linton, I., & Davie, A. (2005). Resistance training for chronic heart failure patients on beta blocker medications. *International Journal of Cardiology, 102*(3), 493–499. https://doi.org/10.1016/j.ijcard.2004.05.061.

Liou, K., Ho, S., Fildes, J., & Ooi, S.-Y. (2016). High intensity interval versus moderate intensity continuous training in patients with coronary artery disease: a meta-analysis of physiological and clinical parameters. *Heart, Lung and Circulation, 25*(2), 166–174. https://doi.org/10.1016/j.hlc.2015.06.828.

Maiorana, A. J., Naylor, L. H., Exterkate, A., Swart, A., Thijssen, D. H., Lam, K., & Green, D. J. (2011). The impact of exercise training on conduit artery wall thickness and remodeling in chronic heart failure patients. *Hypertension, 57*(1), 56–62. https://doi.org/10.1161/hypertensionaha.110.163022.

Mann, S., Beedie, C., & Jimenez, A. (2014). Differential effects of aerobic exercise, resistance training and combined exercise modalities on cholesterol and the lipid profile: review, synthesis and recommendations. *Sports Medicine, 44*(2), 211–221. https://doi.org/10.1007/s40279-013-0110-5.

Marzolini, S., Oh, P. I., & Brooks, D. (2012). Effect of combined aerobic and resistance training versus aerobic training alone in individuals with coronary artery disease: a meta-analysis. *European Journal of Preventive Cardiology, 19*(1), 81–94. https://doi.org/10.1177/1741826710393197.

McCartney, N., & McKelvie, R. S. (1996). The role of resistance training in patients with cardiac disease. *Journal Of Cardiovascular Risk, 3*(2), 160-166.

McKelvie, R. S., Teo, K. K., Roberts, R., McCartney, N., Humen, D., Montague, T., & Yusuf, S. (2002). Effects of exercise training in patients with heart failure: the Exercise Rehabilitation Trial (EXERT). *American Heart Journal, 144*(1), 23–30.

Miche, E., Herrmann, G., Nowak, M., Wirtz, U., Tietz, M., Hürst, M., & Radzewitz, A. (2006). Effect of an exercise training program on endothelial dysfunction in diabetic and non-diabetic patients with severe chronic heart failure. *Clinical Research in Cardiology, 95*(1), i117–i124. https://doi.org/10.1007/s00392-006-1106-z.

Milani, R. V., Lavie, C. J., & Mehra, M. R. (2004). Reduction in C-reactive protein through cardiac rehabilitation and exercise training. *Journal of American College of Cardiology, 43*(6), 1056–1061. https://doi.org/10.1016/j.jacc.2003.10.041.

Moghadam, B. A., Tavakol, K., Hadian, M. R., Bagheri, H., & Jalaei, S. (2009). Phase III cardiac rehabilitation after CABG: Combined aerobic and strengthening exercise protocols. *International Journal of Therapy and Rehabilitation, 16*(8), 420–430. https://doi.org/10.12968/ijtr.2009.16.8.43480.

Moholdt, T., Wisløff, U., Nilsen, T. I. L., & Slørdahl, S. A. (2008). Physical activity and mortality in men and women with coronary heart disease: a prospective population-based cohort study in Norway (the HUNT study). *European Journal of Cardiovascular Prevention and Rehabilitation, 15*(6), 639–645. https://doi.org/10.1097/hjr.0b013e3283101671.

Mora, S., Cook, N., Buring, J. E., Ridker, P. M., & Lee, I. M. (2007). Physical activity and reduced risk of cardiovascular events: potential mediating mechanisms. *Circulation, 116*(19), 2110–2118. https://doi.org/10.1161/circulationaha.107.729939.

Munch, G. W., Rosenmeier, J. B., Petersen, M., Rinnov, A. R., Iepsen, U. W., Pedersen, B. K., & Mortensen, S. P. (2018). Comparative Effectiveness of Low-Volume Time-Efficient Resistance Training Versus Endurance Training in Patients With Heart Failure. *Journal of Cardiopulmonary Rehabilitation and Prevention, 38*(3), 175–181. https://doi.org/10.1097/hcr.0000000000000304.

Munk, P. S., Staal, E. M., Butt, N., Isaksen, K., & Larsen, A. I. (2009). High-intensity interval training may reduce in-stent restenosis following percutaneous coronary intervention with stent implantation A randomized controlled trial evaluating the relationship to endothelial function and inflammation. *American Heart Journal, 158*(5), 734–741. https://doi.org/10.1016/j.ahj.2009.08.021.

Neto, M. G., Durães, A. R., Conceição, L. S. R., Saquetto, M. B., Ellingsen, Ø., & Carvalho, V. O. (2018). High intensity interval training versus moderate intensity continuous training on exercise capacity and quality of life in patients with heart failure with reduced ejection fraction: A systematic review and meta-analysis. *International Journal of Cardiology, 261*, 134–141. https://doi.org/10.1016/j.ijcard.2018.02.076.

Nichols, M., Townsend, N., Scarborough, P., & Rayner, M. (2013). Cardiovascular disease in Europe: epidemiological update. *European Heart Journal, 34*(39), 3028–3034. https://doi.org/10.1093/eurheartj/eht356.

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. https://doi.org/10.1016/j.amjcard.2008.07.016

Palevo, G., Keteyian, S. J., Kang, M., & Caputo, J. L. (2009). Resistance exercise training improves heart function and physical fitness in stable patients with heart failure. *Journal of Cardiopulmonary Rehabilitation and Prevention, 29*(5), 294–298. https://doi.org/10.1097/hcr.0b013e3181ac784b.

Pamukoff, D. N., Haakonssen, E. C., Zaccaria, J. A., Madigan, M. L., Miller, M. E., & Marsh, A. P. (2014). The effects of strength and power training on single-step balance recovery in older adults: a preliminary study. *Clinical Interventions in Aging, 9*, 697. https://doi.org/10.2147/cia.s59310.

Parrinello, G., Torres, D., Paterna, S., di Pasquale, P., Trapanese, C., & Licata, G. (2010). Short-term walking physical training and changes in body hydration status, B-type natriuretic peptide and C-reactive protein levels in compensated congestive heart failure. *International Journal of Cardiology, 144*(1), 97–100. https://doi.org/10.1016/j.ijcard.2008.12.130.

Pattyn, N., Beulque, R., & Cornelissen, V. (2018). Aerobic interval vs. continuous training in patients with coronary artery disease or heart failure: an updated systematic review and meta-analysis with a focus on secondary outcomes. *Sports Medicine*, *48,* 1189. https://doi.org/10.1007/s40279-018-0885-5.

Paul, J. D., Powell, T. M., Thompson, M., Benjamin, M., Rodrigo, M., Carlow, A., & Cannon, R. O., 3rd. (2007). Endothelial progenitor cell mobilization and increased intravascular nitric oxide in patients undergoing cardiac rehabilitation. *Journal of Cardiopulmonary Rehabilitation and Prevention, 27*(2), 65–73. https://doi.org/10.1097/01.hcr.0000265031.10145.50.

Pearson, M., Mungovan, S., & Smart, N. (2018). Effect of aerobic and resistance training on inflammatory markers in heart failure patients: systematic review and meta-analysis. *Heart Failure Reviews, 23*(2), 209–223. https://doi.org/10.1007/s10741-018-9677-0.

Pearson, M., & Smart, N. (2017). Effect of exercise training on endothelial function in heart failure patients: a systematic review meta-analysis. *International Journal of Cardiology, 231*, 234–243. https://doi.org/10.1016/j.ijcard.2016.12.145.

Piepoli, M. F., Corra, U., Benzer, W., Bjarnason-Wehrens, B., Dendale, P., Gaita, D., & Schmid, J. P. (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. *Europena Journal of Cardiovascular Prevention and Rehabilitation, 17*(1), 1–17. https://doi.org/10.1097/hjr.0b013e3283313592.

Pu, C. T., Johnson, M. T., Forman, D. E., Hausdorff, J. M., Roubenoff, R., Foldvari, M., & Singh, M. A. F. (2001). Randomized trial of progressive resistance training to counteract the myopathy of chronic heart failure. *Journal of Applied Physiology, 90*(6), 2341–2350. https://doi.org/10.1152/jappl.2001.90.6.2341.

Salehi, Z., Salehi, K., Moeini, M., Kargarfard, M., & Sadeghi, M. (2017). The effect of resistance exercise on lipid profile of coronary artery disease patients: a randomized clinical trial. *Iranian Journal of Nursing and Midwifery Research, 22*(2), 112. https://doi.org/10.4103/ijnmr.ijnmr_385_14.

Sandri, M., Viehmann, M., Adams, V., Rabald, K., Mangner, N., Höllriegel, R., & Kirsch, K. (2016). Chronic heart failure and aging–effects of exercise training on endothelial function and mechanisms of endothelial regeneration: Results from the Leipzig Exercise Intervention in Chronic heart failure and Aging (LEICA) study. *European Journal of Cardiovascular Prevention and Rehabilitation, 23*(4), 349–358.

Santos, F. V., Chiappa, G. R., Ramalho, S. H. R., de Lima, A. C. G. B., de Souza, F. S. J., Cahalin, L. P., & Cipriano, G. (2018). Resistance exercise enhances oxygen uptake without worsening cardiac function in patients with systolic heart failure: a systematic review and meta-analysis. *Heart Failure Reviews, 23*(1), 73–89. https://doi.org/10.1007/s10741-017-9658-8.

Scharhag-Rosenberger, F., Meyer, T., Gäßler, N., Faude, O., & Kindermann, W. (2010). Exercise at given percentages of $VO_2$max: heterogeneous metabolic responses between individuals. *Journal of Science and Medicine in Sport, 13*(1), 74–79. https://doi.org/10.1016/j.jsams.2008.12.626.

Schnohr, P., Marott, J. L., & O'Keefe, J. H. (2015). Reply: Exercise and Mortality Reduction: Recurring Reverse J-or U-Curves. *Journal of the American College of Cardiology, 65*(24), 2674–2676. https://doi.org/10.1016/j.jacc.2015.04.023.

Schulze, P. C., Gielen, S., Schuler, G., & Hambrecht, R. (2002). Chronic heart failure and skeletal muscle catabolism: effects of exercise training. *International Journal of Cardiology, 85*(1), 141–149.

Shirazi, L. F., Bissett, J., Romeo, F., & Mehta, J. L. (2017). Role of inflammation in heart failure. *Current Atherosclerosis Reports, 19*(6), 27. https://doi.org/10.1007/s11883-017-0660-3.

Steg, P. G., James, S. K., Atar, D., Badano, L. P., Blomstrom-Lundqvist, C., Borger, M. A., & Zahger, D. (2012). ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *European Heart Journal, 33*(20), 2569–2619. https://doi.org/10.1093/eurheartj/ehs215.

Swardfager, W., Herrmann, N., Cornish, S., Mazereeuw, G., Marzolini, S., Sham, L., & Lanctôt, K. L. (2012). Exercise intervention and inflammatory markers in coronary artery disease: a meta-analysis. *American Heart Journal, 163*(4), 666-676. e663. https://doi.org/10.1016/j.ahj.2011.12.017.

Taylor, C., Tsakirides, C., Moxon, J., Moxon, J. W., Dudfield, M., Witte, K., & Carroll, S. (2017). Exercise dose and all-cause mortality within extended cardiac rehabilitation: a cohort study. *Open Heart, 4*(2), e000623. https://doi.org/10.1136/openhrt-2017-000623

Trippel, T. D., Holzendorf, V., Halle, M., Gelbrich, G., Nolte, K., Duvinage, A., & Wachter, R. (2017). Ghrelin and hormonal markers under exercise training in patients with heart failure with preserved ejection fraction: results from the Ex-DHF pilot study. *ESC Heart Failure, 4*(1), 56–65. https://doi.org/10.1002/ehf2.12109.

Tschopp, M., Sattelmayer, M. K., & Hilfiker, R. (2011). Is power training or conventional resistance training better for function in elderly persons? A meta-analysis. *Age and Ageing, 40*(5), 549–556. https://doi.org/10.1093/ageing/afr005.

Valkeinen, H., Aaltonen, S., & Kujala, U. M. (2010). Effects of exercise training on oxygen uptake in coronary heart disease: a systematic review and meta-analysis. *Scandinavian Journal of Medicine and Science in Sports, 20*(4), 545–555. https://doi.org/10.1111/j.1600-0838.2010.01133.x.

Van Linthout, S., & Tschöpe, C. (2017). Inflammation–Cause or Consequence of Heart Failure or Both? *Current Heart Failure Reports, 14*(4), 251–265. https://doi.org/10.1007/s11897-017-0337-9.

Vanhees, L., Geladas, N., Hansen, D., Kouidi, E., Niebauer, J., Reiner, Ž., & Börjesson, M. (2012). Importance of characteristics and modalities of physical activity and exercise in the management of cardiovascular health in individuals with cardiovascular risk factors: recommendations from the EACPR (Part II). *European Journal of Preventive Cardiology, 19*(5), 1005–1033. https://doi.org/10.1177/1741826711430926.

Villelabeitia-Jaureguizar, K., Vicente-Campos, D., Berenguel Senen, A., Veronica Hernandez Jimenez, V., Lorena Ruiz Bautista, L., Barrios Garrido-Lestache, M. E., & Lopez Chicharro, J. (2018). Mechanical efficiency of high versus moderate intensity aerobic exercise in coronary heart disease patients: A randomized clinical trial. *Cardiology Journal*, *May*, 10. https://doi.org/10.5603/cj.a2018.0052.

Walther, C., Mobius-Winkler, S., Linke, A., Bruegel, M., Thiery, J., Schuler, G., & Halbrecht, R. (2008). Regular exercise training compared with percutaneous intervention leads to a reduction of inflammatory markers and cardiovascular events in patients with coronary artery disease. *Europena Journal of Cardiovascular Prevention and Rehabilitation, 15*(1), 107–112. https://doi.org/10.1097/hjr.0b013e3282f29aa6.

Wolpern, A. E., Burgos, D. J., Janot, J. M., & Dalleck, L. C. (2015). Is a threshold-based model a superior method to the relative percent concept for establishing individual exercise intensity? a randomized controlled trial. *BMC Sports Science, Medicine and Rehabilitation, 4*(7), 16. https://doi.org/10.1186/s13102-015-0011-z.

Yamamoto, S., Hotta, K., Ota, E., Mori, R., & Matsunaga, A. (2016). Effects of resistance training on muscle strength, exercise capacity, and mobility in middle-aged and elderly patients with coronary artery disease: A meta-analysis. *Journal of Cardiology, 68*(2), 125–134. https://doi.org/10.1016/j.jjcc.2015.09.005.

Yang, Y. J., He, X. H., Guo, H. Y., Wang, X. Q., & Zhu, Y. (2015). Efficiency of muscle strength training on motor function in patients with coronary artery disease: a meta-analysis. *International Journal of Clinical and Experimental Medicine, 8*(10), 17536.