High-Intensity Aerobic Interval Exercise in Chronic Heart Failure

Philippe Meyer · Mathieu Gayda · Martin Juneau · Anil Nigam

Abstract Aerobic exercise training is strongly recommended in patients with heart failure (HF) and reduced left ventricular ejection fraction (LVEF) to improve symptoms and quality of life. Moderate-intensity aerobic continuous exercise (MICE) is the best established training modality in HF patients. For about a decade, however, another training modality, high-intensity aerobic interval exercise (HIIE), has aroused considerable interest in cardiac rehabilitation. Originally used by athletes, HIIE consists of repeated bouts of high-intensity exercise interspersed with recovery periods. The rationale for its use is to increase exercise time spent in high-intensity zones, thereby increasing the training stimulus. Several studies have demonstrated that HIIE is more effective than MICE, notably for improving exercise capacity in patients with HF. The aim of the present review is to describe the general principles of HIIE prescription, the acute physiological effects, the longer-term training effects, and finally the future perspectives of HIIE in patients with HF.

Keywords Intermittent exercise · Interval training · Cardiac rehabilitation · Heart failure

P. Meyer
University Hospital of Geneva, Geneva, Switzerland
e-mail: philippe.meyer@hcuge.ch

M. Gayda · M. Juneau · A. Nigam (✉)
Cardiovascular Prevention and Rehabilitation Centre
(Centre ÉPIC), Montreal Heart Institute, Université de Montréal,
5000 Belanger Street, Montreal H1T 1C8, Canada
e-mail: anil.nigam@icm-mhi.org

M. Gayda · M. Juneau · A. Nigam
Department of Medicine, Montreal Heart Institute,
Université de Montréal, Montréal, Canada

Introduction and Historical Perspective

Until the late 1980s, heart failure (HF) was widely regarded as a classical contraindication to exercise training in the belief that patients with a severely reduced left ventricular ejection fraction (LVEF) had an excessive risk for exercise-related morbidity and mortality. In the 3rd edition of Braunwald's heart disease textbook published in 1988, one could read: "Reduced physical activity is critical in the care of patients with HF throughout their entire course" [1]. This fear was supported by a non-randomized study performed in the pre-angiotensin converting enzyme inhibitor and beta-blocker eras, which suggested adverse cardiac remodeling in patients with recent anterior myocardial infarction after a 12-week low-level exercise training program [2]. Since the initial landmark trial conducted by Sullivan et al. [3], many randomized trials demonstrated that regular exercise is safe and provides many benefits in the care of patients with chronic HF and reduced LVEF. Meta-analyses of these studies reported an average increase of peak oxygen uptake (VO_{2peak}) of 15 to 20 % following exercise training, with an improvement of symptoms and quality of life, although the impact on morbidity and mortality remained unclear [4–6]. Finally, the largest multicenter randomized, controlled trial of aerobic training in HF, HF-ACTION, was published in 2009. This trial demonstrated modest but significant benefits related to aerobic training after adjustment for pre-specified prognostic factors, in the primary composite endpoint of all-cause mortality or all-cause hospitalization and did not reveal safety issues compared to the non-exercise group [7]. The training modality used in the vast majority of these studies, including HF-ACTION, was moderate-intensity aerobic continuous exercise (MICE), which therefore forms the basis of training therapies in HF patients. For the first time in 2012, the European Society of

Cardiology acknowledged aerobic exercise as a class I, level of evidence A recommendation in patients with HF, which constitutes a complete paradigm shift in less than 25 years [8].

In more recent years, another aerobic training modality, high-intensity aerobic interval (or intermittent) exercise (HIIE), has emerged and appears to be more beneficial in patients with HF [[9•], [10, 11], [12•]]. HIIE consists of repeated periods of high-intensity exercise in alternation with periods of low-intensity exercise or rest. First described in 1959 by Reindell and Roskamm in a scientific journal [13], HIIE has been used since the beginning of the 20th century by elite athletes and definitely popularized by the long-distance runner Emil Zatopek, triple Olympic Champion at the Helsinki Olympic Games in 1952 [14]. Since the early 1990s, Meyer et al. began studying HIIE in patients with coronary artery disease [15], and later in patients with HF [16], but a real interest in this training modality only arose a decade ago.

Principles of HIIE Prescription

The fundamental principle of HIIE is that periods of high-intensity exercise are interspersed with recovery periods, which allows the individual to re-engage in high-intensity exercise multiple times during the same session. The rationale is to accumulate more time in high-intensity zones compared to a continuous exercise where exhaustion would occur more prematurely, and therefore to produce a stronger stimulus for cardiovascular and muscular adaptations [10, 17]. A parameter frequently used to quantify the overall aerobic stimulus induced by a HIIE training protocol is the time spent at a high percentage of VO_{2peak} [12•, 18–25]. HIIE can take the form of cycling, walking, rowing, swimming or other activities, although stationary cycling and treadmill walking have been the most utilized. There are an unlimited number of possible HIIE protocols using different intensities and durations of work/recovery intervals. Different interval combinations have been tested in various populations and induce profound variations in acute physiological responses to exercise that must be taken into consideration during exercise prescription [14, 24–27]. In sports training, three different categories of HIIE have been described [12•]: (1) long intervals: 3 to 15 minutes at an intensity corresponding to 85–90 % of maximal oxygen uptake (VO_{2max}); (2) moderate intervals: 1 to 3 minutes at 95–100 % of VO_{2max}; and (3) short intervals: 10 seconds to 1 minute at 100–120 % of VO_{2max}.

In patients with HF, many protocols have been employed, differing not only in the duration and intensity of work/-recovery intervals but also in the parameters used to quantify and monitor exercise intensity. Table 1 describes several

HIIE protocols used in recent HIIE training studies, which will be detailed further in this review. In most studies, protocols were chosen empirically. Only two studies have compared the acute physiological effects of different HIIE protocols, while no study to our knowledge has compared the training effects of different HIIE protocols over a longer period. Meyer et al. performed a comparison of three HIIE protocols in 16 men with HF and reduced LVEF [28]. Exercise intensity was prescribed as a percentage of the maximal short-term exercise capacity (MSEC) determined by a cycle ergometer steep ramp test (unloaded pedaling for 3 minutes followed by increments of 25 Watts every 10 seconds until exhaustion). The MSEC corresponded on average to slightly more than twice the power output reached at VO_{2peak} (peak power output or PPO). In a cross-over study, 3 different work/recovery interval durations were investigated: 30/60 seconds, 15/60 seconds and 10/60 seconds, with respective work intensities of 50 %, 70 % and 80 % of MSEC and the same recovery intensity of 15 Watts. All three protocols provided similar results with respect to rate-pressure product, gas exchange, catecholamine levels and rate of perceived exertion, such that all three were recommended by the authors. A limitation of this study is the questionable validity of the steep ramp test that has never been widely implemented in cardiac rehabilitation [29]. Furthermore, time spent at a high percentage of VO_{2peak} was not evaluated in the study.

More recently, our group compared four different HIIE protocols on a cycle ergometer in 20 men with HF and reduced LVEF [30]. In this cross-over study, all patients performed four different randomly-ordered HIIE protocols with measurement of gas exchange, continuous blood pressure, and ECG monitoring. Based on previous studies in coronary patients, exercise intensity was set at 100 % of peak power output (PPO) for all protocols (A, B, C, and D) [24, 25, 31]. Work/recovery interval duration was 30/30 seconds (A and B) or 90/90 seconds (C and D), and recovery was passive (A and C) or active (50 % of PPO in B and D). There were no differences between protocols regarding time spent above 85 % of VO_{2peak}. Protocol A with short intervals and passive recovery was found to be superior to protocols B,C, and D, given that it was associated with a significantly longer total exercise time and better tolerance as assessed by the rating of perceived exertion. Most importantly, no ventricular arrhythmias were detected during the 80 continuously-monitored HIIE sessions, and no adverse clinical events occurred. Interestingly, patients with severely reduced exercise capacity appeared to be able to spend considerably more time at a high percentage of VO_{2peak} in protocols with passive recovery, especially protocol A, whereas patients with relatively preserved exercise capacity were able to spend more time at a high percentage of VO_{2peak} in protocols with active recovery, especially

Table 1 HIIE protocols investigated in different randomized training studies

| Studies	Mode	Interval duration		Interval intensity		Duration/ session	Sessions/ week	Weeks of training
		Work	Recovery	Work	Recovery			
Dimopoulos 2006 [45] Roditis 2007 [46]	Ergometer cycling	30 seconds	30 seconds	100 % of PPO	Rest	40 minutes	3	12
Wisloff 2007 [32]	Treadmill walking	4 minutes	3 minutes	90–95 % of peak HR	50–70 % of peak HR	38 minutes	3	12
Smart 2011 [44•]	Ergometer cycling	60 seconds	60 seconds	70 % of PPO	Rest	60 minutes	3	16
Fu 2011 [49•]	Ergometer cycling	3 minutes	3 minutes	80 % of HRR	40 % of HHR	36 minutes	3	12
Iellamo 2012 [48]	Treadmill walking	4 minutes	3 minutes	75–80 % of HRR	45–50 % of HRR	37 minutes	41 sessions	12
Freyssin 2012 [47]	Ergometer cycling / treadmill walking	30 seconds	60 seconds	50 to 80 % of MSEC	Rest	71 minutes	6	8

HIIE, high intensity interval exercise; HR, heart rate; HRR, heart rate reserve; MSEC, maximal short-term exercise capacity; PPO, peak power output.

protocol B (Fig. 1). This suggests that a single HIIE protocol is probably not suitable for all patients and should be individualized (see below).

A considerable body of evidence has been accumulated in recent years with regards to HIIE in HF and other medical conditions thanks to several Norwegian groups [10, 11]. Their HIIE protocol in HF consisted of 4/3 minute work/recovery intervals of uphill treadmill walking that were repeated 4 times, at respective work/recovery intensities of 90–95 % and 50–70 % of peak heart rate [32]. As will be discussed later, very impressive improvements in terms of exercise capacity and cardiac reverse remodeling were demonstrated using this protocol in a small randomized trial in patients with HF [32]. We believe, however, that velocities or power output corresponding to a percentage of VO_{2peak} should be employed to prescribe HIIE intensity because the use of target heart rate zones is often not reliable for the following reasons in HF: (1) frequent chronotropic incompetence due to maximally titrated

Fig. 1 Oxygen uptake (VO_2) during 4 protocols of high intensity interval exercise (**a**, **b**, **c** and **d**) in a patient with low baseline exercise capacity (VO_{2peak}=11.8 ml/kg/min, black line) and a patient with preserved exercise capacity (VO_{2peak}=25.9 ml/kg/min, grey line). **a** 30/30 seconds, 100 %/ 0 % of peak power output (PPO); **b** 30/30 seconds, 100 %/ 50 % of PPO; **c** 90/90 seconds, 100 %/0 % of PPO; **d** 90/ 90 seconds, 100 %/50 % of PPO. Reproduced from Meyer P, et al., "High-intensity interval exercise in chronic heart failure: protocol optimization," *Journal of Cardiac Failure* 2012, 18:126–133, with permission from Elsevier
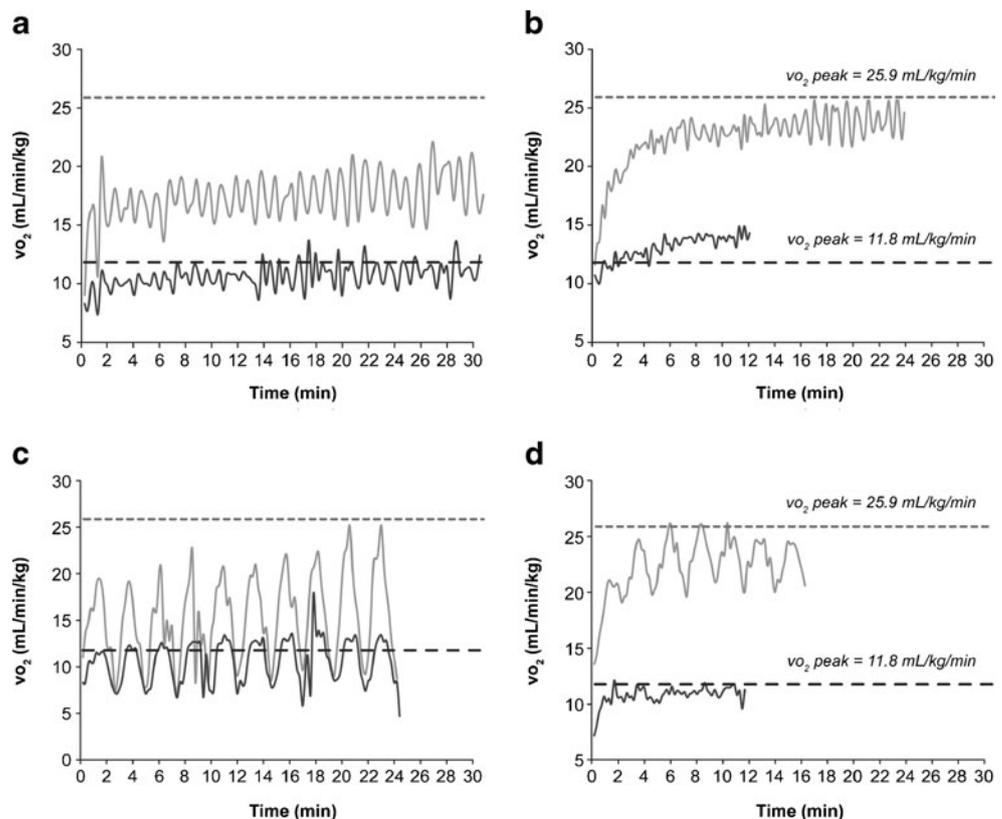
beta-blockers, (2) a high prevalence of chronic atrial fibrillation, and (3) the constant occurrence of heart rate drift during exercise requiring frequent workload adaptations [33, 34].

In summary, no single approach to HIIE prescription can be recommended at present. The most frequently used interval durations range from 30 seconds to 4 minutes, usually with equal work/recovery duration. The work and recovery intensities range respectively from 80 % to 120 % of VO_{2peak} and from 0 % (passive recovery) to 50 % of VO_{2peak}. Warm-up and cool-down periods must be included at the start and end of HIIE sessions that usually have a total duration of 15 to 45 minutes and may be repeated two to five times weekly.

Acute Effects of HIIE

Several studies have investigated the acute physiological responses to HIIE compared to MICE in HF. Meyer et al. compared on a cycle ergometer HIIE (30/60 seconds work/-recovery intervals at intensities of respectively 50 % of MSEC and 15 Watts) with MICE at an intensity of 75 % of VO_{2peak} [35]. HIIE resulted in a higher power output during interval work phase, but with lower rate-pressure product, rating of perceived exertion and plasma catecholamine levels, despite higher blood lactate levels. The authors concluded that HIIE provided a greater peripheral muscular stimulus with a lower central cardiac stimulus in HF patients. Using the same protocol, LVEF measured by radionuclide ventriculography increased significantly and by the same magnitude during HIIE and MICE at the same average power output, both in HF patients and controls [36, 37]. This finding is important given the persistent fear that HIIE may acutely further deteriorate left ventricular function. Recently, Tomczak et al. examined in nine patients with mild HF (NYHA functional class I and II, mean LVEF=35.8±7.2 %), the acute effects of HIIE using the same protocol as described by Wisloff et al. [32] on biventricular function assessed by cardiac magnetic resonance, 6 and 30 minutes post-exercise [38]. Overall, they demonstrated an improvement of biventricular systolic function with a 2.4 % absolute increase of LVEF at 30 minutes post-exercise (P <0.05), which adds further evidence about the safety of HIIE in patients with mild HF and reduced LVEF.

Our group performed in 20 patients (90 % men; aged 61± 9.9 years) with HF and reduced LVEF (mean 26±7 %) a comparison of acute responses after HIIE (2×8 minutes of 30/30 seconds work/recovery intervals at respectively 100 % of PPO and rest) compared to isocaloric MICE (22 minutes at 60 % of PPO) [39]. A greater proportion of subjects completed the prescribed HIIE session compared to MICE (85 % vs. 40 %, P<0.0075) with similar time spent over 90 % of VO_{2peak} and similar mean cardiopulmonary responses (VO_2, ventilation, heart rate and O_2 pulse) during MICE and HIIE.

However, during HIIE, patients exercised for a shorter effective cycling time (7.5±1.5 vs. 17±5 minutes), at a higher power output (51±21 vs. 46±20 Watts), which translated into superior efficiency (energy expenditure/effort time) of HIIE compared to MICE. Finally, HIIE was well tolerated with ratings of perceived exertion that tended to be lower compared to MICE. We did not observe any significant arrhythmias, abnormal blood pressure responses, or increase in troponin-t, B-type natriuretic peptide (BNP) or high-sensitivity C-reactive protein. Using the same protocol, we further evaluated the central hemodynamic changes by cardiac bioimpedance during HIIE and MICE in 13 patients (age, 59±6 years; LVEF, 27±6 %) [40]. Compared to MICE, HIIE elicited similar mean cardiac output (9.26±1.93 L/min vs 10.06±3.14 L/min), mean stroke volume (96 mL±22 vs. 93±21 mL) and mean calculated difference in arterio-venous oxygen content. When examining the kinetics of these variables, our study demonstrated the relative stability of central hemodynamics during HIIE, which is in line with the lack of complications observed in our previous studies. We also compared carbohydrate and lipid oxidation during HIIE and MICE using gas exchange analysis (Frayn equation) in 18 patients with HF and reduced LVEF [41]. HIIE and isocaloric MICE elicited a 4.8- to 5-fold higher carbohydrate oxidation and a 1.22- to 1.42-fold higher lipid oxidation compared to resting values but absolute and relative values of substrate muscle oxidation were similar during both exercise modalities. Finally, with respect to the arrhythmogenic potential of HIIE, Labrunee et al. performed three consecutive 24-hour Holter recordings in 12 patients with HF following an HIIE session, a MICE session or a control period without physical exercise [42]. Interestingly, the number of premature ventricular contractions, ventricular couplets or episodes of non-sustained ventricular tachycardia was clearly and significantly lower after HIIE compared to MICE and no exercise. This novel finding may be due to an improvement in sympatho-vagal balance following HIIE, which was corroborated by a greater reduction of heart rate and better indices of heart rate variability after HIIE compared to MICE.

Overall, these studies indicate that HIIE results in similar mean cardiorespiratory responses but probably superior peripheral effects compared to isocaloric MICE. HIIE appears better tolerated with lower ratings of perceived exertion allowing more patients to complete their planned exercise sessions. When taking into account the effective exercise time without resting intervals, HIIE is a more efficient exercise modality compared to MICE. Finally, in these selected HF patients HIIE appeared safe and did not induce significant arrhythmias, signs of myocardial injury, or acute deteriorations of left or right ventricular function.

HIIE Training Studies

The first HIIE training study in patients with HF was performed by the group of K. Meyer [16]. They performed a random-order crossover study comparing the effects of 3-week HIIE training versus activity restriction in 18 patients with severe chronic HF (mean LVEF 21 ± 1 %, mean VO_{2peak} 12.2 ± 0.7 ml/kg/min). The HIIE protocol consisted of 30/60 second work/recovery intervals at respectively 50 % of MSEC (corresponding to slightly more than 100 % of PPO) and 15 Watts, during 15 minutes, 5 times/week. They demonstrated a 24 % increase in VO_{2peak} [16] and a 6 5 % improvement in the 6-minute walk test [43] in the exercise group.

Since then, several small single-center randomized training studies comparing HIIE to MICE have been performed (Table 2) [32, 44•, 45–48, 49•]. Other studies that have investigated HIIE in addition to strength training [50–53] or exclusively in comparison to sedentary controls [54–57] will not be discussed here. A recent meta-analysis including the majority of these studies was also recently been published [58]. The most spectacular and comprehensive HIIE randomized training study was published by Wisloff et al. in 2007 [32]. A total of 27 patients with severe HF of ischemic etiology (mean age 75 years, VO_{2peak} 13.0 ml/kg/min, LVEF 29 %) were randomized to either MICE or HIIE 3 times per week for 12 weeks or to a control group that received standard advice regarding physical activity. The HIIE protocol was detailed previously in this review and in Table 1. The MICE protocol consisted of isocaloric steady-state walking at 70–75 % of peak heart rate during 47 minutes. HIIE training resulted in superior improvements in VO_{2peak} compared to MICE (46 % vs. 14 %, $p<0.001$) and led to major benefits in cardiac remodelling parameters (35 % increase of LVEF, 40 % decrease of BNP). There was also a greater impact of HIIE on endothelial function as assessed by ultrasound-guided brachial artery flow-mediated dilation and quality of life, compared to MICE.

These impressive findings have generated a wave of enthusiasm in the cardiovascular rehabilitation community. Subsequently, several other groups have demonstrated the benefits of HIIE training in HF patients. Using a similar protocol with 3/3 minutes work/recovery intervals at respectively 80 % and 40 % of PPO, Fu et al. demonstrated a 23 % increase in VO_{2peak} in the HIIE group ($p<0.05$) compared to no significant change in the MICE group [49•]. Ventilatory efficiency and cardiac output were also significantly increased in the HIIE group compared to the MICE group. Comparable improvements in VO_{2peak} (respectively 21 % and 13 % in the HIIE and MICE groups) were observed by Smart et al. after 16 weeks of stationary cycling thrice a week. However, no significant changes in ventricular dimensions or systolic or diastolic function were detected over the study period. A particularity of this study was that HIIE and MICE protocols only differed by the addition of 60 seconds of rest each minute in the HIIE group, and otherwise used the same moderate intensity (70 % of VO_{2peak}) for exercise intervals [44•]. Finally, in a short but very intensive intervention (6 times per week during 8 weeks), using 30/60 second work/recovery intervals at

Table 2 Randomized training studies comparing HIIE to MICE

Studies	Age (years)	Men (%)	LVEF (%)	Baseline VO_{2peak} (ml/kg/min)	MICE protocol	↑ VO_{2peak} (HIIE vs. MICE)	Other outcomes
Dimopoulos 2006 [45] (N=24)	60	96	32	15.4	40 minutes at 50 % of PPO	8 % vs. 6 %	↑ HR recovery at 1 min in MICE only
Roditis 2007 [46] (N=21)	60	90	32	~14.7	40 minutes at 50 % of PPO	8 % vs. 9 %	↑ phase II O$_2$ kinetics in MICE only
Wisloff 2007 [32] (N=27)	75	74	29	13.0	47 minutes at 70–75 % of peak HR	46 % vs. 14 %	↑ LVEF, ↑ endothelial function, ↑ quality of life superior in HIIE
Smart 2011 [44•] (N=23)	~61	91	~28	~12.3	30 minutes at 70 % of PPO	21 vs. 13 %	No change in cardiac volumes, LVEF and endothelial function
Fu 2011 [49•] (N=45)	67	64	38	~16.0	30 minutes at 60 % of HRR	22.5 % vs. no significant change	↑ ventilatory efficiency, ↑ cardiac output, in HIIE only
Iellamo 2012 [48] (N=16)	62	100	33	18.6	30–45 minutes at 45–60 % of HRR	22 % vs. 22 %	No change in cardiac output, in cardiac dimensions, and in LVEF
Freyssin 2012 [47] (N=26)	54	50	~29	~10.6	61 minutes at VT1 + aquagym + gymnastics	27 % vs. 2 %	↑ 6-minute walk test by 12 % in HIIE (6 % in MICE)

HIIE, high intensity interval exercise; HR, heart rate; HRR, heart rate reserve; LVEF, left ventricular ejection fraction; MICE, moderate intensity continuous exercise; PPO, peak power output; VT1, first ventilatory threshold.

intensities of up to 12 0 % of VO_{2peak} for work intervals and employing a passive recovery, Freyssin et al. demonstrated a VO_{2peak} increase of 22 % compared to 2 % only in the MICE group [47].

However, not all training studies have demonstrated the superiority of HIIE over MICE for improving VO_2. Using a protocol with 30/30 seconds work/recovery intervals at high intensity (100 % of PPO) and passive recovery, Dimopoulous et al. only found a modest 8 % increase in VO_{2peak} in the HIIE group ($P=0.01$) compared to 6 % in the MICE group ($P<0.05$) without significant differences between groups [45]. Moreover, examining markers of parasympathetic activity, they reported a significant increase in heart rate recovery at one minute post-exercise only in the MICE group. In a subsequent study using the same protocol, these authors obtained similar results in terms of exercise capacity improvements and they also demonstrated that only MICE training improved phase II O_2 kinetics, an indirect index of muscle oxidative capacity [46]. More recently, Iellamo et al. performed a very similar intervention as described by Wisloff et al. but with slightly lower intensities (75–80 % of heart rate reserve versus 90–95 % of peak heart rate) [48]. VO_{2peak} improved by 22 % in both HIIE and MICE groups while neither training modality influenced ventricular remodelling parameters or cardiac output.

In summary, these studies overall suggest that HIIE training elicits larger improvements of VO_{2peak} compared to MICE in patients with HF whereas the impact on cardiac dimensions and function and on endothelial function remains uncertain. Differences in results may be due to differences in patient characteristics and/or in training protocols. However, we believe it is currently not possible to conclude that a specific HIIE protocol is superior to another. Furthemore, all studies were single-centre, and, in the vast majority, investigators were not blinded to outcome assessments, which represent limitations.

Conclusions and Future Directions

When considering the current body of evidence of HIIE in HF summarized in this review, several conclusions can be drawn. First of all, HIIE is more effective than MICE to improve VO_{2peak} in patients with HF and reduced LVEF. This is an important finding given that better functional capacity translates into an improvement of symptoms and quality of life. Secondly, HIIE was shown to be more efficient, meaning that the same energy expenditure can be performed in a shorter time period, which may be an important practical aspect to consider during a rehabilitation program. Thirdly, HIIE acute and training studies performed in selected HF populations, including predominantly men with ischemic heart disease in NYHA functional class II, did not reveal safety issues.

However, more research of HIIE in HF is definitely warranted to further explore several issues.

Will HIIE have an impact on clinical outcomes? VO_{2peak} being one of the strongest predictors of outcomes in this population [59], HIIE may potentially contribute, among other therapeutic strategies, in further reducing HF morbidity and mortality. However, to demonstrate such an effect would require many more randomized training studies or a very large "HF-ACTION-like" trial investigating HIIE, which is hardly conceivable at present. In a similar vein, the impact of HIIE on cardiac reverse remodeling parameters and especially LVEF, which is also a known predictor of outcomes in HF, remains uncertain and should also be further investigated.

Is HIIE really safe in HF patients? Even if HIIE training appeared safe in a recent large observational study in coronary patients [60], more data are needed in HF patients who are older, more fragile, and often equipped with defibrillators. Future investigations should include a larger sample and a broader representation of HF patients. This will not only confirm the safety of HIIE in this population but also help to better identify predictors of response to that training modality.

What is the optimal HIIE protocol to be used? As mentioned earlier in this review, no specific HIIE protocol has been proven superior, and therefore no single regimen can be recommended. Future training studies should compare different HIIE protocols to establish the optimal one. However this is a rather complex issue not only because there are countless possible interval combinations but also because protocols should probably be individualized and tailored to patients, especially according to their baseline exercise capacity and training level. As mentioned earlier, very deconditioned patients may benefit from protocols using shorter intervals, lower intensities and passive recoveries whereas patients with higher training levels could better improve with longer intervals, higher intensities and active recoveries.

Will HIIE improve adherence to exercise training in HF patients? Non-adherence was a major issue in the HF-ACTION study where only 30 to 40 % of patients followed training recommendations after 3 months despite a close follow-up by study personnel [7]. There is no data yet about the adherence to HIIE in HF patients. In coronary patients, the long-term adherence to HIIE was superior to MICE [61] and it was perceived as a more enjoyable training modality in healthy adults [62]. In our experience, HIIE may be very motivating for HF patients when performed in groups in the same way as the very popular "spinning" sessions proposed by fitness centers.

Some of these issues will be addressed in an ongoing multicenter European randomized trial, SMARTEX-HF [63]. A total of 200 patients with HF and LVEF ≤35 % will be randomized for a 12-week exercise program to one of three different arms: HIIE as proposed by Wisloff et al. [32], MICE, and regular exercise according to patients' preferences. The primary endpoint will be cardiac reverse remodeling whereas secondary endpoints will include VO_{2peak}, biomarkers, quality of life and level of physical activity assessed by questionnaires.

In a recent position statement, the European Society of Cardiology has incorporated HIIE as a recommended training modality in patients with HF [64•]. In agreement with this paper, we believe that HIIE should not replace other training modalities in HF, such as MICE, strength and respiratory training but should rather complement them. To be effective, exercise training should be progressive and varied. Therefore, analogous to optimizing pharmacotherapy, combining and tailoring different exercise training modalities according to each patient's baseline exercise capacity, personal needs, preferences and goals seem the most judicious approach to exercise prescription.

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