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Clinical Review

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Cardiovascular disease, Cardiac rehabilitation, Heart failure, High intensity interval training

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Abstract

Cardiac rehabilitation is a key component in the secondary prevention of cardiovascular disease. However, uptake and adherence to programmes is suboptimal, especially for patients with heart failure. Traditionally, cardiac rehabilitation programmes have involved moderate-intensity continuous training; however, there is growing evidence that high-intensity interval training can produce equal or superior effects in both healthy and diseased populations. High-intensity interval training has already been shown to be both safe and effective, but the optimal protocols and delivery mechanisms are yet to be determined. Despite this, high-intensity interval training has the potential to offer an alternative mechanism of cardiac rehabilitation delivery to patients with heart failure, with the possibility of overcoming some of the challenges usually faced (e.g. patients' lack of time) in implementing successful cardiac rehabilitation programmes. This article aims to summarise the current knowledge surrounding the inclusion of high-intensity interval training in cardiac rehabilitation programmes, specifically focusing on those patients living with heart failure.

Introduction

Cardiovascular disease, including coronary heart disease and heart failure, is the leading cause of death worldwide (World Health Organization (WHO), 2018). An important intervention in the secondary prevention of cardiovascular disease is comprehensive cardiac rehabilitation, which involves education, lifestyle behaviour modification, psychological support and exercise (Anderson et al, 2016). These exercise programmes have traditionally involved moderate-intensity continuous training, which has been shown to be effective in reducing cardiovascular mortality, incidence of myocardial infarction and hospital readmissions, as well as improving quality of life for patients with coronary heart disease (Anderson et al, 2016). Although a more recent Cochrane review, carried out by Long et al, focusing specifically on heart failure, showed that compared to a no-exercise control, cardiac rehabilitation had no impact on mortality in the short term (<12 months) (Long et al, 2019). This same review did show however that for patients with heart failure, cardiac rehabilitation reduces hospital readmissions and improves quality of life. It is worth noting that the evidence for these are

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of low-moderate and low-quality respectively. Currently, uptake and adherence to current cardiac rehabilitation programmes is suboptimal with participation of eligible patients (both coronary heart disease and heart failure) reported as a mean of 50% in England, Wales and Northern Ireland (British Heart Foundation, 2019). Both locally and nationally, the referral of patients with heart failure to cardiac rehabilitation programmes is even less, with a recent report finding that only 10% of eligible patients with heart failure were referred for exercise-based cardiac rehabilitation (Golwala et al, 2015).

This is in part due to the majority of NHS cardiac rehabilitation services having no specific heart failure programme, with a national survey conducted in 2011/2012 indicating that only 16% of UK centres provide a specific rehabilitation programme for those with heart failure (Dalal et al, 2012). Clearly, novel approaches and new ways of thinking are required in order to increase participation and completion of cardiac rehabilitation programmes for patients with heart failure. One area of growing interest is around the use of high-intensity interval training, with recent systematic reviews showing that it is safe and effective for improving cardiovascular fitness in patients with both cardiovascular disease and heart failure (Hannan et al, 2018; Wewege et al, 2018).

Heart failure

Currently in the UK, around 920 000 people are affected by heart failure (Conrad et al, 2018)—predominantly within the older population, with incidence and prevalence increasing steeply with age. The average age of diagnosis is 77 years (Conrad et al, 2018). Patients with heart failure experience many symptoms including breathlessness, fluid retention, fatigue and marked reductions in exercise capacity. These symptoms have detrimental effects on daily living, health-related quality of life, hospital admission rate and mortality (Working Group on Cardiac Rehabilitation and Exercise Physiology and Working Group on Heart Failure of the European Society of Cardiology, 2001), all of which contribute to higher healthcare costs (Ziaeian and Fonarow, 2016). It is estimated that the total annual cost of heart failure to the UK NHS is currently around £1 billion—with approximately 70% of this attributed to hospitalisation (The Lancet, 2011).

Heart failure has two main subcategories; approximately half of patients have impaired left ventricular contraction, known as heart failure with reduced ejection fraction, while the other half do not have impaired ventricular contraction and are described as having heart failure with a preserved ejection fraction (Yancy et al, 2013). The majority of drug and device trials showing benefit have focused on patients with heart failure with reduced ejection fraction. The drug and device trials in patients with heart failure with a preserved ejection fraction have produced disappointing results and have been unable to demonstrate any treatment for the benefit of patients with heart failure with a preserved ejection fraction or which lowers their mortality (Holland et al, 2011). The lack of effective pharmacological treatments for patients with heart failure with a preserved ejection fraction is perhaps partly owing to the limited understanding of the disease's complex pathophysiology.

Heart failure and exercise

A major symptom in patients with heart failure (both heart failure with a preserved ejection fraction and heart failure with reduced ejection fraction) is reduced exercise tolerance, which is also a principal predictor of hospital readmission and mortality (Kato et al, 2015). Heart failure severity can be measured by this reduction in exercise tolerance and O_2 transport-use pathway impairment (Weber et al, 1982; Poole et al, 2011; Rossiter et al, 2011). Pathophysiological mechanisms of impaired exercise tolerance in heart failure are summarised in *Figure 1*; it is worth noting that much more is known and understood about the causes of dysfunction in heart failure with reduced ejection fraction than heart failure with a preserved ejection fraction. Reduced exercise tolerance can be measured as a decreased peak oxygen consumption (VO_{2peak}) during a cardiopulmonary exercise test.

Figure 1. Mechanisms of decreased exercise tolerance in heart failure patients include decreased myocardial contractility, diastolic impairment, increased peripheral resistance, functional mitral regurgitation, chronotropic incompetence, inadequate distribution of blood flow (i.e. failure to direct CO to the exercising muscles), abnormal skeletal muscle metabolism, endothelial dysfunction, abnormally high ergoreflex activation and functional iron deficiency (Piña et al, 2003; Conraads et al, 2013).

Exercise has long been established as a safe and effective therapy for patients with heart disease. As far back as 250 years ago, William Heberden discovered that regular exercise helped restore physiological function and improved morbidity and mortality in patients with angina (Willius and Keys, 1961). There is a wealth of evidence supporting the use of exercise training and cardiac rehabilitation in the ongoing treatment of patients with heart failure (Coats et al, 1992; Golwala et al, 2015; Fleg et al, 2015; Benjamin et al, 2018; National Institute for Health and Care Excellence (NICE), 2018). Recent studies have demonstrated the ability of exercise therapy to improve VO_{2peak}, muscle strength, exercise tolerance, health-related quality of life and left-ventricular remodeling, and reduce heart failure-specific hospitalisation (Haykowsky et al, 2007; O'Connor et al, 2009; Haykowsky et al, 2013; Taylor et al, 2014; Forman et al, 2015).

Although drug treatment can help to achieve some of these outcomes, to date, only exercise training has the ability to reverse deficits in skeletal muscle oxygenation and improve exercise tolerance. Given the lack of effective pharmacological treatment available for heart failure with a preserved ejection fraction, exercise and cardiac rehabilitation may have the potential for even more benefit in this group of patients, than in those patients with heart failure with reduced ejection fraction.

As previously mentioned, despite the well-recognised benefits and recommendations in clinical guidelines, the referral and uptake of cardiac rehabilitation by patients with heart failure remains low. One reason for this could be the lack of heart failure-specific cardiac rehabilitation (CR_{HF}) (Dalal et al, 2012). Within those that are referred, attendance and completion is low. To date, issues surrounding adherence (classified as meeting at least 80% of the recommended dose) to exercise programmes has mainly been documented in heart failure with reduced ejection fraction (Deka et al, 2017); however, it can be hypothesised that similar issues would be present in a population with heart failure with a preserved ejection fraction. When considering exercise adherence and how to improve it, it is important to consider barriers to participation. Some of the barriers cited, among others, are: lack of time, lack of perceived need, and difficulties accessing specialist equipment (Dalal and Doherty, 2015; Doherty et al, 2018). However, it is worth noting that much of the reported data is for cardiac rehabilitation for patients with coronary heart disease or for general cardiac rehabilitation with no disease type stated.

Exercise training has been shown to be a safe and low-cost intervention to improve heart failure symptoms and survival (Fleg et al, 2015). However, a lack of dedicated cardiac rehabilitation programmes for heart failure and low adherence to current exercise protocols support the need for new strategies in delivering cardiac rehabilitation to all patients with heart failure. One such strategy is high-intensity interval training. Although formal recommendations continue to focus on aerobic continuous training, guidelines are broadening to recognise the potential benefit of high-intensity interval training for certain populations within patient groups (NICE, 2018).

High-intensity interval training

High-intensity interval training has developed over the years since first being described in the 1920s and 1930s in the training regimes of middle-distance athletes (Hill et al, 1924; Seiler and Tønnessen, 2009). It is defined as either repeated short (<45 seconds) to long (2–4 minutes) bouts of high (not maximal)-intensity exercise or short (≤10 seconds, repeated sprint sequences) or long (20–30 second sprint interval session) all-out sprints interspersed with recovery periods (Buchheit and Laursen, 2013). The height of intensity has yet to be clearly defined (Biddle and Batterham, 2015), with most research quoting intensities 85% to 95% of VO_{2peak}/max heart rate. There is robust evidence of the efficacy of high-intensity interval training to improve cardiovascular and metabolic function in both healthy and disease populations (Jelleyman et al, 2015; Ramos et al, 2015), with meta analyses consistently demonstrating the association of exercise intensity and improvement in VO_{2peak} (Ismail et al, 2013).

High-intensity interval training protocols vary widely, in part as a result of the broad definition of high-intensity interval training, with physiological adaptations determined by intensity, duration and number of intervals performed, as well as the duration and intensity of recovery. Despite this variation, when compared on a matched-work basis or equivalent energy expenditure, high-intensity interval-based training elicits equal or even superior changes in physiological performance and health-related markers when compared with moderate-intensity continuous training (Wisløff et al, 2007). High-intensity interval training also has the additional benefits of being relatively time-efficient compared with moderate-intensity continuous training, with the ability to elicit equal or greater enjoyment compared with moderate-intensity continuous training and show similar training adherence compared to moderate-intensity continuous training in both laboratory and clinical environments (Jung et al, 2014; Martinez et al, 2015; Vella et al, 2017)

Despite the reduced total exercise volume and the lower time commitment, the physiological benefits/remodelling seen as a result of high-intensity interval training are comparable to moderate-intensity continuous training (Gibala et al, 2012). In response to high-intensity interval training, the body undergoes changes in cardiovascular function and improved skeletal muscle metabolic control

(Burgomaster et al, 2008; Rakobowchuk et al, 2008; Gibala et al, 2012). The molecular mechanisms underlying these adaptations are described in detail elsewhere (Gibala et al, 2012; Hirai et al, 2015; MacInnis and Gibala, 2017).

These adaptations were initially studied in healthy/athletic individuals; however, high-intensity interval training has more recently been shown to improve cardiorespiratory fitness in a range of populations, including those with coronary heart disease and heart failure (Warburton et al, 2005; Wisløff et al, 2007).

Heart failure and high-intensity interval training

Systematic reviews have shown that high-intensity interval training is safe and more effective than moderate-intensity continuous training at improving VO_{2peak} in patients with heart failure with reduced ejection fraction (Haykowsky et al, 2013; Gomes Neto et al, 2018; Wewege et al, 2018). The largest of these reviews by Gomes Neto et al (2018) looked at 13 randomised controlled trials up to October 2017, comparing high-intensity interval training with moderate-intensity continuous training in patients with heart failure with reduced ejection fraction. Meta analyses reported a significantly greater increase in VO_{2peak} following high-intensity interval training compared with moderate-intensity continuous training.

Five of these studies also looked at health-related quality of life using the Minnesota Living with Heart Failure Questionnaire; four of these were included in a meta-analysis which showed that there was no significant difference between high-intensity interval training and moderate-intensity continuous training groups (1.2 at 95% CI). However, both groups did show an improvement in scores (high-intensity interval training 30.7 to 24.8, and moderate-intensity continuous training 31.8 to 24). When interpreting the results from this systematic review, it is worth noting that only one of the studies reported training intensities alongside the prescribed protocol intensities. This was the largest study included in the systematic review and meta analyses and was undertaken by Ellingsen et al (2017).

In Ellingsen et al (2017), 80% of the patients in the moderate-intensity continuous training group exercised above the target level, whereas 51% of the patients in the high-intensity interval training group exercised below their target level. This resulted in only a 10% difference in actual exercise intensity. Although not often reported, the intensities of exercise in either moderate-intensity continuous training or high-intensity interval are an important consideration when interpreting results, designing protocols and prescribing high-intensity interval training. The results reported by Gomes Neto et al (2018) are consistent with an earlier meta-analyses including seven randomised controlled trials (Haykowsky et al, 2013).

Randomised controlled trials for high-intensity interval training interventions in patients with heart failure include a wide variety of high-intensity interval training protocols, differing modes of intervention and various durations of prescribed programmes as summarised in *Table 1*. High-intensity interval training protocols range from 30 seconds of intense exercise with 30 seconds of rest to a maximum of 4 minutes of intense exercise followed by 4 minutes rest, with other protocols lying in between. There is clearly more research needed to determine the optimal dose of high-intensity interval training for patients with heart failure and, indeed, 'one size' may not fit all.

Table 1. High-intensity interval training and moderate-intensity continuous training protocols for randomised controlled trials in patients with heart failure.

Author (year)	Number of randomised patients (HIIT/MICT)	Intervention frequency (times per week)	Intervention duration (weeks)	HIIT protocol		
				Mode / Type	Exercise intensity	Programme
Nechwatal et al (2002)	25/25	6	3	Bike	Load is increased by 25 W every 10s. 50% max watts for AR	5 × 90s with 30s
Dimopoulos et al (2006)	12/12	3	12	Bike	1st month - 100% baseline pWR 2nd and 3rd month 110–120% baseline pWR	40 × 30s with 3 complete res
Roditis et al (2007)	10/10	3	12	Bike	1st month - 100% baseline pWR 2nd and 3rd month 110–120% baseline pWR	40 × 30s with 3 complete res
Wisloff et al (2007)	9/9	3 (2 x supervised 1 x at home)	12	Treadmill	90–95% peak HR 50–70% peak HR AR	4 × 4 min with 3 AR
Freyssin et al (2012)	13/13	5	8	Bike	50–80% maximal power	3 × (12 ×30s wi min complete r
Smart and Steele (2012)	9/9	3	16	Bike	70% peak VO2	30 × 1 min wit min complete r
Fu et al (2013)	15/15	3	12	Bike	80% HR reserve 40% HR reserve AR	5 ×3 min with 3 AR
Iellamo et al(2013)	10/10	3	12	Treadmill	75–80% HR reserve	4 × 4 min with 3 AR
Koufaki et al (2014)	16/17	3	24	Bike	100% PPO 20–30% PPO AR	2 × 15 min as 3 with 1 min A
Benda et al (2016)	12/12	2	12	Bike	90% max workload 30% max work load AR	10 ×1 min with min AR
Ulbrich et al (2016)	15/12	3	12	Treadmill	95% peak HR 70% peak HR AR	4 – 6 × 3 min w min AR
Ellingsen et al (2017)	82/73	3	12	Treadmill / Bike	90–95% max HR 60–70% max HR AR	4 × 4 min with 3 AR

Abbreviations: HIIT= high intensity interval training; MICT = moderate intensity continuous training; AR = Active Recovery; HR = heart rate; Watt = maximal workload; pWR = peak work rate; VT1 = first ventilatory threshold; PPO = peak power output.

Ballesta Garcia et al (2018) conducted a meta-analysis to determine the optimal dose of high-intensity interval training for patients with coronary heart disease and heart failure, with a total of 19 studies, including 10 exclusively focused on heart failure. Results demonstrated no significant difference between high-intensity interval training programmes >12 weeks compared to <12 weeks and no significant difference between programmes with short or long exercise intervals. However, there was a statistical difference in the recovery intensity, with passive recovery and recovery at <40% VO_{2peak} unable to demonstrate adaptations in VO_{2peak}. There was also no significant difference in VO_{2peak} seen for protocols performed <2 days a week, leading to a suggestion that training sessions should be at least 3 times a week with an active recovery >40% VO_{2peak} for patients with heart failure.

Although not included in meta-analyses, randomised controlled trials have also shown benefits in a number of other outcomes. Included in these are decreased hospitalisations, decreased plasma levels of BNP and increased distances in the 6-minute walk test. All randomised controlled trials report high-intensity interval training to have either comparable or improved outcomes to moderate-intensity continuous training.

High-intensity interval training potentially offers an appealing option to patients with heart failure who may not be able to maintain longer periods of activity. Patients with heart failure typically become severely deconditioned, having VO_{2peak} levels well below threshold levels; as a result, many activities of daily living require near maximal or maximal effort. For example, Kitzman et al found that the oxygen cost for a patient with heart failure vacuuming was equal to 89% of maximal effort (Kitzman et al, 2002). To date, much of the work looking at time-efficient high-intensity interval training has tested 'all-out' sprint protocols, which demand a very high level of motivation and are not strictly high-intensity interval training protocols due to its definition as NOT maximal effort, thus highlighting the need for further research in this area.

The transferability and feasibility of all-out high-intensity interval training to the heart failure population is unclear. However, if patients with heart failure were to perform short bouts of exercise at a higher relative intensity with a rest period or period of lower-intensity exercise, this may allow patients with heart failure to accumulate a greater time at higher intensity compared with moderate-intensity continuous training. The optimal high-intensity interval training protocol for patients with heart failure, with respect to interval duration and intensity remains unclear. Despite its clear benefits, high-intensity interval training may not be suitable for all patients with heart failure; but, according to current guidelines, may provide another option for those patients who feel it is achievable and suitable for them (NICE, 2018).

Current trials for high-intensity interval training in a heart failure population have mostly been lab- or centre-based and, although results are supportive of high-intensity interval training as a form of cardiac rehabilitation for patients with heart failure, the application and usefulness in a real-world setting is less well understood. One potential stumbling block could be the need for patients to undergo a cardiopulmonary exercise test before commencing cardiac rehabilitation involving high-intensity interval training, as many centres would not have access to cardiopulmonary exercise testing, especially in cases of more community-based cardiac rehabilitation programmes. Another point for consideration is how short blocks of high-intensity interval training—usually a maximum of 12 weeks—can be introduced to longer-term cardiac rehabilitation programmes. There is a clear need to investigate alternative delivery methods and settings when considering cardiac rehabilitation for patients with heart failure, to both suit patient needs and achieve maximum participation levels, along with establishing how high-intensity interval training protocols designed 'in lab' can be applied to 'real-world settings'.

Limitations of current research

A major limitation of current research is the relatively limited number of randomised controlled trials and the small sample sizes in trials, typically ranging from 20–30 patients. There has only been one larger multicentre trial (Ellingsen et al, 2017). This was the SMARTEX trial, which recruited 261 patients with left-ventricular ejection fraction ≤35% and randomly assigned them to either high-intensity interval training or moderate-intensity continuous training. Contrary to many of the single-centre randomised controlled trials, the SMARTEX study found no significant difference between groups in $VO_{2peak.}$ However, results from this trial must be interpreted with caution, as only 33% of patients trained at the prescribed intensity (80.5% of those in the high-intensity interval training group exercised at too low an intensity and 50.8% of the moderate-intensity continuous training group exercised at too high an intensity).

Training at the intensity prescribed is a factor which must be considered when conducting future trials. The way in which intensity is measured is another consideration; often % of max heart rate is used as a measure of intensity. However, patients are often on medication which may attenuate their heart rate response; they may have chronotropic incompetence or have implanted devices which augment their heart rate. For this reason, it may be useful to measure perceived exertion alongside heart rate, as some studies have (Nilsson et al, 2008). It is also worth noting that, to date, there are no protocols prescribing high-intensity interval training without the need for a cardiopulmonary exercise test first; clearly this is something which needs to be addressed if high-intensity interval training is to successfully be introduced into cardiac rehabilitation programmes.

Women are severely underrepresented in heart failure exercise intervention trials (whether high-intensity interval training or moderate-intensity continuous training). Some trials only recruit men and even those that recruit women have very low numbers (Long et al, 2019). This, along with the relatively young age of trial participants leads to a study population which is not truly representative of the clinical population of heart failure. This is also true when considering the lack of trials recruiting those patients with heart failure with a preserved ejection fraction; particularly with the lack of proven pharmacological interventions for this group of patients, they surely warrant more research into the possible benefits of exercise interventions.

Conclusions

The benefits of cardiac rehabilitation in patients with heart failure are clear, from reduced hospital admissions, to improved $VO_{2max/peak}$ and improved quality of life; however, challenges lie in increasing patient participation and adherence. Patient preferences are also important in defining uptake and outcomes (Dalal et al, 2007) and, for this reason, more work needs to be done examining what motivates people living with heart failure to exercise, as well as the barriers they face to participation and adherence. The type of exercise and preferred setting of patients with heart failure is also an important factor to determine, not only to increase participation but also to maintain attendance for the duration of exercise programmes.

The use of high-intensity interval training within cardiac rehabilitation programmes for patients with heart failure still requires much research, especially in order to translate laboratory findings for application to real-world settings. The safety and ability of high-intensity interval training to improve VO_{2peak} in heart failure has been well documented; however, questions remain over the ability of high-intensity interval training to reduce all-cause mortality and rehospitalisation, especially in the longer term (>12 months). Trials looking at a longer follow-up period would also allow us to understand whether or not high-intensity interval training-based cardiac rehabilitation can elicit a long-term change in physical activity in patients with heart failure. Future research into cardiac rehabilitation for patients with heart failure must also aim to give a fairer representation of the heart failure population with less bias towards younger males.

Cardiac rehabilitation for patients with heart failure is constantly developing and adapting to reflect and suit the current patient population with heart failure. There are still many questions unanswered; however, guidelines and research continue to strive to improve outcomes for patients living with heart failure.

Conflict of interest: The authors have no conflicts of interest to declare.

Key points

- Current referral, uptake and adherence to cardiac rehabilitations programmes for patients with heart failure is suboptimal; nurses can play a role in making referrals
- The challenges to delivering appropriate and successful cardiac rehabilitation for patients with heart failure are not fully understood, but nurses should encourage participation
- High-intensity interval training is both safe and effective for use in a heart failure population, but the optimal protocol remains unclear
- Longer-term follow-up following high-intensity interval training interventions is needed to understand the long-term benefits and promote maintenance
- Future studies need to include populations that are more representative of those living with heart failure (i.e. more older people and women)

Reflective questions

1. What might be some of the reasons for lack of heart failure-specific cardiac rehabilitation programmes?
2. What potential barriers/challenges might patients with heart failure face when accessing cardiac rehabilitation services?
3. Why are the populations represented in randomised controlled trials not fully representative of the 'real-world' heart failure population?
4. What role could high-intensity interval training play in increasing participation in cardiac rehabilitation for patients with heart failure?

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