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High-Intensity Interval Training vs. Moderate-Intensity Continuous Training in the Prevention/Management of Cardiovascular Disease

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ABSTRACT

Moderate-intensity continuous training (MICT) has long been considered the most effective exercise treatment modality for the prevention and management of cardiovascular disease, but more recently high-intensity interval training (HIIT) ~~has emerged into the clinical environment~~ **has been viewed** as a potential alternative to MICT in accruing such benefits. HIIT was initially found to induce significant improvements in numerous physiological and health-related indices, to a similar if not superior extent to MICT. Since then, many studies have attempted to explore the potential clinical utility of HIIT, relative to MICT, with respect to treating numerous cardiovascular conditions such as coronary artery disease, heart failure, stroke, and hypertension. Despite this, however, the efficacy of HIIT ~~compared to MICT with respect to~~ **in** reversing the specific symptoms and risk factors of these cardiovascular pathologies ~~for improved health and wellbeing as well as reduced morbidity and mortality~~ is not well understood. ~~In addition,~~ HIIT is often perceived as very strenuous, which could ~~potentially~~ render it unsafe for those at risk of or afflicted with cardiovascular disease, but these issues are also yet to be reviewed. Furthermore, the optimal HIIT protocol for each of the cardiovascular disease cohorts has not been established. Thus, the purpose of this review article is to (i) evaluate the efficacy of HIIT relative to MICT in the prevention and management of cardiovascular conditions, and (ii) explore any potential safety issues surrounding the suitability and/or tolerability of HIIT for patients with cardiovascular disease, as well as the potential optimal prescriptive variables of HIIT for application in the clinical environment.

Key Words: exercise; interval training; continuous training; cardiovascular disease

A sedentary lifestyle is accompanied by changes to the cardiovascular structure and function which, with their complications, increase cardiovascular disease (CVD) risk and contribute to increased morbidity and mortality in all age groups.[1-5] Indeed, declines in cardiorespiratory fitness and endothelial function are greatly implicated in the development and progression of CVDs.[6] Low levels of cardiorespiratory fitness are associated with an increased risk for cardiovascular and all-cause mortality in people of all ages,[2] while impaired endothelial function results in a chronic inflammatory process accompanied by a loss of antithrombotic factors and an increase in vasoconstrictor and prothrombotic factors in addition to abnormal vasoreactivity. **This sequence leads**~~, leading~~ to atherosclerosis and, in turn, cardiovascular events.[7] The current epidemiological state of CVD is such that by the year 2030, it will be responsible for approximately 23 million deaths on an annual basis,[8] thus emphasising a great need to develop potent, cost-effective interventions that alleviate the associated health burdens.

Modifiable lifestyle changes such as increasing physical activity levels are widely acknowledged to be the first-line of approach to CVD prevention and/or management. Endurance exercise training, in particular, is known to induce numerous favorable adaptations including improved skeletal muscle oxidative capacity,[9] peripheral vascular structure and function, including popliteal artery distensibility and flow-mediated dilation (FMD),[10] muscle microvascular density,[11] and muscle O_2 utilization kinetics.[11] These adaptations have significant scientific and clinical relevance linked with the effective management of people at risk of developing, or afflicted with, many chronic cardiovascular disorders including coronary artery disease (CAD),[12-14] heart failure,[15-18] stroke,[19,20] and hypertension.[12,21] However, the specific modality of exercise and associated prescriptive variables required to accrue such clinical benefits is a contentious issue, with no clear recommendations for the prevention and/or management of cardiovascular disorders.

Moderate-intensity continuous training (MICT) has traditionally been considered the most beneficial training modality for patients with CVD.[22-25] In fact, current CVD prevention and rehabilitation guidelines suggest performing 150 – 180 minutes of MICT (50 – 70% peak oxygen uptake [VO_{2peak}]) per week for the delivery of health benefits.[23] More recently, however, high-intensity interval training (HIIT) has raised considerable interest in the clinical context as a potential alternative to MICT for reducing the risk of CVD as well as improving the health and wellbeing outcomes of those affected.[26-34] It may be thought that the higher intensity of exercise ~~as with HIIT~~ may increase the risk of an acute cardiovascular event in comparison to MICT. However, HIIT applied in the settings discussed in this paper has been shown to be low risk and is adapted to maintain safety (See safety issues/clinical perspectives section).

HIIT is characterized by brief, intermittent bursts of high intensity exercise, interspersed with periods of rest or low-intensity exercise (active recovery). A growing body of research suggests that HIIT has the capacity to induce changes in numerous physiological and health-related markers to a similar or even superior extent to MICT.[35-37] As such, the use of HIIT has also been shown to be very beneficial for CVD cohorts, with particular relevance to improving numerous risk factors ~~in cardiovascular disease cohorts,~~ including cardiorespiratory fitness (VO_{2peak}),[26-29] endothelial function,[30,31] left ventricular[32,33] and overall myocardial function,[34] and specific blood pressure dynamics,[34] to a similar, if not superior magnitude to MICT. What is perhaps most intriguing about these findings is that the volume of exercise and time spent training has generally been significantly lower with HIIT relative to MICT. Given that “lack of time” remains one of the most commonly cited barriers to regular exercise participation,[38-40] the use of HIIT may be particularly important from a clinical and public health perspective in the prevention/management of chronic disease.

HIIT has long been used in the athletic setting as a means of enhancing physical performance,[41-46] but only more recently in the clinical context for the prevention and management of chronic disease. Thus, the utility of HIIT, relative to MICT, in ameliorating the specific symptoms and adverse effects of those at risk of or afflicted with CVD is not well understood. Indeed, previous reviews have attempted to explore the efficacy of HIIT in comparison to MICT in the prevention/management of CVD,[17,35,36,47,48] but it is noteworthy that the number of studies providing a direct comparison between HIIT and MICT in relation to treatment effects were limited at their respective times, making it difficult to determine the dominant exercise treatment modality in the clinical environment. However, recently, a number of comparative studies have **been published** ~~emerged into the literature~~,[19,20,49-55] making it timely to once again revisit, update and summarize the available information. Thus, the aim of the current work is to build on previous literature exploring the effectiveness of HIIT relative to MICT in the prevention/management of numerous cardiovascular pathologies including coronary artery disease, heart failure, stroke, and hypertension, with particular relevance to physiological adaptations, clinical benefits and potential underlying mechanisms. A further aim is to explore any potential safety issues of HIIT for clinical populations, and provide optimal prescriptive variables of HIIT for effective therapeutic exercise prescription and application in the clinical setting.

LITERATURE SEARCH METHODOLOGY

The National Library of Medicine (PubMed) database was used to search for relevant articles between January 2000 and August 2015. The specific search terms used in isolation and/or combination were ‘high-intensity’, ‘interval’ ‘intermittent’, ‘continuous’, ‘endurance’, ‘training’, ‘cardiovascular’, ‘cardiac’, and ‘disease’. Reference lists of all articles obtained from this search were also examined for additional relevant articles. The inclusion/exclusion criteria for all articles in this review were such that they needed to provide information relating to the physiological responses induced by HIIT and/or MICT with particular relevance to the prevention and/or management of cardiovascular disease.

HIIT VS. MICT IN THE MANAGEMENT OF CVD

HIIT has been shown to be potentially beneficial for patients with specific cardiovascular pathologies including coronary artery disease,[13,14,51,52,55,56] heart failure,[15-18,49,50,54] stroke,[19,20] and hypertension.[12,21,34,53] ~~The following sections discuss the effectiveness of HIIT relative to MICT with regards to the prevention/management of the above outlined cardiovascular conditions in detail.~~

CAD

CAD is one of the leading causes of mortality, with more than 17 million deaths worldwide.[57] CAD is a result of atherosclerosis, which has been associated with low levels of cardiorespiratory fitness (VO_{2peak}),[2] endothelial dysfunction and inflammatory reaction.[58,59] In fact, the level of cardiorespiratory fitness, in particular, appears to have the greatest impact on cardiac and all-cause mortality in patients with CAD,[2,60] given its known influence on numerous cardiovascular risk factors such as levels of inflammatory/hemostatic biomarkers, blood pressure, lipids, anthropometric measures, glucose tolerance and insulin sensitivity.[61] Thus, physical exercise that improves VO_{2peak} is strongly recommended for this cohort, and previous research suggests that HIIT may be equivalent to or even superior to MICT in producing such benefits in patients with CAD.[29,52,55,62,63] Moholdt et al[62] and Tschentscher et al[55] reported similar increases in VO_{2peak} (~3.3 vs. ~2.3 $ml.kg^{-1}.min^{-1}$) and peak work capacity (~22.8% vs. ~21.1%) following a period (4 and 6 weeks) of HIIT and MICT, **respectively??** In addition, Rognmo et al[29] examined 11 weeks of HIIT (80 – 90% VO_{2peak}) vs. MICT (50 – 60% VO_{2peak}) with respect to improving aerobic capacity and reported greater increases (17.9% vs. 7.9%) in VO_{2peak} following the HIIT program. Moreover, a meta-analysis by

Elliot and colleagues[52] on HIIT vs. MICT, which included 229 CAD patients in total, found a significantly greater increase in VO_{2peak} (~1.53 $ml.kg^{-1}.min^{-1}$) following HIIT relative to MICT, respectively. Based on these findings, HIIT may be more effective than MICT in improving aerobic exercise capacity in CAD patients, which could have many benefits with respect to improving quality of life as well as morbidity and mortality rates. The specific mechanisms underpinning the increased VO_{2peak} in CAD patients following HIIT have not been well documented, but could perhaps be related to increased protein levels of peroxisome proliferative activated receptor-γ coactivator-1α (PGC-1α), a critical factor coordinating the activation of metabolic genes required for substrate utilization and mitochondrial biogenesis.[33,35]

With regard to HIIT-induced cardiovascular (endothelial) adaptations in patients with CAD, previous research has also shown promising results, comparable to those found following MICT. Specifically, HIIT has been shown to improve FMD, a marker of brachial artery endothelial-dependent function, both acutely (pre, 0.25 ± 0.13 mm vs. post, 0.29 ± 0.13 mm) and chronically (pre, 4.6 ± 3.6% vs. post, 6.1 ± 3.4%) to a similar magnitude as MICT,[64-66] perhaps due to increased nitric oxide bioavailability (i.e., a pivotal regulator of FMD and endothelial function).[33] In addition, heart rate recovery (i.e., change in heart rate from peak exercise to one minute after peak exercise with the patient standing)[67] and heart rate variability (i.e., cardiac autonomic function), which are inversely related to risk of mortality in CAD patients,[68] have also been shown to improve with HIIT,[56,69] although this is not consistent with all trials,[70] perhaps due to the variability of the pre-training states of the samples employed. Nevertheless, the improved FMD and vascular endothelial function seen with HIIT[64,65] may be of significant importance given that stiffening of the large elastic arteries and concomitantly impaired endothelial function play central roles in the etiology of atherogenesis and endothelial dysfunction which are associated with an increased risk of mortality in CAD patients.[6]

Unfortunately, very little evidence currently exists concerning the long-term effects of HIIT in comparison to MICT in patients with CAD. The one study of Moholdt et al[62] included a 6-month follow-up after the initial 4 weeks of HIIT vs. MICT, and found VO_{2peak} to be significantly higher with HIIT, indicating that HIIT provides more favorable long-term effects than MICT for CAD patients. Other available long-term HIIT intervention studies in these patients have omitted the use of a full MICT program,[13,69] making comparative judgements between HIIT and MICT difficult. Another study by Moholdt and colleagues[69] compared the long-term effects of a 4-week HIIT program against a standard care, hospitalized residential rehabilitation program (consisting of outdoor walking, cross-country skiing, indoor cycling, ball games and strength training (80% of sessions were endurance based)) in patients with CAD, and reported increases in VO_{2peak} (~18.8% and ~17.4%) and quality of life following both interventions at a 6-month follow-up, with no significant differences between interventions. Madssen et al[13] determined whether a 12-month maintenance program consisting of home-based HIIT (3 sessions per week) would improve VO_{2peak} in CAD patients any more than usual care offered by the rehabilitation clinic (i.e., patients are encouraged to be physically active but not given any concise exercise prescription) and found no changes in VO_{2peak}, quality of life and blood biomarkers at 12 months' follow-up. However, since the home-based HIIT program in the latter study was unsupervised with only one-third of patients reporting full adherence to the program, the lack of improvements in VO_{2peak} at 12 months follow-up could be attributed to a lack of adherence to the prescribed HIIT program.

Collectively, evidence supporting the use of HIIT in improving the health and wellbeing of patients with CAD is promising and, for the most part, may also suggest that

HIIT is somewhat more beneficial than MICT. However, additional long-term studies in this patient group that directly compare HIIT with MICT in terms of induced physiological adaptations (i.e., VO_{2peak}, FMD, endothelial function), quality of life, morbidity and mortality are required before HIIT can be widely recommended in this cohort as an alternative to MICT.

Heart Failure

Heart failure constitutes a serious health problem in modern societies as a major cause of morbidity and mortality.[5,71] Patients with heart failure suffer from a severely reduced quality of life due to their exercise intolerance and associated inability to perform daily activities.[72-76] Such adverse effects, however, can be ameliorated by exercise training. Previous studies have also compared the utility of HIIT against MICT in patients with heart failure, with respect to improving exercise capacity and quality of life.[16,28,32,33,77] Angadi et al[32] reported significantly greater increases in VO_{2peak} (pre, ~19.2 vs. post, ~21.0 ml/kg^{-1}/min^{-1}) in a cohort of heart failure patients with preserved ejection fraction (HFpEF) following 4 weeks of HIIT, whereas no such changes were observed following MICT. Wisloff et al[33] also reported similar findings, in that VO_{2peak} increased markedly more in post-infarction heart failure patients with HIIT than MICT (~46% vs. ~14%). In addition, a meta-analysis by Haykowsky and colleagues[28] which included 7 randomized trials on the efficacy of HIIT vs. MICT with regards to improving VO_{2peak} in heart failure patients with reduced ejection fraction (HFrEF), found HIIT to be more effective (weighted mean difference, 2.14 ml/kg^{-1}/min^{-1}). Furthermore, increases in VO_{2peak} concomitant with improved functional capacity (distance walked during a 6-minute walk test)[77] and quality of life[33] have also been shown to be greater with HIIT relative to MICT in patients with heart failure. These findings suggest that HIIT may be superior to MICT in alleviating the symptoms and adverse effects seen in patients with heart failure. Although it is currently unknown whether treatment effects may vary between specific heart failure populations (HFpEF, HFrEF, post-infarction), the use of HIIT indeed appears to be more promising than MICT in each of these cohorts, and thereby has some potential to be considered ~~ahead of~~ **superior to** MICT for the effective management of the condition. The greater beneficial effects of HIIT may be, in part, due to a greater generation of large shear stress forces within the endothelium leading to improvements in endothelial function, and promotion of an increase in muscle mass, hence improving oxygen metabolism.[78] However, it must be noted that endurance training-induced increases in VO_{2peak} could also occur independent of any changes in endothelial function in patients with heart failure,[79] suggesting that other mechanisms ~~(i.e., skeletal muscle adaptations)~~ such as a greater O_2 utilization in skeletal muscle via PGC-1α-mediated mitochondrial function and/or Ca^{2+} cycling in skeletal muscle by sarcoplasmic reticulum (SR) ATPase (SERCA) may be more responsible for the superior increase in VO_{2peak} seen with HIIT in patients with heart failure.[33,80-82] **edit ok???**

~~It is also of relevant~~ **Of** note, ~~that~~ not all studies have shown superior results with HIIT. Koufaki et al[16] reported similar increases in VO_{2peak} following HIIT and MICT in a group of HFrEF patients, which contrasts with the studies above. As the training protocols were not isocaloric (of similar dose), the authors suggested that the lack of a superior HIIT effect could perhaps be attributed to the lower amount of total work performed with HIIT compared to MICT in the study (HIIT, ~588 kcal/week vs. MICT, ~705 kcal/week). However, this explanation seems rather flawed when considering the work of Iellamo and colleagues[83] where similar improvements in VO_{2peak} were also found in post-infarction heart failure patients following isocaloric HIIT and MICT training programs. It is thus feasible that other factors, such as inconsistencies in methodologies, subject characteristics, as well as the physical activity levels of the subjects employed, are more responsible for the lack of a superior HIIT effect seen in these two studies. Nevertheless, it must be noted that HIIT was not found to be inferior to MICT, indicating that it is still a very potent, time-efficient modality that improves exercise capacity in HF patients.

A known cardiac feature of heart failure is the progressive chamber dilation and deterioration in pump function resulting in increased hemodynamic load and neurohormonal stress. This process, termed left ventricular (LV) remodeling, is also associated with increased morbidity and mortality.[32,33,84,85,86,87,88] Interestingly, HIIT has also been shown to reverse LV remodeling more favorably than MICT.[32,33] Wisloff et al[33] found 12 weeks of HIIT to significantly reduce LV end-diastolic (18%) and end-systolic volumes (25%) and increase LV EF (35%), compared to MICT. Similarly, Angadi et al[32] reported significant improvements in LV diastolic function (pre, 2.1 ± 0.3; post, 1.3 ± 0.7) with 4 weeks of HIIT, but no changes were seen following MICT. The mechanisms by which HIIT may improve LV function in patients with heart failure are not well understood, but may relate to improved atrial myocyte Ca^{2+} handling via increased activity of SERCA 2a, resulting in increased SR Ca^{2+} content, and improved myocyte contractility, as reported by Johnsen et al.[86] Thus, HIIT also appears to be more effective than MICT in terms of improving LV function which may, in fact, promote a greater quality of life and reduce the rate of morbidity and mortality among the population.

Stroke

Stroke is a leading cause of disability worldwide, associated with various physical impairments that trigger a vicious cycle of limited activity and deconditioning, which in turn exacerbates the risk of recurrent stroke and major cardiovascular events.[89,90,91,92,93] Cardiorespiratory fitness levels among stroke patients have been found to be as low as 50 – 80% of the age- and sex-matched values in sedentary individuals,[94,95] which even falls short of the level required for independent living.[96] The use of aerobic exercise training may therefore be of significant importance among stroke patients, as it could theoretically break the vicious cycle of physical inactivity and functional decline by improving VO_{2peak}, physical function, and quality of life. Despite the sound theoretical rationale for aerobic exercise training, no data currently exist concerning the comparison of HIIT with MICT for improving aerobic fitness and functional performance in stroke patients, and the available research is thus limited to studies that have examined the utility of HIIT and MICT independently.[19,20,27,97-101]

MICT has been shown to improve VO_{2peak} (6.3 ml/kg^{-1}/min^{-1} and ~17%) in patients with stroke significantly more than conventional care (physiotherapy)[98] and reference rehabilitation programs (stretching and low-intensity walking).[96] In addition, meta-analyses[100,101] have also confirmed the potent beneficial effects of MICT, with documented significant effect sizes in favor of MICT to improve VO_{2peak} in patients with chronic stroke. To the authors' knowledge, the only MICT intervention study that failed to show a significant effect on cardiorespiratory fitness was Moore et al.[102] It has been suggested that the 4-week training period used in their study may have been too short to induce a substantial cardiovascular effect in chronic stroke patients who may have lived an inactive lifestyle for extended periods.[43] The fact that the total duration of MICT has been at least 8 weeks among the studies that found positive effects on VO_{2peak} may also support this notion.[97,98,100,101,103-110]

On the other hand, the application of HIIT in stroke rehabilitation appears to be sparse and conflicting. Askim et al[19] reported no changes in VO_{2peak} following 6 weeks of HIIT in a selected group of stroke patients, although significant improvements were observed in the 6-minute walk test (pre, ~410 m vs. post, ~461 m). In contrast, Gjellesvik et al[27] demonstrated considerable increments in VO_{2peak} (pre, ~2.32 vs. post, ~2.60 L/kg^{-1}/min^{-1}) following initial HIIT which also remained significantly elevated at 1-year follow-up (2.59 L/kg^{-1}/min^{-1}). Given that exercise prescriptive variables were similar between studies (4 x 4-minute work periods at an intensity between 85 – 95% of peak heart rate, interspersed with 3-minute rest periods), one may speculate that inter-study differences in subject characteristics (level of stroke [mild, moderate], pre-training state) led to this discrepancy.

Thus, both HIIT and MICT could perhaps prove beneficial for stroke patients with respect to improving cardiorespiratory fitness, which in most cases also seems to associate with improved functional performance and general wellbeing, as reflected by numerous studies showing improvements in walking endurance (6-minute walk test) (~53 m), speed (~0.14 m/s), economy (pre, 1.12 vs. post, 1.04 $L/kg^{-1}/min^{-1}$), and quality of life, parallel to VO_{2peak}.[27,97,98,100,101,107] The underlying mechanisms for the HIIT- and MICT-mediated improvement in VO_{2peak} in those with stroke remain to be determined but could perhaps be attributable to an enhanced ability of the skeletal muscles to utilize O_2 via improved mitochondrial function.[100] However, in view of the current literature, the use of MICT appears to be more promising than HIIT for improving aerobic fitness and health outcomes among stroke patients. But more research is obviously required on the use of HIIT and, more importantly, on the direct comparison of HIIT to MICT with respect to stroke rehabilitation, before definitive judgements can be made. Furthermore, it must be noted that because up to 75% of stroke patients have coexisting cardiac disease,[111] which has been shown to be a major causative factor increasing the risk of cardiac arrest during exercise,[112] the foremost priority in formulating any form of aerobic exercise training into stroke rehabilitation should be to screen and monitor all exercise prescriptions carefully on an individual basis before making any practical applications.[113]

Hypertension

Hypertension is the most common risk factor for cardiovascular events such as CAD, heart failure and stroke, affecting approximately one billion individuals worldwide.[1,114,115] In fact, the association between blood pressure (BP) and greater incidence of CVD begins with BP levels as low as 115/75 mmHg, and then becomes stronger for each 20/10 mmHg increase in systolic/diastolic BP.[116] Regular exercise is a well-established intervention for the prevention and treatment of hypertension, since it can reduce the risk of hypertension in normotensive populations,[117,118] reduce BP in hypertensive cohorts,[30,119-121] and also improve several factors involved in the pathophysiology of hypertension.[26,122,123] Traditionally, MICT has been recommended as part of the battery of interventions for effective management of the condition,[124,125] however, several studies suggest that HIIT may be superior to MICT for improving various health indices in hypertensive individuals as well as those at high familial risk for hypertension.[26,30,122,126]

Higher levels of cardiorespiratory fitness (VO_{2peak}) are associated with a lower incidence of hypertension.[127-129] In fact, 21% of hypertension cases could be avoided simply by increasing cardiorespiratory fitness levels,[129] and the use of HIIT has generally been shown to be more effective than MICT in this context.[26,31,53,122] In a pilot study by Tjønna et al[31] on subjects with metabolic syndrome (including hypertension patients), VO_{2peak} was found to increase significantly more with HIIT (~35%) than with MICT (~16%). Similarly, Ciolac et al[26] reported HIIT to be superior to MICT for improving VO_{2peak} (~15% vs. ~8%) in a cohort at high familial risk for hypertension. This potential advantage of HIIT for improving VO_{2peak} in hypertensive and high-risk cohorts may have many important clinical implications with regards to reducing the risk of cardiovascular events and mortality, but additional longer-term studies with follow-ups are required to confirm this.

Studies examining HIIT vs. MICT with respect to mediating cardiovascular adaptations in hypertensive patients or those at high risk for hypertension also suggest greater benefits with the use of HIIT.[26,30,31,122] Although resting[31] and ambulatory[30,120] BP seem to reduce to a similar extent with HIIT and MICT, the BP response to exercise[120] and heart failure response following the cessation of exercise[122] have been shown to improve considerably more with HIIT compared to MICT. Such hemodynamic changes may have important implications for hypertension prognosis given that exaggerated BP responses to exercise and impaired heart failure responses following exercise are associated with several pathophysiological abnormalities of hypertension,[130-133] and are independent risk factors for CVD and mortality.[130-134] Moreover, arterial stiffness, which is accelerated with hypertension[135] and purported to be an independent predictor of cardiovascular and all-cause mortality in hypertensive patients,[136] has also been shown to improve significantly more with HIIT (pre, ~9.44 vs. post, ~8.90 ms^{-1}).[26,30,31] In fact, MICT interventions have thus far failed to show any significant effect on arterial stiffness in hypertensive patients.[30,137,138] Furthermore, Tjønna and colleagues[31] showed HIIT to be more effective than MICT with respect to improving nitric oxide availability (36%) and endothelial function (~9% vs. ~5%) in subjects with metabolic syndrome (most of which were hypertensive). This finding of a greater endothelial benefit with HIIT is also corroborated by Ciolac et al[26] where HIIT was found to be superior to MICT in improving resting, exercise and recovery levels of plasma nitrite/nitrate and endothelin-1 in subjects at high risk for hypertension. Based on these findings, HIIT appears to be more effective than MICT with respect to reversing the cardiovascular abnormalities associated with hypertension which may, in turn, reduce the risk of cardiovascular events and mortality. The mechanisms underpinning the superiority of HIIT in mediating cardiovascular adaptations in hypertensive patients (or those at high risk) are not fully understood, but it seems reasonable to suggest that HIIT and MICT affect shear stress in the arterial wall differently during exercise training, and this may in fact yield differential molecular responses.[26,31,126]

Although the specific mode of action contributing to hypertension is not fully understood, increased activation of the sympathetic nervous system has been documented to play a pivotal role in the pathogenesis.[139] Interestingly, HIIT has also been shown to reduce markers of sympathetic activity (norepinepherine levels) to a greater extent than MICT in a cohort at high familial risk for hypertension.[26] Notwithstanding that more research is needed examining HIIT vs. MICT with respect to mediating sympathetic activity, the use of HIIT also currently appears to be more promising for the improvement of neural/hormonal factors involved in the pathogenesis of hypertension.

PRACTICAL PERSPECTIVES AND APPLICATIONS

Safety Issues/Clinical Perspectives

HIIT may be superior if not similar to traditional MICT for managing and offsetting cardiovascular-related disease, despite a considerably lower training volume and time commitment compared to MICT.[28,29,33,53,55,63,98] Such findings could indeed lead some to question the longstanding utility of MICT, in that it should perhaps be replaced with HIIT. This is a potentially controversial paradigm shift given the potential increase in adverse event risk associated with exercising at higher intensities, particularly in the clinical population where the likelihood of an untoward episode is already at a heightened state. It must be noted, however, that the HIIT protocols employed by studies for clinical populations[29,33,62,140-144] have generally been modified to be less strenuous for greater tolerance and applicability.

These "low-risk" HIIT protocols are usually characterized by a lower absolute intensity of the work bout but with a longer duration of work and shorter rest periods compared to the more traditional sprint interval training protocols,[145,146] and have been shown to be effective in the treatment of the above reviewed CVDs.[28,29,33,53,55,63,98] Rognmo et al[147] also reported the use of such a HIIT protocol to be safe for clinical populations with the risk of a cardiovascular event being low. Moreover, evidence suggests that HIIT is perceived to be more enjoyable than traditional MICT,[148] which may have certain important clinical implications in terms of exercise adherence. Thus, the use of HIIT could perhaps be considered ahead of MICT in the clinical environment owing to its similar/superior potency in the treatment of CVD, and more enjoyable and time-efficient nature.

Exercise Prescriptive Variables

There is currently no clear consensus on the optimal HIIT prescriptive variables that elicit the greatest benefits for each clinical population, as there is a lack of evidence ~~available concerning the comparison of~~ **comparing the** ~~varying~~ HIIT prescriptive variables with ~~respect to~~ the effective management of a specific pathology. Also, it does not seem ideal to provide optimal recommendations for HIIT protocols based on those used by previous studies in clinical populations, given that the protocols have greatly varied in terms of exercise intensity, timing of the work:recovery cycles, type and intensity of recovery, and the number of intervals.[28,29,33,53,55,63,98,140-144] Moreover, it is feasible that the optimal HIIT protocol for the management of one condition may not be the optimal protocol for others.

However, of all the established risk factors for CVD, impaired aerobic fitness appears to have the strongest relationship to mortality.[2,149] Hence, improving aerobic capacity should be the most important clinical target, particularly for CVD populations with a higher than normal risk of morbidity and mortality. Improved aerobic fitness would also, for the most part, reduce the symptoms of any such associated CVD and subsequently improve general health, wellbeing, and quality of life.[29,31,33,97,98,100,101,107] Based on these considerations, it seems more meaningful to determine the optimal HIIT prescriptive variables for CVD populations with respect to improving VO_{2peak} rather than ameliorating any other symptoms and risk factors associated with a specific pathology. **Table 1** displays the HIIT prescriptive variables used by previous studies to improve VO_{2peak} in patients with CVD.

It is evident from the literature[26,27,29,31,32,33,55] that the use of 4 bouts of 4-minute work intervals at 85 – 95% MHR with 3 minutes of active recovery at 70% MHR, performed 3 times a week for as little as 2 weeks can promote significant improvements in aerobic capacity in numerous CVD cohorts. Thus, a HIIT protocol with similar prescriptive variables should, in theory, improve the aerobic fitness levels of those at risk of, or afflicted with CVD, and subsequently prove beneficial with respect to the prevention/management of any such symptoms associated with cardiac pathologies. However, whether this particular prescription of HIIT is optimal with regards to improving the aerobic capacity of patients with CVD and reducing morbidity and mortality rates within the clinical population, is currently unknown and requires further research.

CONCLUSIONS

The current guidelines for the prevention/management of CVD emphasise the importance of incorporating endurance exercise training into daily routines, as it is known to induce numerous favorable physiological adaptations which are linked with the reversal of risk factors associated with the development and progression of cardiac pathologies.

Reports of HIIT being similar to or even superior to MICT with respect to stimulating physiological remodelling, ~~despite having a considerably lower exercise volume and time commitment,~~ have prompted many researchers to question the longstanding utility of MICT in the clinical environment and explore the efficacy of HIIT in the treatment of many cardiovascular disorders including CAD, heart failure, stroke, and hypertension. Indeed, the use of HIIT also appears to be very promising in the prevention/management of all of these cardiac pathologies, with similar, or in many cases superior effects to MICT with respect to improving aerobic capacity, endothelial function, LV function, and BP. Such improvements will have important clinical implications for the improvement of health, wellbeing, and quality of life, as well as morbidity and mortality rates within the CVD population. What is more, in the vast majority of studies, the total exercise volume and time commitment has been significantly lower with HIIT, and yet its use still showed an array of positive physiological benefits that are at least comparable to MICT. Thus, HIIT has the potential to be a particularly useful treatment modality for those at risk of or afflicted with CVD, by serving as a more time-efficient alternative to MICT that ~~nonetheless~~ still induces significant positive adaptations aligned with reduced morbidity and mortality.

It is also important to note that HIIT has been shown to be safe, tolerable and enjoyable for patients with CVD, thus eliminating any major concerns of an increased adverse event risk with the use of such exercise. The optimal prescriptive variables of HIIT, however, that induce the greatest benefits with respect to successfully preventing and/or managing each of the cardiovascular pathologies are unknown, as there is virtually no research available on the comparison of varying HIIT prescriptive variables for the optimal treatment of a specific cardiac pathology. Hence, while more research is required on the optimal HIIT prescriptive variables, it is noteworthy that of all established risk factors, impaired aerobic capacity appears to be the most greatly implicated in the development and progression of CVD, and also has the strongest link to morbidity and mortality. Thus, it may be more useful to develop optimal HIIT programs for CVD patients based on improving aerobic fitness rather than reversing the specific symptoms and risk factors associated with a pathology. In this context, the use of 4 bouts of 4-minute work intervals at 85 – 95% MHR, interspersed with 3 minutes of active recovery at 70% MHR, performed 3 times a week for as little as 2 weeks has been shown to be very promising, and can, theoretically, induce the relevant physiological responses constituting to increased aerobic fitness and act to improve health and wellbeing, as well as morbidity and mortality. In view of the current literature, this particular prescription appears to be optimal and thus may have an important clinical relevance.

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