

High-Intensity Intermittent Exercise Training for Cardiovascular Disease

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Abstract

Exercise training is widely recommended in health and some conditions diseases. It is well established that physical active behaviour is related to decrease in cardiovascular diseases and consequently longer life expectancy. Talking about exercise training involves some methodological approaches such as type of exercise, volume, duration, frequency and intensity; and intensity is exactly what this review is focused, especially high-intensity intermittent exercise training, also known as interval training. Prescribing this model of training according to literature makes it difficult to reach a consensus about the methodology and true effects of it, especially for cardiac patients. For that reason, the aim of this review is to present the current context about the different types of high-intensity intermittent exercise training, its benefits and risks compared to endurance training in some diseases such as coronary artery disease and chronic heart failure.

Keywords: Intermittent exercise; Cardiovascular disease; Exercise intensity; Interval training

Abbreviations: CHF: Chronic Heart Failure; HIIE: High-Intensity Intermittent Exercise; CAD: Coronary Artery Disease; P_{peak} : Peak Workload Intensity; t_{peak} : Peak Workload Duration; P_{rec} : Recovery Load; t_{rec} : Recovery Duration; P_{mean} : Mean Load; VO_{2R} : Reserve Oxygen Consumption; HRR: Reserve Heart Rate; HR_{max} : Maximum Heart Rate; VO_{2max} : Maximum Oxygen Consumption; AT: Anaerobic Threshold; RCP: Respiratory Compensation Point; LV: Left Ventricular; ACSM: American College of Sports Medicine

Introduction

It is well known that continuous moderate-intensity exercise (endurance) training is recommended both in health and disease conditions [1]. Exercise training has the power of changing metabolism [2], increasing functional capacity and skeletal muscle mass, restoring the reduced oxidative capacity and exercise intolerance in Chronic Heart Failure (CHF) [3,4]. More important is the fact that low cardiorespiratory fitness, one common condition in sedentary adults, is associated with an increased prevalence of cardiovascular disease risk factors and death risk [5,6]. Furthermore, endurance training is able to cause autonomic nerve system adaptations, such as sympathetic outflow decrease [7], reversion of β -adrenergic receptor dysfunction [8] and parasympathetic modulation increase that is mainly related to resting bradycardia [9,10]. The decreasing in sympathetic outflow is a desirable response for CHF patients since sympathetic hyperactivity is associated with high morbidity and mortality [11]. In addition, endurance training contributes to remodel cardiac mass [12] and improves endothelial dysfunction in patients with CHF [13]. However, when discussing about endurance training it is important to consider the type of exercise, frequency, duration of session and exercise intensity [1,14,15]. The magnitude of health benefits provided by exercise programs depends mainly on exercise intensity and volume. Based on the concept of a positive continuum of health/fitness benefits with increased exercise intensity, the old method of training applied for athletes [16] "the interval training" had been used to improve aerobic power and causes metabolic adaptations in sedentary healthy individuals and recreationally active adults [17-23]. In recent years, it has also been used as an effective method to improve functional capacity, cardiac function and peripheral muscular adaptation in cardiac patients [24-27]. Some studies have shown that this technique could be superior in comparison with endurance training for improving long-term

effects of exercise on cardiovascular system in cardiac patients [28-31]. Moreover, the time commitment for most High-Intensity Intermittent Exercise (HIIE) training programmes is considerably lower than that traditionally prescribed in endurance training programmes and also the variation provided by this method could contribute to motivate the subjects and increase the adherence to the program. However, there are many ways of prescribing this model of training according to literature that make it difficult to reach one consensus about the methodology and real effects of it, especially for cardiac patients. Therefore, the aim of this review is to present the current context about the different types of HIIE training, their benefits and risks compared to endurance training in some diseases such as Coronary Artery Disease (CAD) and CHF.

History and Concept of High-Intensity Intermittent Exercise Training

The concept of interval training was developed across several decades [32,33] and was first used by athletes who trained at velocities close to their specific competition velocity. Long and middle distance runners as Hannes Kolehmainen (3-fold champion in Summer Olympics, 1912) and Pavoo Nurmi (9-fold champion in Olympics between 1920 and 1928) are examples of successful athletes that used this method. The method was based on the possibility of intensifying the action of the training upon the body throughout the increase on exercise intensity and decrease on exercise duration (short bouts of high-intensity exercise) interspersed by short periods of rest or low-intensity exercise. The rationale behind interval training is that the total amount of high-intensity exercise is higher than could be attained during a single bout of continuous exercise at the same intensity until

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exhaustion [34]. This method was applied in the Swedish running training and was named “Fartlek” by G. Holmer. In the decade of 1930s, W. Gerschler used the interval training method to train German athletes applying a very wide range of distances (100m to 3,000m) for the intense exercise phase, according to the athlete’s capacity. The hallmark of the modern interval training era was established by the consecutive victories of Emil Zatopek in 1950s (Gold medals for 5,000m, 10,000m and marathon running) who adopted 2 to 3 hours of repetitive intense running at the distances between 100m to 400m with active recovery of less intensity. From the 1950s, the researches H. Reindell and W. Gerschler set the Freiburg interval training constituted of short periods of intense exercise (30 seconds) interspersed with less intense exercise or rest of 60 to 90 seconds establishing the relation between work and recovery of 1:2 or 1:3. Meanwhile, the Swedish researcher Erik Christensen and coworkers developed several studies using different relations between effort and recovery [33,35,36] and observed a higher economy of interval training when using 30:30 seconds, that is a work: recovery ratio of 1:1. These and other results brought the practical form of short interval training or sprint interval training [33,37]. New varieties of interval training for endurance athletes were created in the 1960s and 1970s. Years later the researches started focusing in the possibility of using this method to train cardiac patients. Although the concept of interval training is quite easy to understand the wide manners of applying it make difficult the establishment of a consensus about this technique and the understanding of its effects on health.

The Components of High-Intensity Intermittent Exercise

Because of the wide variety of definition for this method in the literature we decided to adopt the HIIE (High-Intensity Intermittent Exercise) nomenclature, as suggested by Tschakert and Hofmann in a recent review [38]. Exception will be made when referring to a specific study.

According to these authors [38] there are 5 main components for HIIE:

- Peak workload intensity (P_{peak})—The intensity level used during work phase in each bout of the HIIE intervals.
- Peak workload duration (t_{peak})—The work duration performing P_{peak} .
- Recovery load (P_{rec})—The intensity level used during recovery phase in each bout of the HIIE intervals.
- Recovery duration (t_{rec})—The recovery duration performing P_{rec} .
- Mean load (P_{mean})—The mean load. It is the result of the handling of the latter 4, as following: $P_{mean} = (P_{peak} \times t_{peak} + P_{rec} \times t_{rec}) / (t_{peak} + t_{rec})$.

Before defining P_{peak} it is important to review the concept of high-intensity exercise mainly when studying HIIE for cardiac patients. The American College of Sports Medicine (ACSM) recommends a combination of moderate (i.e., 40% to <60% reserve oxygen consumption – VO_2R) and vigorous (i.e., $\geq 60\% VO_2R$) intensity exercise for most adults [1,14]. However, how is vigorous exercise defined?

Peak workload intensity (P_{peak}) and recovery load (P_{rec})

Exercise intensity may be estimated using reserve heart rate (HRR), VO_2R , percentage-predicted maximum heart rate (HR_{max}), percent estimated maximum oxygen consumption (VO_{2max}) and perceived exertion. According to ACSM’s classification, the exercise intensity for VO_2R/HRR and HR_{max} is presented as the following [1]: light: 20-39%

and 50-63%; moderate: 40-59% and 64-76%; hard (vigorous): 60-84% and 77-93%; very hard: $\geq 85\%$ and $\geq 94\%$, respectively. However, the use of HR_{max} to calculate HRR is restricting in cardiac patients because usually these patients are taking β -blockers which attenuate the HR response to exercise. Thus, the estimative of exercise intensity could only be feasible when it is obtained by maximum exercise testing. In this case, the ventilatory thresholds determined in a preliminary incremental exercise test might provide an accurate reference for exercise intensity prescription since they are based on actual metabolic response to physical exercise. The use of ventilatory thresholds has been adopted during cyclist’s training session [39] and might be also appropriated for patients. According to the cardiopulmonary exercise testing, the Anaerobic Threshold (AT) is the light intensity; the range between ventilatory thresholds (AT to Respiratory Compensation Point –RCP) is the moderate-intensity and the level above RCP is the high-intensity [39]. Thus, the P_{peak} will be set between the power output at RCP and “all-out” exercise [16] and the P_{rec} in the power output at AT. This technique allows an individual and accurate setting of each single interval components, as reported by previous authors [38].

Recovery phase

The t_{peak} ranges from a few seconds up to several minutes and the P_{peak} phases are separated by periods of low- or moderate-intensity exercise or passive recovery with a t_{rec} that can be shorter than, equal to, or longer than t_{peak} [38]. The management of P_{rec} and t_{rec} would influence the VO_2 recovery and consequently the time of reaching VO_{2max} in the following P_{peak} phases and also the recovery of the muscle metabolism that is essential to get a better work capacity. All we need is to provide a faster decrease on blood H^+ and lactate concentrations after the high-intensity exercise and Del Coso et al. [40] observed that low-intensity prolonged recovery between repeated bouts of high-intensity exercise maximized H^+ and lactate removal. It is believed that the best recovery intensity would be at AT power output or even passive, since there is no lactate formation during light-intensity exercise. Two previous studies showed that the best lactate removal occurs for recovery intensities of 52% [41] and 63% of VO_{2max} [42]. When comparing active and passive recoveries, Abderrahmane et al. [43] demonstrated that interval training in moderately trained individuals with active recovery increased VO_{2max} and maximal aerobic velocity. The study of Dupont et al. [44] evaluated healthy physically active male subjects who performed intermittent runs (15 seconds) at supra-maximal velocity (120% of maximal aerobic speed) to exhaustion with active recovery (50% of maximal aerobic speed) and passive recovery. Results showed a longer time to exhaustion with passive recovery than with active recovery probably due to a blockade of the replenishment of the alactacid and oxyhemoglobin energy sources which were partially depleted during the previous work interval. In the same way, Thevenet et al. [45] observed in athletes that active recovery led to a shorter time to exhaustion with longer time spent at 90% VO_{2max} ($t_{90VO_{2max}}$) and 95% VO_{2max} ; whereas passive recovery allows a longer running time to exhaustion for similar $t_{90VO_{2max}}$ and $t_{95VO_{2max}}$ during a 30 seconds intermittent exercise session at 105% of maximal aerobic velocity. They concluded that both recovery modes are efficient to stimulate the aerobic system during intermittent exercise and the choice of recovery mode depends on training objectives. If the objective is to improve VO_{2max} , active recovery should be chosen, while a passive recovery is preferred to improve VO_{2max} and induce muscular adaptations. To our knowledge there is no studies comparing the effect of active versus passive recovery in cardiac patients and considering the fact that the HIIE training studies with this population do not stress the patients

to their maximum or even supra-maximum effort, the active recovery could be better.

Different High-Intensity Intermittent Exercise Training Protocols

Although HIIE training has been used as a success method to improve endurance performance in athletes [16], the perception that it is unsafe and or unfeasible for less 'fit' populations and cardiac patients is now being challenged. The wide combinations of the 4 components of HIIE (P_{peak} , t_{peak} , P_{rec} , and t_{rec}) result in a large variety of HIIE prescriptions used in exercise training programs. Despite this diversity, beneficial effects have been observed even among ill individuals. However, it is important to assume that the isolated or combined manipulation of each component of HIIE prescription could have a direct impact on acute metabolic and cardiopulmonary responses to exercise [30,46]. These acute responses will lead to specific medium- and long-term training adaptations. Regarding Table 1, it is possible to observe that the training frequency used in the studies was of 2 to 3 sessions per week. We consider 2 sessions as the minimum but it was not yet observed if 3 or more sessions could maximize the benefits of HIIE in patients. Some studies used 1 home-based session as additional session training and despite the objective of motivating the patient to remain active for a longer period of time at the end of the protocol; it cannot be safe for more complicated patients. The training duration varied more, with a minimum of 10 weeks and one study evaluating the 1 year effect of HIIE. The most common training duration was of 12 weeks (3 months). However, not all studies that had this length of training found a positive response or a greater response with HIIE compared to endurance training. Most likely, the effect of training length can be directly related to the initial state of the patient and maybe patients in a better functional capacity will demand longer training duration to present positive effects. Furthermore, the exercise type varied importantly and it can result in differences between the studies. More importantly is that the effects of HIIE may be underestimated when using different types of exercises and the use of only one type of ergometer to evaluate the improvement caused by HIIE could lead to a mismatch. Moreover, the great variability in HIIE's prescription makes it difficult to conclude the positive or negative or even similar effect of HIIE compared to endurance training in cardiac patients. We should consider 3 important points about this subject: 1) the majority does not use the ventilatory thresholds to prescribe HIIE's intensities even when they had evaluated the patients with a cardiopulmonary exercise testing; 2) the majority used an inverse relation between work: recovery with higher exercise than recovery duration. It could impose a higher cardiovascular stimulus that in a long-term training would not be sustainable to the patients. Work: recovery relations of 1:3, 1:2 or 1:1 could be more suitable for cardiac patients; and 3) finally, not all studies had implemented the same total work when comparing HIIE and endurance training and this difference may be an influential factor in the responses to training and causes misunderstanding about the true effects of HIIE.

High-Intensity Intermittent Exercise Training in Coronary Artery Disease

Exercise training is highly recommended for patients with CAD [47] since it improves functional capacity, decreases cardiac ischemia and angina pectoris, and improves endothelial function [48]. Rognmo et al. [28] studied high-intensity aerobic interval exercise compared to moderate exercise in CAD patients and observed 17.9% increase in VO_{2peak} in the interval training group versus 7.9% in the moderate-

intensity group. The authors suggest that high-intensity was a key factor to this huge improvement on functional capacity since both programs had similar total amount of work. In one randomized controlled trial [49] that evaluated 89 post-myocardial infarction patients showed a higher increase in VO_{2peak} after aerobic interval training than after usual care rehabilitation. However, this superior result observed by HIIE in functional capacity in CAD patients is controversial. Currier et al. [50] observed similar training effect in relative VO_{2peak} with no differences between low-volume high-intensity interval exercises training versus endurance training. However, they highlight that the increase in VO_{2peak} (24%) observed after high-intensity exercise training was larger than the changes observed in previous HIIE investigations [28,49,51]. Also, Warburton et al. [29] found similar increase in VO_{2peak} and time to exhaustion after 16 weeks of high-intensity interval training compared to moderate training in CAD patients. However, the treadmill time to exhaustion at 90% VO_{2R} and the AT were greater after interval training. Thus, high-intensity interval training results in greater tolerance to an anaerobic challenge enabling individuals to perform daily life activities with less effort and for a longer period of time. The similar improvement on VO_{2peak} with the interval training and moderate continuous training might be due to the differences in HIIE protocols since Warburton's study used a shorter time at high-intensity (2 minutes) followed by the same time recovery when compared to Rognmo's study [28]. The authors also used a mix of exercise types for training (treadmill, stair climber and cycle ergometer for arms and legs) which may have limited the maximal functional gain on treadmill test.

Increase in sympathetic nerve outflow in CAD is a physiopathology condition which can be modulated by exercise training. Six months of moderate-intensity exercise at AT to <10% below RCP, decreased peripheral sympathetic nerve activity measured directly in fibular nerve and improved baroreflex sensitivity in myocardial infarction patients [52]. However, this autonomic control adaptation using HIIE is not well established. If on one hand high-intensity interval training program improved 24-hour HR variability that was correlated to changes in VO_{2peak} in patients following percutaneous coronary intervention for angina pectoris [53], on the other hand, in a recent study [54], HR variability and HR recovery (which is related to cardiac autonomic control) were unchanged in patients with CAD following 12 weeks of interval training and moderate training. However, in the latter the authors attributed the negative results to the optimal pharmacological treatment and pre-training state of the patients. If patients are in a good and stable cardiovascular condition, maybe the HIIE could be optimized to get positive results. Therefore, differences in protocols and population vary in some studies and the results should be seen with cautions.

Endothelial function with different exercise intensities training has been tested in CAD patients [49-51,55]. Increased brachial artery flow-mediated dilation was observed after 6 months of supervised high-intensity interval exercise training in coronary artery disease patients [51]. However, in this study, the authors compared high-intensity with a control sedentary group. Could high-intensity exercise be better than moderate-intensity exercise to improve the endothelial function? Either acute exercise [55] or chronic exercise [49,50] comparing moderate- and high-intensity exercises increased brachial artery flow-mediated dilation with no differences between groups, suggesting that both trainings improved endothelial function in patients with CAD.

Summarizing, studies with HIIE in CAD patients show greater benefits of this training type to improve functional capacity and anaerobic tolerance. However, the effects of HIIE on autonomic modulation and endothelial function are not well established.

	Subject number in each group	Training frequency	Training duration	Exercise mode CPET equipment	HIIE training methods	HIIE total time; Total work	Main findings
CAD studies							
Rognmo et al. [28]	21 CAD patients (11 for high-intensity aerobic interval exercise-mean LVEF=54.8%/10 for moderate-intensity exercise-mean LVEF=51.9%)	3 days/week	10 weeks	Uphill treadmill walking CPET=on treadmill	4× (4 min at 80-90%VO _{2peak} (85-95%HR _{peak}) int by 3 min at 50-60% VO _{2peak} Work: Recovery ratio of 1:0.75	33 min; Similar total work between groups	Higher ↑ on VO _{2peak} with high-intensity aerobic interval exercise versus moderate exercise.
Warburton et al. [29]	14 male CAD patients (VO _{2peak} >9 METs) (7 for interval training/7 for traditional training)	2 days/week Each group was instructed to engage in 3 additional sessions/week of continuous exercise	16 weeks	3 bouts of 10 min on 3 types of exercise (treadmill, stairclimber and combined arm and leg cycle ergometer) CPET=on treadmill	(2 min at 90% HR/VO _{2R} (85-95%) int by 2 min at 40% HR/VO _{2R} (35-45%)) Work: Recovery ratio of 1:1	30 min; Similar training volume between groups	Similar ↑ on VO _{2peak} between training programs. Higher anaerobic tolerance with interval training.
Munk et al. [51]	40 CAD patients (after PCI with stent implantation) (20 for high-intensity interval training-mean LVEF=65%/20 for sedentary control group-mean LVEF=65%)	3 days/week	24 weeks	Cycling, running CPET=on cycle ergometer	(4 min at 80-90% HR _{max} int by 3 min at 60-70% HR _{max}) Work: Recovery ratio of 1:0.75	Missing data about total time and total work between groups	↓ in late luminal loss in the stented coronary segment, ↑ in VO _{2peak} , ↑ in endothelium function, and ↓ in inflammation with high-intensity interval training compared with sedentary group.
Munk et al. [53]	40 CAD patients (after PCI with stent implantation) (20 for high-intensity interval exercise training-mean LVEF=63%/20 for sedentary control group-mean LVEF=64%)	According to Wisloff et al. [31]	24 weeks	According to Wisloff et al. [31]	According to Wisloff et al. [31]	According to Wisloff et al. [31]	↑ in HR variability, ↑ in VO _{2peak} with high-intensity interval training compared with sedentary group.
Moholdt et al. [49]	89 post-myocardial infarction patients (2-12 weeks) (30 for aerobic interval training/59 for group exercise-usual care rehabilitation) Mean LVEF not referred	3 days/week (2 supervised sessions and 1 home session)	12 weeks	Aerobic exercises like walking, jogging, lunges and squats. CPET=on treadmill	4 × (4 min at 85-95% HR _{max} int by 3 min at 70% HR _{max}) Work: Recovery ratio of 1:0.75	38 min; Missing data about total work between groups	Higher ↑ in VO _{2peak} with aerobic interval training versus usual care rehabilitation.
Currie et al. [54]	14 male CAD patients (7 for high-intensity interval exercise/7 for moderate-intensity endurance exercise) Mean LVEF not referred	2 days/week	12 weeks	Cycling CPET=on cycle ergometer	10×(1 min at 88% PPO int by 1 min at 10% PPO) Intensity was increased every month Work: Recovery ratio of 1:1	Missing data about total time; Less total work for HIIE group	↔ in cardiac autonomic function with endurance or high-intensity interval exercise programs.
Currie et al. [50]	22 CAD patients (11 for high-intensity interval exercise training/11 for moderate-intensity endurance exercise) Mean LVEF not referred	3 days/week (2 supervised sessions and 1 home session)	12 weeks	Cycling CPET=on cycle ergometer	10×(1 min at 89% PPO (80-104%) int by 1 min at 10% PPO) Work: Recovery ratio of 1:1 Workload was increased every 4 weeks	30-35 min; Less total work for HIIE group	Similar ↑ in VO _{2peak} and flow-mediated dilation for both training programs.
CHF studies							
Wisloff et al. [31]	27 post-infarction HF patients (9 for aerobic interval training-mean LVEF=28%/9 for moderate continuous training-mean LVEF=32.8%/9 for control group- mean LVEF=26.2%)	3 days/week (2 supervised sessions and 1 home session)	12 weeks	Uphill treadmill walking CPET=on treadmill	4×(4 min at 90-95% HR _{peak} int by 3 min at 50-70%HR _{peak}) Work: Recovery ratio of 1:0.75 Weekly home-based training=outdoor uphill walking. Interval training patients performed 4×(4 min with an exercise intensity that made them breathe heavily without becoming too stiff in their legs)	38 min; Training protocols were isocaloric	Aerobic interval training was superior to reverse LV remodeling, ↑ VO _{2peak} , ↑ endothelial function and quality of life than moderate continuous training.

Nilsson et al. [26]	80 stable CHF patients (40 for high-intensity aerobic interval training-mean LVEF=30%/40 for sedentary control group-mean LVEF=31%)	2 days/week The patients attended exercise classes as outpatients in groups of 8 to 12	16-24 weeks	Aerobic dance movements (with music) using both upper and lower extremities (endurance, strength, and stretching exercises) CPET=not performed Tests: 6-minute walking distance and exercise test on cycle ergometer	3x(5-10 min at 15-18 on the Borg scale) int by 2x(5-10 min at 11-13 on the Borg scale). Work: Recovery ratio of 1:0.67 Patients were encourage to gradually reach the right exercise intensity	50 min;	↑ in functional capacity and quality of life with high-intensity aerobic interval training versus sedentary group.
Nilsson et al. [27]	80 stable CHF patients (40 for high-intensity aerobic interval training -mean LVEF=31% / 40 for sedentary control group-mean LVEF=31%)	the same as above	16-24 weeks and 1 year	the same as above	the same as above	the same as above	↑ in functional capacity and quality of life in long-term high-intensity aerobic interval training versus sedentary group.
Koufaki et al. [57]	17 CHF (8 for high-intensity interval training-mean LVEF=41.7% / 9 for continuous aerobic exercise training- mean LVEF=35.2%)	3 days/week	24 weeks	Cycling CPET=on cycle ergometer	2x15 min (30 seconds at ≈ 100% PPO int by 1 min at ≈ 20-30% PPO) Work: Recovery ratio of 1:2	30-33.6 min; Training protocols were not isocaloric	Similar ↑ in VO_{2peak} for both training programs

The studies are present in chronological order in disease groups. CAD=coronary artery disease; LVEF=left ventricular ejection fraction; CPET=cardiopulmonary exercise testing; VO_{2peak} =peak oxygen consumption; VO_{2R} =reserve oxygen consumption; HR=heart rate; min=minutes; int=interspersed; PCI=percutaneous coronary intervention; CHF=chronic heart failure; HIIE=high-intensity intermittent exercise; PPO= peak power output; ↑=increase; ↓=decrease; ↔=no changes.

Table 1: High-Intensity Intermittent Exercise Training Types in Cardiac Patients.

High-Intensity Intermittent Exercise Training in Chronic Heart Failure

As well as in CAD, exercise training is widely recommended for CHF patients due to positive improvements in functional class, functional capacity and quality of life [56]. Decreasing on sympathetic nerve activity and enhancement on skeletal muscle blood flow and VO_{2peak} were observed in endurance trained CHF patients compared to sedentary ones [7]. However, recent studies have shown a higher effectiveness of high-intensity aerobic interval training to improve functional capacity and quality of life in CHF patients compared to sedentary standard care group, both in short and long-term effects [26,27]. When comparing HIIE to endurance training in CHF patients, Koufaki et al. [57] observed similar improvement on VO_{2peak} and quality of life. On the other hand, Wisloff et al. [31] showed that aerobic interval training was superior to moderate training to increase VO_{2peak} (46% versus 14%) in CHF patients, and it was associated with reverse Left Ventricular (LV) remodeling with increased ejection fraction by 35%. The different results observed in both studies [31,57] could be explain by differences between HIIE prescriptions (Table 1), initial clinical status of the patients and CHF etiologies. In a recent meta-analysis in CHF patients [58], it was shown a higher increase in VO_{2peak} with aerobic interval training compared to moderate continuous aerobic training, reinforcing this finding. In addition, Wisloff et al. [31] showed a positive periphery adaptation with improvement in brachial dilatation and mitochondrial function of lateral vastus muscle with aerobic interval training.

Reverse LV remodeling seen with HIIE is a great result to improve cardiac function [31]. However, the exactly molecular mechanisms of adaptations in human heart of CHF patients after an HIIE training program is not well known, but in post-infarction heart failure rats, interval training reduced sarcoplasmic reticulum Ca^{2+} ATPase activity in atrial myocytes, increased Na^{+}/Ca^{2+} exchanger activity and increased diastolic Ca^{2+} leak through ryanodine receptors [59]. Accordingly, impaired Ca^{2+} transient is a characteristic of LV contractile dysfunction in heart failure and perhaps the improvement in this mechanism could

also explain upper cardiac function in CHF patients after HIIE training.

Recently, skeletal muscle waste has been focused on in the CHF patients' treatment because it is an important determinant of exercise intolerance [3]. Shifting from oxidative to glycolytic skeletal muscle fiber types in CHF has been reported [3] and it was possible to observe functional alterations in oxidative enzymes, mitochondria and capillary density in human skeletal muscle cells. Exercise training is one important strategy to change muscle waste with improvement on oxygen delivery, oxidative metabolism and strength [3] and it has been reported that moderate-intensity exercise training increases mitochondrial structure and function, increasing consequently the VO_{2peak} [60]. Unfortunately, skeletal muscle adaptations in CHF patients using HIIE training are still missing in the literature. However, in the Cunha et al. study in heart failure humans and heart failure rats, moderate-intensity exercise training restored oxidative stress and ubiquitin proteasome system (proteasomal activity) in the skeletal muscle in both humans and animals, suggesting the role of exercise training to prevent muscle atrophy [61]. Now, it is time to test the hypothesis that HIIE training could be superior to moderate-intensity exercise training to improve skeletal muscle hypertrophy and quality of life in CHF patients.

Summarizing, as well as in CAD patients, HIIE seems to be superior to improve functional capacity and exercise intolerance in CHF patients. However, improvement in cardiac function with HIIE is not yet a consensus. Besides, studies addressing autonomic nerve system and HIIE are still missing in the literature.

Is High-Intensity Intermittent Exercise Training Safe for Cardiac Patients?

To our knowledge only one study with a large numbers of CAD patients has addressed this question and deserves attention [62]. The risk of cardiovascular events during high- versus moderate-intensity aerobic exercise among 4,846 patients was studied. In a total of 175,820 exercise training hours, they found 1 fatal cardiac arrest during

moderate-intensity exercise (129,456 exercise hours) and 2 nonfatal cardiac arrests during high-intensity interval exercise (46,364 exercise hours). The results indicated that the risk of a cardiovascular event in CAD patients is low after both training types. However, the data should be interpreted more critically. Halle [63] has discussed that the rates of complications calculated to the number of patient-exercise hours were >5-fold higher during high-intensity interval training (1/23,182 hours) compared to moderate continuous training (1/129,456 hours). Also, moderate continuous training was performed 2.8 times more often which may have statistically increased the chance for a fatal event. Despite no study has been designed to test the safety of HIIE training for CHF patients, this prescription should be done with caution. It is important to take into account the etiology of disease, drugs therapy, the presence of ischemia and/or arrhythmia, blood pressure levels, LV ejection fraction, functional class (New York Heart Association) and orthopedic disorders. It seems a little early to reach a conclusion about the safety of HIIE in cardiac patients.

The Long-Term Practice of High-Intensity Intermittent Exercise

To our knowledge, the long-term effect of HIIE on cardiovascular and musculoskeletal systems in cardiac patients has not been investigated yet. It is important to take into consideration the fact that excessive training intensity and abrupt increases in training volume increase the risk for injury to bones, joint and muscles [64] mainly to middle-aged and older adults. Accordingly, it is essential to create an intermittent exercise session plan that includes warm-up, stretching and cool-down exercises. Also, a variety of exercise modalities could be proposed to avoid the potential for overuse syndromes [1] and the inclusion of resistance exercises on exercise training programs to maintain adult's bone health is recommended by the ACSM [1,14].

For the purpose of using HIIE in a rehabilitation program we suggest the manipulation of some components of the HIIE, such as t_{rec} and t_{peak} as previously proposed for athletes at their preparatory period of training [38]. However, we recommend applying lower volume of training in cardiac patient population. The authors used the following rationale: given a short t_{peak} (which is associated with a low La production), P_{mean} and cardiorespiratory strain can be substantially reduced by an extension of t_{rec} . In contrast, if t_{rec} is shortened (or t_{peak} is lengthened), P_{mean} (and cardiorespiratory strain) will increase. We also propose a training periodization (up to 1 year) that could prepare the patients for keeping a long-term use of HIIE. The exercise physiologists, trainers and physical therapists could begin with endurance training, secondly introduce a HIIE with short t_{peak} and long t_{rec} and finally introduce a HIIE with longer or kept t_{peak} and proportionally shorter t_{rec} . It is possible to think about the work: recovery relations of 1:3, 1:2 and 1:1 progressively. It is important to consider the frequency of HIIE session. It is advisable not to train more than 3 times per week using this exercise method since your metabolic recovery is longer. Finally, we suggest that HIIE takes part in a comprehensive rehabilitation program but it should not be used as the only tool to improve health in cardiac patients.

Conclusion

HIIE is a very easy and feasible exercise for all individuals and may provide an alternative to current exercise prescriptions for most people who reports "lack of time". However, the use of this method in cardiac patients deserves additional studies. It is early to conclude that HIIE is better than moderate endurance training since there is a large variability in the application of this method in this population. Likewise,

it is desirable to get more conclusive studies about the potential risk of practicing HIIE in cardiac patients. Standardization of this method should be intensively required in rehabilitation programs and we truly suggest the use of ventilatory thresholds as an effective individualized approach for intensity range definition. The relation between work: recovery should also be standardized. Maybe of less importance is the exercise type used for HIIE training. However, the evaluation test should be as similar as possible to the exercise adopted during HIIE training. The hypothesis of superior effects of HIIE should be tested using a standardized HIIE in a wide range of populations and larger multicenter randomized settings comparing HIIE versus moderate endurance training. A comprehensive review of the physiological adaptations induced by a standardized HIIE will allow more convinced conclusions about HIIE prescription for cardiac patients.

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