REVIEW ARTICLE

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High-Intensity Interval Training in Cardiac Rehabilitation

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Abstract

High-intensity interval training (HIIT) is frequently used in sports training. The effects on cardiorespiratory and muscle systems have led scientists to consider its application in the field of cardiovascular diseases. The objective of this review is to report the effects and interest of HIIT in patients with coronary artery disease (CAD) and heart failure (HF), as well as in persons with high cardiovascular risk. A non-systematic review of the literature in the MEDLINE database using keywords 'exercise', 'high-intensity interval training', 'interval training', 'coronary artery disease', 'coronary heart disease', 'chronic heart failure' and 'metabolic syndrome' was performed. We selected articles concerning basic science research, physiological research, and randomized or non-randomized interventional clinical trials published in English.

To summarize, HIIT appears safe and better tolerated by patients than moderate-intensity continuous exercise (MICE). HIIT gives rise to many short- and long-term central and peripheral adaptations in these populations. In stable and selected patients, it induces substantial clinical improvements, superior to those achieved by MICE, including beneficial effects on several important prognostic factors (peak oxygen uptake, ventricular function, endothelial function), as well as improving quality of life. HIIT appears to be a safe and effective alternative for the rehabilitation of patients with CAD and HF. It may also assist in improving adherence to exercise training. Larger randomized interventional studies are now necessary to improve the indications for this therapy in different populations.

1. Introduction

High-intensity interval training (HIIT) consists of alternating periods of intensive aerobic exercise with periods of passive or active moderate/mild intensity recovery.[1] The principal interest lies in the fact that it offers the possibility to maintain high-intensity exercise for far longer periods than during continuous exercise.[2,3] Therefore, HIIT elicits a greater training stimulus, which further improves maximal aerobic capacity.[4]

The central and peripheral adaptations induced by HIIT have been clearly shown in animal models[5-9] and healthy subjects.[10-15] In addition, HIIT appears to be of particular interest since high-intensity exercise (85–100% of peak oxygen uptake [$\dot{V}O_{2peak}$]), apart from its greater ability to improve the limiting factors of $\dot{V}O_{2peak}$, and $\dot{V}O_{2peak}$ itself,[16,17] is also more effective than moderate-intensity continuous exercise (MICE) in improving cardiovascular risk factors.[18-20] The clinical implications appear to be major since (i) $\dot{V}O_{2peak}$ is a strong independent predictor of morbimortality in patients with coronary artery disease (CAD)[21,22] and heart failure (HF);[23] and (ii) the control of risk factors such as diabetes, dyslipidaemia, being overweight and hypertension is a fundamental component of secondary prevention in these patients.[24-26]

Given the above, interest in HIIT in the scientific literature continues to grow.[27] During the last decade, several studies have demonstrated the benefits of this type of exercise in patients referred to cardiac rehabilitation programmes. Wisloff et al.,[28] Warburton et al.[29] and Rognmo et al.[30] showed that HIIT was more effective than MICE in inducing cardiovascular adaptations in patients with mild to severe heart disease. The American Heart Association[24] recently included this exercise technique in its recommendations for patients with heart disease, although without clearly indicating the prescription modalities. Prescription of HIIT is complex since there are an unlimited number of possible exercise/recovery interval combinations,[31] which should be adapted to a wide range of patients referred to cardiac rehabilitation.

Though a majority of studies demonstrate that MICE is sufficient to reduce the risk of developing cardiovascular disease, or suffering a recurrence, moderate- to high-intensity continuous exercise (6 and 12 metabolic equivalents [METs], corresponding to 21 and 42 mL/min/kg of O_2) has also been shown to reduce all-cause mortality in healthy individuals, independently of activity duration,[32] and to reduce the risk of heart disease in elderly individuals,[33] supporting the need to further investigate the health effects of HIIT. In 5106 apparently healthy subjects, it has been shown that the relative intensity, and not the duration of cycling, is of more importance in relation to all-cause and coronary heart disease mortality.[34] This finding is in line with the previous study of Andersen et al.[35] showing that the time spent in leisure physical activity was inversely associated with all-cause mortality in both men and women irrespective of age. The benefits were also found from moderate physical activity, with further benefits from sports activity. In addition, a single session of high-intensity exercise per

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week was found to be sufficient to reduce the risk of cardiovascular death both in men (relative risk [RR] 0.61, 95% confidence interval [CI] 0.49, 0.75), and women (RR 0.49, 95% CI 0.27, 0.89), compared with those reporting no activity.[36] These data suggest that HIIT is both very efficient and particularly cost effective. The question of determining the most appropriate exercise intensity for cardiac patients is still, however, a matter of debate given the heterogeneity of exercise protocols, patient types and timing of the implementation. The modification of a single parameter, such as the duration, the intensity or the type of recovery, significantly modifies the acute physiological response[37,38] and presumably long-term adaptations.

The aim of this review is to take stock of current knowledge concerning the short- and long-term adaptations induced by HIIT in patients with heart disease (CAD and HF) or at high risk of cardiovascular disease (including only studies in patients with the metabolic syndrome[39]), and to discuss practical clinical applications.

We conducted a review of the literature in November 2011. The review included studies published in English before 31 October 2011. We searched the electronic databases of PubMed, MEDLINE, CINAHL®, Google Scholar, SPORTDiscus™, EMBASE and Web of Science using the keywords 'exercise', 'high-intensity interval training', 'interval training', 'coronary artery disease', 'coronary heart disease', 'chronic heart failure' and 'metabolic syndrome'.

2. General Principles of Interval Training Prescription

In healthy trained subjects, the improvement in $\dot{V}O_{2peak}$ with exercise training appears to correlate with the time spent at a high level of oxygen uptake ($\dot{V}O_2$).[40] It is thus usual to measure this parameter to determine the acute physiological requirements of different interval-training protocols.[37,40-44] In training for sports, three categories of interval training inducing different physiological responses are usually described: long intervals (3–15 minutes, intensity 85–90% maximal oxygen uptake [$\dot{V}O_{2max}$]), moderate intervals (1–3 minutes, intensity 95–100% $\dot{V}O_{2max}$), short intervals (10 seconds to 1 minute, 100–120% $\dot{V}O_{2max}$).[45] A new form of interval training has recently been described and consists of repeated 30-second periods of exercise at an intensity of approximately 250% of $\dot{V}O_{2peak}$, interspersed with 4-minute recovery periods at 65% $\dot{V}O_{2peak}$.[12]

Saltin et al.[31] characterized the different parameters of interval training and compared the different physiological responses induced by them. This classification is based on three parameters: (i) ratio, which is the relationship between the exercise duration and the recovery duration; (ii) mean intensity, which is the mean of the intensity during the exercise and recovery; and (iii) amplitude, which corresponds to the difference between exercise and recovery intensities divided by mean intensity and expressed as a percentage (table I).

There are thus many possible combinations that all induce varying acute physiological responses. In healthy subjects, for the same mean intensity, but with different exercise intensities during recovery, time to exhaustion (Tlim) at 85% of $\dot{V}O_{2peak}$ ranged from 7.4 to 14.5 minutes.[37] Even though mean intensity alone is not sufficient to quantify the volume of exercise training, it is more relevant when exercises with the same amplitude (passive recovery) are prescribed because it then has an inverse relationship with performance.[43] It also retains all of its relevance when the ratio is the only variable that is modified. By diminishing recovery time, the mean exercise intensity is increased, which also increases

Table I. Examples of calculations using Saltin's parameters for two different interval-training protocols (A, B)

Saltin's parameters	Mode A	Mode B
Duration of exercise phase	15 sec	1 min
Exercise intensity (PPO)	120% of PPO	100% of PPO
Duration of recovery phase	15 sec	30 sec
Type and intensity of recovery	Passive (0%)	Active (50% of PPO)
Ratio	1/1	2/1
Mean intensity	60%	83%
Amplitude	200%	60%

PPO = peak power output.

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energy expenditure.[46,47] The type of recovery therefore has a major impact on performance. Passive recovery allows a greater number of exercise repetitions in young subjects, in endurance athletes[38,48] and in patients with heart disease.[49,50]

3. Acute Physiological Effects of High-Intensity Interval Training (HIIT)

3.1 Patients with Stable Coronary Artery Disease (CAD)

The short-term cardiovascular and bioenergetic responses to HIIT with different exercise protocols have recently been studied in patients with heart disease. These studies made it possible to characterize the optimal HIIT protocol on a cycle ergometer for patients with stable CAD according to their short-term response.[49] The method used aimed to identify the interval training protocol that resulted in the maximum amount of time spent at a high percentage of $\dot{V}O_{2peak}$, as proposed for athletes by Dupont et al.[51] and Millet et al.,[52] while taking into account Tlim and the subjective patient comfort. Two variables were modified: duration of the exercise/recovery phases and the type of recovery (passive or active) [figure 1]. Exercises phases were conducted at 100% of maximal aerobic power (MAP).

The results showed that the Tlim of interval exercises incorporating passive recovery phases was significantly greater than during interval training sessions incorporating active recovery phases. When exercises were performed until exhaustion, the time spent at a high percentage of $\dot{V}O_{2peak}$ was independent of the recovery protocol, which is in accordance with the results of Dupont et al.[38] in healthy individuals. Depend-

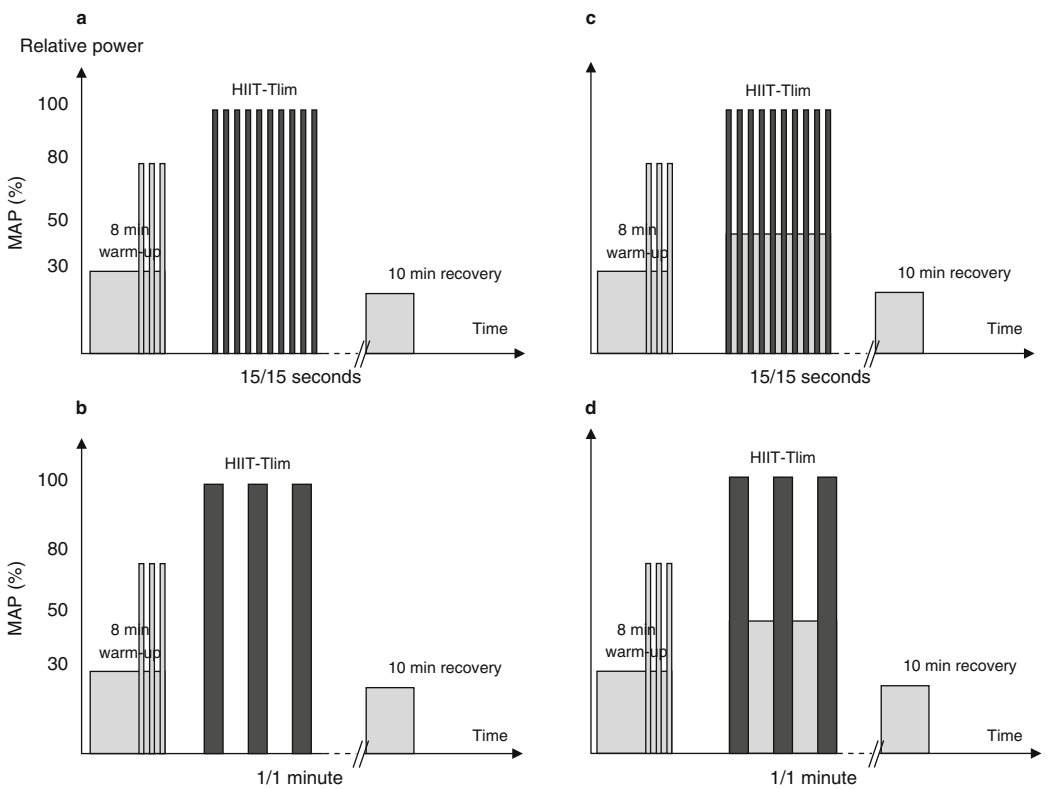

Fig. 1. Different training protocols. Mode (**a**) and (**b**) ratio 1 : 1, mean intensity 50%, amplitude 200%; mode (**c**) and (**d**) ratio 1 : 1, mean intensity 75%, amplitude 66%. **HIIT** = high-intensity interval training; **MAP** = maximal aerobic power; **Tlim** = time to exhaustion.

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ing on the type of interval training used, CAD patients were able to spend between 223 and 337 seconds at a training intensity greater than 95% of $\dot{V}O_{2peak}$, and between 585 and 819 seconds at a training intensity greater than 80% of $\dot{V}O_{2peak}$. Using the Borg scale to measure the rating of perceived exertion (RPE), the effort was perceived to be less intense during protocols with passive recovery periods. It appeared that HIIT, with 15-second periods of exercise interspersed with short (15 second) phases of passive recovery, was the optimal protocol among the four tested. Tlim was significantly longer, perceived difficulty was lower[53] and time spent near $\dot{V}O_{2peak}$ was similar to that achieved during the other three protocols. This was the first study to employ exercise phases at very high intensity (15-second phases at 100% of the MAP) in CAD patients. This exercise intensity was very well tolerated, notably when interspersed with passive recovery, which resulted in an exercise time limit of a mean ± standard deviation of 1724 ± 482 seconds. It was hypothesized that passive recovery may allow better reoxygenation of muscles thus enabling restoration of phosphorylcreatine stores, which may explain why subjects experienced lower levels of fatigue. These elements confirm in a practical context, the magnetic resonance imaging (MRI) study of Yoshida et al.,[54] which showed that depletion of phosphorylcreatine stores during intense exercise is rapid, but that passive recovery permits a significantly greater replenishment of phosphorylcreatine than does active recovery. Oxyhaemoglobin (HbO_2) also fell more slowly with interval training that included passive recovery, which enabled the synthesis of greater amounts of phosphorylcreatine.[55]

We compared short-term responses of the optimal HIIT protocol with those induced by an isocaloric continuous exercise session at 70% of MAP.[56] All patients rated the interval training protocol as their preferred one, with a mean Borg score of 14 ± 2 for HIIT versus 16 ± 2 for continuous exercise ($p < 0.05$). This may be explained by better recovery in terms of metabolism during the passive phases (reduction in $\dot{V}O_2$, reconstitution of energy stores). Nonetheless, even though patients did not pedal during the 15-second passive-recovery phases, energy expenditure remained high. The method used to calculate energy expenditure gave precise estimations of the amount used during exercise and showed that 10 minutes of exercise using the optimal HIIT protocol induced an energy expenditure equivalent to that achieved during 10 minutes of exercise at 60% of peak power. Patients generally preferred HIIT to MICE, which may also be a reflection of the less intense sensation of dyspnoea, since mean ventilation was far lower (58.9 ± 14.2 and 49.8 ± 8.2 l/min^{-1} for MICE and HIIT, respectively; $p < 0.001$), whereas the difference in mean $\dot{V}O_2$, even though significant, was relatively small (respectively, 1773 ± 589 and 1604 ± 468 l/min^{-1}; $p < 0.01$) [figure 2]. This protocol could therefore be particularly useful for weight loss in overweight and obese individuals for whom continuous moderate-intensity exercise may be limited by fatigue and dyspnoea.[57]

As dyspnoea was an exercise-limiting factor in these patients, HIIT could be an interesting training modality to improve long-term adherence in cardiac rehabilitation programmes. In addition, because of the rhythm change imposed by the exercise protocol, patients may treat it like a game, which may help them forget the amount of exertion required.[53] Apart from the undeniable and enhanced physiological benefit of this type of exercise compared with continuous exercise, HIIT appears to a potential tool to improve adherence to exercise training.

Concerning safety, no significant clinical, haemodynamic, electrical or biological signs of ischaemia or arrhythmia have been observed with HIIT. Two recent studies showed that, in patients with stable ischaemic CAD, continuous exercise above the ischaemic threshold is safe and well tolerated.[58,59] Our data suggest that HIIT may be a more attractive training modality in CAD than high-intensity continuous exercise for the simple reason that ischaemia would be intermittent rather than continuous. Current guidelines state that in patients with stable angina,[60] MICE is recommended (target heart rate [HR] fixed at 10 beats per minute [bpm] below the ischaemic threshold), because the risk-benefit ratio goes against higher intensities.[61,62] This opinion,

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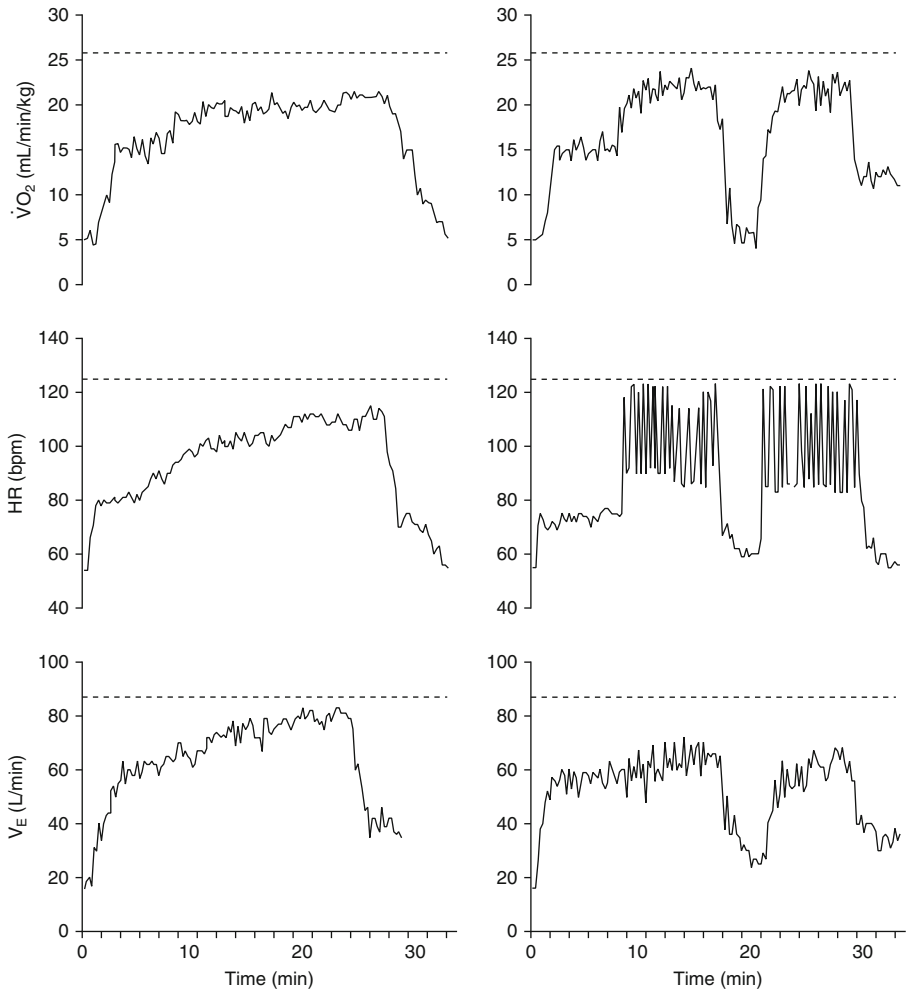

Fig. 2. Oxygen consumption, heart rate and ventilation in a patient during continuous exercise (left panel) and interval training (right panel). The continuous exercise consisted of maintaining an intensity of 70% of MAP for 28.7 minutes, and high-intensity interval training after a 10-minute warm-up at 50% of MAP consisted of two series of 10 minutes each comprising 15-second periods of exercise at 100% of MAP interspersed with 15-second phases of passive recovery. The two series were separated by 4 minutes of rest and ended with a 5-minute recovery period (ratio 1 : 1, mean intensity 50%, amplitude 200%). The dotted line shows the maximal values for this coronary artery disease patient for the three criteria. **bpm** = beats per minute; **HR** = heart rate; **MAP** = maximal aerobic power; $\mathbf{V_E}$ = ventilation; $\mathbf{\dot{V}O_2}$ = oxygen consumption.

however, is based on a single study in 21 patients with ischaemic CAD.[63] These patients exercised for 10 minutes on a cycle ergometer at 75% of the maximal HR, twice a week, for 12 weeks. From Holter ECG recordings, the authors identified ten episodes of ischaemia associated with ventricular rhythm disturbances in five patients. However, the exercise protocol took patients to 75% of maximal HR within the first 2 minutes. This rapid start could have caused the rhythm disturbances, since the importance of a warm-up period in CAD patients with regard to the risk of ischaemia[64,65] and arrhythmias is well known.[66] Moreover, in a recent case report, our team presented the acute cardiopulmonary responses of a patient with ischaemia and angina during a time-limited exercise performed according to the HIIT protocol presented above (15-second periods of exercise at

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100% of the MAP interspersed with 15-seconds of passive recovery phases).[67] The exercise protocol lasted 34 minutes, and was well tolerated with no rhythm disturbances either during or after exercise, and without any increased biomarkers of cardiac injury. In addition, there was complete disappearance of all clinical and electrical signs of ischaemia after 24 minutes, with no recurrence thereafter (figure 3).

This observation is similar to the phenomenon of warm-up angina, which leads to a significant decrease in the ECG signs of ischaemia on a second stress test conducted shortly after the first one.[68] Moreover, periods of intermittent ischaemia could lead to the phenomenon called ischaemic preconditioning,[69] provided that exercise intensity at the end of the test is high enough and that the period between the two stress tests is short.[64-66] Ischaemic preconditioning corresponds to the phenomenon in which exposure to brief episodes of ischaemia and reperfusion before coronary occlusion reduces infarct size.[70,71] This phenomenon was first described in 1978 in an animal model and has since been confirmed in a series of studies, even though the underlying mechanisms have yet to be elucidated.[72,73] Converging data indicate that this phenomenon also occurs in humans. During coronary angioplasty, ST-segment elevation can be progressively reduced by repeated balloon inflation and intermittent arterial occlusion.[74] This could explain why successive phases of high-intensity exercise interspersed with periods of rest might induce adaptations that are beneficial for the ischaemic myocardium. Recent studies have shown that in a relatively short timeframe (8 weeks), intermittent ischaemia induced by HIIT fosters the formation of collateral coronary vessels in animal models[75] without causing myocardial injury. Noteworthy, is the fact that HIIT has also been shown to improve endothelial function.[28,76]

Although regular exercise training improves endothelial function in patients with CAD,[77] a single high-intensity exercise session may also have acute beneficial effects on the endothelium. Guiraud et al.[78] recently measured endothelial microparticles (EMP), specific biological markers associated with the dysfunction, apoptosis and/or damage to endothelial cells[79-82] during single isocaloric sessions of optimized HIIT and MICE in patients with CAD.[78] No elevation in EMP levels was observed 20 minutes, 24 hours and 72 hours after either exercise session. These data suggest that repetitive short phases of high-intensity aerobic exercise do not cause vascular shear stress that is sufficient to damage the underlying endothelium. These results are in keeping with those of Möbius-Winkler et al.[83] who showed

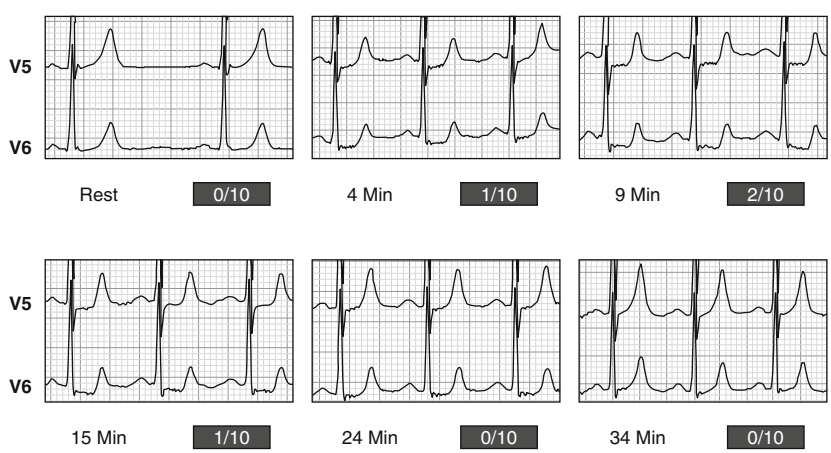

Fig. 3. ECG (leads V5 and V6) and perception of angina (scale of 0–10) during a 34-minute session of high-intensity interval training in a patient with ischaemia and angina.

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that 4 hours of cycling at 70% of the anaerobic threshold (approximately 50% of $\dot{V}O_{2peak}$) did not increase EMP levels in healthy subjects.

In summary, most studies on acute exercise showed that HIIT incorporating short exercise/recovery intervals are safe, well tolerated and are associated with maintenance of a high percentage of $\dot{V}O_{2max}$ during exercise sessions, while generally enabling subjects to exercise longer relative to isocaloric MICE. Furthermore, use of passive recovery phases is even more preferred by patients and does not come at the expense of significantly lower mean $\dot{V}O_2$ response.

3.2 Patients with Heart Failure (HF)

The team led by K. Meyer, a pioneer in this field,[84] was the first to show the interest of HIIT adapted to HF patients. Exercise intensity was prescribed as a percentage of the maximal short-term exercise capacity (MSEC), which is approximately equivalent to peak power measured during a standard cardiopulmonary exercise test,[85] using a steep ramp test on a cycle ergometer (increase in work rate by 25 Watts [W]/10/sec^{-1}).[84] The most widely used exercise protocol consisted of alternating 30-second periods of exercise at 50% of the MSEC with 60-second periods of active recovery at 10 W (ratio 1 : 2, MI 23%, amplitude 173%). Other exercise combinations (15 seconds at 70% of the MSEC or 10 seconds at 80% of the MSEC interspersed with 60 seconds of active recovery at 10 W, that is to say ratio 1 : 4, MI 27%, amplitude 222%; and ratio 1 : 6, MI 23%, amplitude 304%) were also studied.[86] For the three protocols, participants were asked to perform as many repetitions as possible. Meyer et al.[86] reported that the participants were able to produce an effort greater than 70% $\dot{V}O_{2peak}$ for 17–35 minutes, that is to say 3–4 times longer than the true duration of pedalling, which ranged from 5 to 8 minutes. The result of this study once again highlights the excellent effort – benefit ratio of HIIT. Compared with continuous exercise at 75% of $\dot{V}O_{2peak}$, interval training resulted in greater power developed during the exercise phases, but with a lower HR-pressure product (HR × systolic blood pressure), a lower level of perceived exertion and lower levels of plasma catecholamines, despite a higher level of blood lactate. In other words, HIIT induced a greater degree of peripheral stimulation (adequate short-term strength despite reduced endurance due to muscular deconditioning) while increasing the impact on central factors.[86] However, the validity of the maximal short-term exercise capacity in evaluating the prescription of HIIT is debatable, since this evaluation protocol has never been widely used in cardiac rehabilitation, which is a major limitation for these training protocols.[85]

Following on from our work in CAD patients, we compared acute cardiopulmonary responses induced by four HIIT protocols to characterize the optimal protocol for HF patients. The four protocols tested are presented in figure 4. The choice of 30 seconds of exercise for the short intervals was justified by the fact that shorter periods would have been less well tolerated by HF patients (time to acclimatize, too frequent interruptions). Taking into account the total exercise time, the preferred protocol, the perception of effort, patient comfort and time spent at a high percentage of $\dot{V}O_{2peak}$, the short-interval protocol (30 seconds) incorporating passive recovery phases appeared optimal in these patients.[50]

The cardiopulmonary and biological responses induced by this optimized HIIT protocol (30 seconds at 100% MAP and 30 seconds of passive recovery; ratio 1 : 1, MI50%, amplitude 200%) were then compared with those induced by an isocaloric MICE session.[87] Efficiency (energy expenditure/effort time), and tolerance (ability to complete exercise sessions, ventilation) were all greater with HIIT relative to MICE. In addition, patients subjectively preferred the optimized HIIT session, which was associated with a lower RPE compared with MICE. Furthermore, HIIT also produced a substantial physiological stimulus: time spent at an intensity greater than 90% of $\dot{V}O_{2peak}$, and central haemodynamic responses were similar to those induced by MICE.[88] Finally, no rhythm disturbances were observed and no elevations in biomarkers of cardiac injury (troponin T), increased ventricular wall stress brain natriuretic peptide (BNP) or inflammation high-sensitivity C-reactive protein (hs-CRP) occurred.

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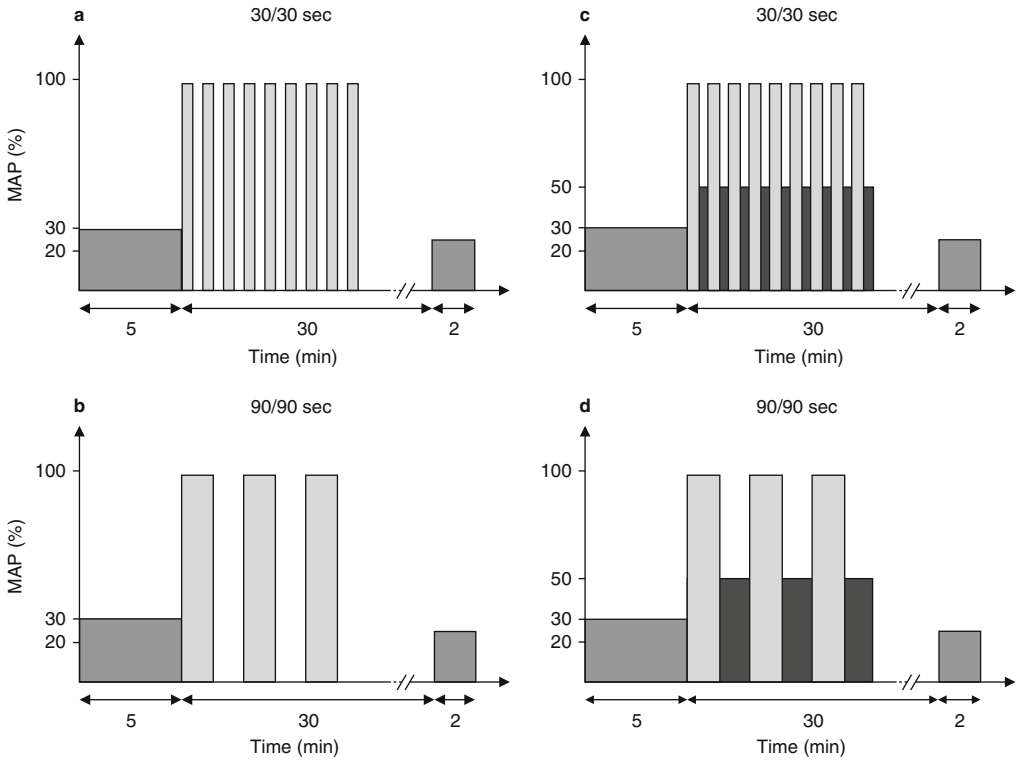

Fig. 4. Different training protocols. Mode (**a**) and (**b**) ratio 1 : 1, MI 50%, amplitude 200%, mode (**c**) and (**d**) ratio 1 : 1, MI 75%, amplitude 66%. **MAP** = maximal aerobic power.

HIIT, therefore, seems to be a promising exercise protocol and should be considered in cardiac rehabilitation for HF patients, even those with a low exercise capacity.

Recently, Tomczak et al.[89] investigated the acute effect of HIIT on biventricular function using cardiac MRI in nine HF subjects with non-ischaemic cardiomyopathy. They observed that immediately after HIIT, left ventricular end systolic volume decreased by 6% ($p < 0.05$) accompanied with a 2.4% absolute increase ($p < 0.05$) of ejection fraction 30 minutes after HIIT, accompanied by a reduction in left ventricular afterload and preserved diastolic function.

Finally, Labrunee et al.[90] recently presented 24 hours of Holter monitoring data from 12 HF subjects following an optimal HIIT session, a continuous exercise session (according to the model used by our group) and following a control period without physical exercise. The number of premature ventricular contractions (PVCs) over 24 hours was significantly lower after HIIT than after both the continuous exercise and no exercise (564 ± 375, 1139 ± 267, 1955 ± 1763 for HIIT, MICE and no exercise, respectively; $p < 0.05$). Similar results were reported for ventricular couplets (32 ± 19 vs 367 ± 278 and 425 ± 317 for HIIT, MICE and no exercise, respectively; $p < 0.05$) and runs of non-sustained ventricular tachycardia (10 ± 6 vs 185 ± 145 and 259 ± 205 for HIIT, MICE and no exercise, respectively; $p < 0.05$). These changes were accompanied with improvements in sympathovagal balance due to better reactivation of parasympathetic tone notably during the first 3 hours after exercise.

In summary, a large number of cardiovascular parameters measured during intense exercise in small samples of selected patients, suggest that HIIT is safe and well tolerated. As will be discussed in section 4.2, larger studies comparing the

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long-term cardiovascular effects of optimized HIIT versus MICE training are required.

4. Long-Term Effects of HIIT

4.1 Patients with CAD

The first studies were conducted by Meyer et al.,[91] who investigated the effects of HIIT during a cardiac rehabilitation programme following coronary bypass surgery (mean = 24 days post-operatively). Subjects performed 20 minutes of either interval training or continuous exercise every day for 3.5 weeks, initially at 86% of maximal HR. The workload was then increased by 20 W/week. During the third week, the interval-training group performed alternating 1-minute phases at 20 W with 1-minute phases at 121 W, whereas the MICE group pedalled continuously at 83 W. Although total energy expenditure was lower in the interval group, peak power improved more in the interval training group (+0.63 vs +0.26 W/kg for interval training and MICE groups, respectively; $p < 0.001$), while resting HR (−9 vs −4 bpm, respectively; $p < 0.04$), and HR at 75 W (−12 vs −2 bpm, respectively; $p < 0.02$) were also reduced more in this group. These results demonstrate the effectiveness of interval training in improving physical performance without placing excessive demands on heart function (similar rate pressure product).[91]

Rognmo et al.[30] studied the impact of 10 weeks of either continuous (50–60% of $\dot{V}O_{2peak}$) or isocaloric interval (ratio 4 : 3, MI 72%, amplitude 42%) exercise performed three times per week on functional capacity in 21 stable CAD patients. There was a significant increase in $\dot{V}O_{2peak}$ in both groups (interval 17.9%; $p = 0.012$ and continuous 7.9%; $p = 0.038$), with a greater improvement in the HIIT group (interaction $p = 0.011$). This improvement in the HIIT group was all the more remarkable since initial $\dot{V}O_{2peak}$ was 32 mL/min/kg, which is far higher than in most reported studies in patients with heart disease. By dividing the increase in $\dot{V}O_{2peak}$ by the number of exercise sessions, the authors noted a 0.6% improvement in $\dot{V}O_{2peak}$ per exercise session after interval training, compared with a 0.3% improvement after MICE training ($p = 0.006$). The results for this parameter must, however, be interpreted with caution, since the adaptation process to exercise training is not linear. These results are consistent with the results of Jensen at al.[92] who revealed the relationship between exercise intensity (50% and 85% of $\dot{V}O_{2peak}$) and improvements in $\dot{V}O_{2peak}$ in a large cohort of CAD patients.

Warburton et al.[29] studied the effects of 16 weeks of aerobic exercise in 14 patients with stable CAD, randomized to aerobic interval (ratio 1 : 1, MI 65%, amplitude 77%) or MICE training. Subjects performed both a maximal cardiopulmonary stress test and a sustained submaximal exercise test (constant intensity = 90% of the reserve HR) continued to exhaustion, before and after exercise training. Surprisingly, $\dot{V}O_{2peak}$ improved to a similar degree in both groups. This could be explained by the fact that baseline $\dot{V}O_{2peak}$ in patients was already high (intensity >9 METs, equivalent to >42 mL/min/kg of O_2). In addition, the small sample size limited statistical power in this study. Nonetheless, Tlim during the submaximal exercise test increased 5-fold in the interval training group and 2.5-fold in the MICE group ($p < 0.05$), which led the authors to suggest that interval training safely improved anaerobic tolerance.[29] However, these results must be interpreted with caution, as the contribution of anaerobic capacity during interval training is rather limited; the intensity of interval training approximately corresponds to 85% of $\dot{V}O_{2peak}$.[93] The improvement in Tlim most likely stems from the positive impact of interval training on aerobic endurance and/or energy costs at high intensity.[94]

More recently, Amundsen et al.[95] compared the effects of two training protocols, interval (ratio 4 : 3, MI 72%, amplitude 42%) and continuous on left ventricular diastolic function in CAD patients. After 10 weeks of training, the improvement in $\dot{V}O_{2peak}$ was significantly greater in the HIIT group (17% vs 8% in HIIT and MICE groups, respectively; $p < 0.01$). Left ventricular filling speed and diastolic relaxation increased only in the HIIT group. HIIT thus improved left ventricular compliance and contributed to the increase in systolic ejection volume and cardiac output witnessed.

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Munk et al.[96] compared the effect of interval training with usual care on in-stent restenosis after coronary angioplasty with stent implantation. After 6 months, restenosis, as measured by late loss in lumen diameter in the stented artery, was significantly lower (median value [range] = 0.10 [0.52] mm) in the exercise group relative to the control group, 0.39 (0.38) mm (interaction $p < 0.01$). Results were similar irrespective of the type of stent implanted (bare or medicated). Furthermore, HIIT resulted in a significant improvement in $\dot{V}O_{2peak}$ and endothelial function (flow-mediated dilatation [FMD] of the brachial artery) and a reduction in inflammation (hs-CRP). The preventive effects of exercise on restenosis can be explained in part by the fact that exercise improves endothelium-dependent vasodilation by activating synthesis of nitric oxide (NO), which increases levels of NO in coronary endothelial cells. Local release of NO seems to inhibit the neo-intimal proliferation, suggesting that exercise has a potential mechanical effect on late loss of lumen diameter.[97] In addition, these results were significantly correlated with the decrease in interleukin-6 and C-reactive protein levels, which may attenuate some inflammatory pathways that are potentially contributing to the beneficial effects of exercise training on restenosis.[98] In the HIIT group only, Munk et al.[99] also showed a significant improvement in regulation of the autonomous nervous system of the myocardium. Moreover, changes in the HR variability (using the standard deviation of NN intervals [SDNN] and the square root of the mean squared difference of successive NNs [RMSSD]) correlated with improved $\dot{V}O_{2peak}$ ($r = 0.47$; $p < 0.01$ and $r = 0.39$; $p = 0.03$, respectively).

Still using the same interval training protocol (ratio 4 : 3, MI 72%, amplitude 42%) compared with continuous exercise, Karlsen et al.[100] showed that the prescription of hyperoxia (65% O_2) during HIIT improved both $\dot{V}O_{2peak}$ and systolic ejection fraction to a similar degree in comparison with normoxic training. In other terms, oxygen supplementation did not provide benefit during exercise training in this CAD sample. Subsequently, Helgerud et al.[101] showed that after 24 sessions HIIT led to an increase in maximal systolic ejection volume (23%; $p < 0.05$) and $\dot{V}O_{2peak}$ (17%; $p < 0.05$), whereas lower-limb muscle building alone had no effect on these parameters.

In a randomized study, Moholdt et al.[102] compared the effects of interval training (ratio 4 : 3, MI 72%, amplitude 42%) and MICE on functional capacity in patients after coronary bypass surgery during a stay in a rehabilitation unit (4 weeks) followed by 6 months of home-based training. Both exercise protocols generated a similar improvement in $\dot{V}O_{2peak}$ in the short term (after 4 weeks: HIIT +12.2%, $p < 0.001$; MICE +8.8%, $p < 0.001$), but the long-term benefits on the maintenance or improvement were clearly greater following interval training (HIIT +5.9%; $p < 0.001$) with no change for MICE. In post-myocardial infarction patients, this team also compared both types of supervised exercise training.[103] Both exercise protocols increased endothelial function, serum adiponectin, quality of life (QoL), and reduced serum ferritin and resting HR. High-density lipoprotein cholesterol (HDL-C) increased only after HIIT. The $\dot{V}O_{2peak}$ increased more after HIIT than after usual care rehabilitation ($p < 0.005$). The difference between groups in terms of $\dot{V}O_{2peak}$ persisted after 30 months of home-based training ($p < 0.005$), which can be explained partly by a higher increase during the initial 12 weeks of supervised training and partly by a lower decline during follow-up.[104]

In summary, HIIT appears to be well suited to CAD patients and its superiority to continuous-type aerobic exercise is almost beyond doubt. However, it is still necessary to define when cardiac rehabilitation incorporating HIIT may commence after an acute coronary syndrome.

4.2 Patients with HF

Meyer et al.[105] compared 3 weeks of interval training with exercise restriction in 18 patients with HF (mean left ventricular ejection fraction 21%, mean peak $\dot{V}O_2$ 12.2 mL/min/kg). Interval training included aerobic exercise on a cycle ergometer (30 seconds of work at 50% of the MSEC/60 seconds active recovery at 15 W, for 15 minutes, 5 times/week) and on treadmill (60 seconds at a mean speed of 2.4 miles per hour/60 seconds

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active recovery at 0.9 miles per hour, for 10 minutes, 3 times a week). This protocol led to an increase of 24% in $\dot{V}O_{2peak}$, associated with a significant improvement in the ventilatory threshold and a decrease in HR measured at a work rate of 56 W. Meyer et al.[106] also compared ventricular function during interval training versus continuous exercise in HF patients. The two exercise protocols led to similar changes in ejection fraction during both exercise and recovery. It therefore appears of interest to recommend HIIT more frequently, because it induces a greater degree of peripheral adaptation than MICE, with no harmful effect on ventricular function.

In 1998, Willenheimer et al.[107] compared a programme comprising 16 weeks of interval training (ratio 3 : 1, MI 60%, amplitude 133%) with restriction of physical activity in 49 patients with mild to moderate HF, with and without ischaemic etiology (ejection fraction 35–36%, $\dot{V}O_{2peak}$ 16.4–16.6 mL/kg/min). The exercise protocol consisted of alternating phases of 90 seconds at 80% $\dot{V}O_{2peak}$ on a cycle ergometer with 30 seconds of passive recovery. Interval training was found to be safe (no adverse events or deterioration of ventricular function) and resulted in a similar improvement in $\dot{V}O_{2peak}$ and quality of life.

More recently, the study by Wisloff et al.[28] confirmed in a randomized trial, the effectiveness of interval training in patients with HF ($\dot{V}O_{2peak}$ 13.0 mL/kg/min, mean systolic ejection fraction 29%). Interval training (ratio 4 : 3, MI 72%, amplitude 42%) was compared with continuous training with respect to variables associated with cardiovascular function and prognosis over 12 weeks at a training frequency of 3 sessions per week. The HIIT protocol was similar to that used by Rognmo et al.[30] in patients with CAD (4×4 minutes at 90–95% of the maximal HR separated by 3 minutes of active recovery at 50–70% of the maximal HR). The continuous exercise was isocaloric at 70–75% of the maximal HR. HIIT led to a greater improvement in $\dot{V}O_{2peak}$ than did MICE (46% vs 14% for HIIT and MICE training, respectively; $p < 0.001$), as well as beneficial effects on cardiac remodelling (reduction in end-diastolic and end-systolic volumes in the interval group only). Furthermore, ejection fraction increased by 35% and pro-BNP decreased by 40% in the HIIT group. These changes were accompanied by an improvement in endothelial function (post-hyperaemic brachial artery ultrasonography) and mitochondrial function (muscle biopsies of the vastus lateralis). These benefits are all the more interesting because they occurred in patients who were already receiving optimal medical treatment.

Deljanin Ilic et al.[108] studied the effect of two exercise protocols (interval and continuous) on NO production. After 3 weeks of training, increases in both NO production and physical capacity in patients with left ventricular dysfunction (ejection fraction <40%) were greater following interval training than continuous training. More recently, Nilsson et al.[109] developed a rehabilitation model based on aerobic dance movements with music (the Norwegian Ullevaal model). Sessions lasted 50 minutes with movements involving the whole body and alternating 3 high-intensity periods (15–18 on the Borg scale) with 2 moderate-intensity periods (11–13 on the Borg scale) lasting 5–10 minutes each. After 4 months, the improvement in exercise capacity and QoL in the exercise group was significantly greater than that achieved in the usual care group (+58 m in the 6-minute walk test vs 15 m, respectively; $p < 0.001$) and (+10 vs 1 point; $p < 0.005$ for QoL).[110,111] Differences between groups remained statistically significant after 12 months of follow-up, suggesting that this protocol provided long-term beneficial effects.[112] Hermann et al.[113] examined whether 8 weeks of HIIT improves $\dot{V}O_{2peak}$ and non-invasively measured endothelial function when compared with a no-training control group. They found that $\dot{V}O_{2peak}$ increased significantly in the HIIT group (+18.4%) compared with controls (–4.9%; $p < 0.001$ exercise vs control). FMD increased in the exercise group compared with controls (8.3 ± 1.1% to 11.4 ± 1.2% vs 5.6 ± 1.0% to 5.3 ± 1.7%; $p = 0.024$). Systolic blood pressure fell in the exercise group (142 ± 4.2 mmHg to 127 ± 3.4 mmHg; $p = 0.01$) and remained unchanged in controls. Finally, it has been shown in 28 HF patients ($\dot{V}O_{2peak}$ 15.7 mL/kg/min, mean systolic ejection fraction 37%) that HIIT associated with strength training induced a greater beneficial effect on vascular reactivity ($p = 0.002$) measured with FMD rather than HIIT alone.[114]

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In summary, HIIT appears to be superior to MICE training and could be particularly suited to subjects with HF. The superiority of HIIT is notably well confirmed for the improvement of $\dot{V}O_{2peak}$ in a recent meta-analysis.[115] Not only are the results in the above-mentioned studies encouraging with respect to physiological parameters, but we are also convinced that this type of exercise will lead to improved adherence. The subjects express that HIIT is more motivating because its effects are felt by the subjects in terms of improved exercise capacity and because the total exercise time is reduced.[25] Further research with larger prospective studies is required in order to confirm the safety and effectiveness of HIIT in subjects with HF.

4.3 High-Risk Primary Prevention

Following on from earlier studies of Rognmo et al.[30] and Wisloff et al.,[28] the same team studied the effect of 16 weeks of continuous or interval training (ratio 4 : 3, MI 72%, amplitude 42%) in patients with the metabolic syndrome and high cardiovascular risk.[116] The study sought to determine whether exercise intensity had an impact on cardiometabolic risk. HIIT improved $\dot{V}O_{2peak}$ (35% and 16%, respectively; $p < 0.01$), reduced the number of cardiometabolic risk factors (respectively, 5.9 pre and 4.0 post; $p < 0.01$ vs 5.7 pre and 5.0 post, intergroup difference; interaction $p < 0.05$), reduced the prevalence of the metabolic syndrome (respectively, −46% [$p < 0.05$] and −37% [$p = 0.23$]; intergroup difference $p < 0.05$), improved endothelial function (increase in post-ischaemic brachial hyperaemia (9% vs 5%; $p < 0.001$), and improved glucose metabolism to a greater degree than did continuous exercise. However, the reduction in weight and waist circumference was similar in both groups, which is discordant with more recent data,[117] notably for longer HIIT programmes in obese subjects with and without the metabolic syndrome.

Recently, Stensvold et al.[118] compared HIIT with strength training (ST) alone, ST with HIIT (ST+HIIT) and no-exercise control group in patients with the metabolic syndrome. After 12 weeks, waist circumference was significantly reduced after HIIT (95% CI −2.5, −0.04 cm), ST+HIIT (95% CI −2.11, −0.63 cm) and ST alone (95% CI −2.68, −0.84) and was associated with an improvement in endothelial function. In contrast, the control group increased waist circumference (95% CI 0.37, 2.9 cm). $\dot{V}O_{2peak}$ increased by 11% and 10% in the HIIT and ST+HIIT groups, respectively. There was, however, no significant improvement in body weight, fasting glycaemia or levels of HDL-C. The absence of any effect of these protocols on body composition or lipid profile could be due to the relatively short study duration. Indeed, a recent retrospective study showed that a longer HIIT programme (9 months) resulted in durable weight loss and had a positive impact on body composition, notably the quantity of visceral fat, which is a strong independent cardiovascular risk factor.[119] This type of prolonged training does not appear to increase the risk of ventricular arrhythmias in this high-risk population, as shown by the same team, which measured electrical stability of the myocardium before and after prolonged HIIT. Drigny et al.[120] compared interval training (2 series of 10 minutes of effort comprising 15–30 seconds at 80% of peak power interspersed with 15–30 seconds of passive recovery; total time including warm-up and recovery = 34 min) with continuous training at 60% of peak power (40 minutes) in 65 patients with the metabolic syndrome over a 9-month period. They observed that QT dispersion (QTd) improved to a similar degree after HIIT and MICE, with a significantly greater improvement in cardiometabolic risk with HIIT.

In summary, the relationship between exercise intensity and peripheral adaptations has already been described in healthy subjects, and has just been confirmed in patients presenting with the metabolic syndrome. HIIT thus seems to be very effective in these patients.

5. Conclusion and Perspectives

Even though exercise intensity is still a source of debate in 2011, there is growing scientific evidence that HIIT presents little danger for selected, stable cardiac patients, provided that the prescribed protocols are respected. The controversy

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surrounding the implementation of HIIT certainly reflects the history of cardiac rehabilitation.[121] Indeed, in the 1950s, it was considered unreasonable to expect patients with heart disease to perform exercise training. It was not until the early 1970s that the benefits of exercise were recognized by the medical community. The benefits of physical exercise in patients with CAD and HF have since been proven and documented in many meta-analyses,[122,123] thanks to a more systematic individualized approach in the management of cardiac rehabilitation. Although the benefits seem to be directly linked to the notion of training volume and intensity, exercise prescription still needs to be clarified to enable the scientific community to develop even more precise recommendations. Furthermore, we must bear in mind that the principal aim is to foster long-term adherence to physical activity in these patients. In addition to physiological efficacy, the recommendations must also orient healthcare professionals and patients to protocols that optimise adherence to cardiac rehabilitation programmes and regular physical activity. The game-like nature of interval training makes it an attractive alternative.[53] In theory, it could be incorporated into every phase of rehabilitation adjusted according to each patient's medical history and functional status. As such, although this review has focused on the efficacy and utility of HIIT, more modest intensity interval training could be employed in the most deconditioned patients and specifically incorporate passive recovery periods.

Our team is spread over a number of different units that welcome patients in phase II and III (Toulouse and Dijon, France; Geneva, Switzerland and Montreal, Canada). To date, our scientific data about acute effects and tolerance lead us to implement HIIT frequently in clinical settings. In phase II, the exercise protocols used according to the severity of the disease, the age and level of training remain empiric, but there is a willingness to structure them, to adapt them to the needs of individual patients and to use them more generally and more systematically. From a practical view, we use the same risk stratification as for MICE, taking into account the time since the acute event, the initial exercise tolerance assessed with a graded maximal exercise test, the left ventricular ejection fraction, the presence of defibrillator or pacemaker and the existence of other co-morbidities such as diabetes and hypertension. We usually observe the following strategy: i.e. for coronary patients with non-altered ejection fraction and exercise tolerance >5 METS, we introduce HIIT using two sessions at 60% of peak power output (PPO) during exercises phases, then we increased the workload to 80% of PPO and, finally, up to 100% of PPO if well tolerated. In case of altered ejection fraction and/or low exercise tolerance, we usually start with a minimum of 2 weeks or 8–10 sessions in continuous mode, before starting HIIT with the same protocol as described in section 3. We have so far totalled 30 000 patient-hours of training without any significant adverse events.

This type of exercise thus appears to be attractive and cost effective. However, one must bear in mind that even if HIIT has become increasingly popular, it has until now been studied only in a small selection of stable cardiac patients, mainly male CAD with high exercise capacity or ischaemic HF (New York Heart Association Functional Classification II or III). Large multicentre trials are now required to demonstrate both the safety and efficacy of HIIT using hard endpoints in various unselected cardiac populations, with lower exercise tolerance, or HF patients with implantable cardioverter defibrillators (ICDs). Indeed, it has been reported that these latter patients experience smaller, but still significant, improvements in $\dot{V}O_{2max}$ compared with non-ICD cardiac controls following cardiac rehabilitation.[124] As the effect of exercise training on aerobic capacity in HF is dependent on exercise intensity, one of the hypotheses is that ICD patients might be afraid of training at high-intensity levels, even if, in a recent review, Isaksen et al.[125] reported that intensity levels ranging from 60% to 80% of maximal HR appeared to be safe in this population. In the study of Meyer et al.,[50] no event was observed among the ICD-patients (n = 15) who exercised at high intensity. A larger trial investigating the safety and effectiveness of HIIT is currently underway for HF patients[126] but more are now warranted.

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