

High intensity interval training vs moderate intensity continuous training in the management of metabolic type disease

Abstract

Previously, the use of moderate-intensity continuous training (MICT) has generally been considered the most beneficial exercise treatment modality for the prevention/management of metabolic type disease. More recently, however, high-intensity interval training (HIIT) has emerged into the clinical setting as a potential alternative to traditional MICT in the management of such diseases, but the comparative effects are not well understood. Use of HIIT has the potential to induce favorable physiological remodeling that is similar or even superior to MICT, despite a considerably lower exercise volume and time commitment. Many studies have therefore examined the efficacy of HIIT relative to MICT with respect to reducing the development and progression of numerous metabolic conditions including obesity, type 2 diabetes, and the metabolic syndrome. Despite this, however, the efficacy of HIIT relative to MICT in reversing the specific symptoms and adverse effects of those at risk of, or afflicted with metabolic disease is not well understood. Moreover, HIIT is often perceived as very stressful and demanding, which could potentially render it unsafe and/or unappealing for clinical populations whom are already at a higher risk of experiencing adverse events. Furthermore, the optimal prescriptive variables (volume, intensity, duration, rest) of a HIIT protocol that elicit the greatest benefits for each of the aforementioned clinical cohorts have not been established. This review article aims to explore the use of HIIT with respect to the above. Firstly, the efficacy of HIIT is examined relative to MICT in the management of metabolic diseases, with particular relevance to physiological adaptations, health outcomes, and potential mechanisms. Secondly, the potential safety issues relating to the suitability and tolerability of HIIT for clinical populations, as well as the optimal HIIT prescriptive variables for such clinical populations are discussed.

Keywords: interval, continuous, disease, endurance

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Background

Obesity

The global epidemic of obesity has become a major health, social and economical burden with approximately 312million people worldwide being obese (body mass index (BMI)>30kg/m²) and at least 1.1billion people being overweight (BMI, 25–29.9kg/m²),^{1,2} mainly due to a physically inactive lifestyle and inappropriate diet habit.^{3–5} Exercise training is a well established intervention for the prevention and management of obesity, and since obesity is also associated with low levels of cardio respiratory fitness and impaired endothelial function,⁶ it is not surprising that the use of aerobic exercise training, in particular, is becoming increasingly recommended in the treatment/management of the condition⁷ given its capacity to improve cardio respiratory fitness and endothelial function.^{8,9} In spite of this, there are still limited data available with regards to the specific type of exercise training that elicits the greatest health benefits in obese individuals. Indeed, most exercise protocols designed to induce fat loss have focused on the use of moderate-intensity continuous training (MICT), but these have resulted in negligible weight loss.^{10–12} It has been reported that high-intensity interval training (HIIT) may in fact be more effective than MICT with respect to reducing body fat.^{12,13} However, these studies have mainly been on healthy subjects with low-moderate levels of fat and, as such, may render any potential

generalization to obese populations invalid. Despite the fact that the efficacy of HIIT in the management of body fat levels in overweight and obese individuals has been demonstrated by numerous studies^{14–21} research is currently very scarce and inconclusive concerning the utility of HIIT, relative to MICT with respect to fat loss among obese cohorts. Schjerve et al.²² examined the effectiveness of HIIT vs. MICT in a group of obese adults and reported similar significant decreases in body fat levels (~2.2% vs. ~2.5%, P<0.04), BMI (~0.6kg/m² vs. ~1.1kg/m², P<0.04 and P<0.007 respectively), and body weight (~2% vs. ~3%, P<0.04). Corte de Araujo et al.²³ also found HIIT and MICT to be equally effective at reducing BMI levels (~5% vs. ~3%, P<0.05) in a cohort of obese children, although HIIT was found to be more effective in reducing body weight (~2.6%, P<0.05 vs. ~1.2% NS). In contrast, Wallman et al.²⁰ reported significantly greater reductions in android fat levels (0.7 effect size) with HIIT relative to MICT in overweight adults. In contrast, Keating et al.²⁴ reported MICT to elicit significantly greater (P<0.05) reductions in trunk fat (~3.1% vs. increase of ~0.7%), android fat (~2.7% vs. increase of ~0.8%), and total body fat (~2.6% vs. ~0.3%) compared to HIIT in a group of overweight adults. Such variability in reported findings could perhaps be accounted for by inter-study differences in HIIT protocols and subjects employed. The latter finding by Keating et al.²⁴ of no significant effect on body fat with HIIT is perhaps most surprising given that HIIT has consistently been shown to improve body composition among obese cohorts.^{9,12,14–22} Thus, although the

authors utilized a HIIT protocol which has previously been shown to reduce body fat in overweight individuals,²⁰ one may speculate that the protocol was insufficient to promote significant improvements in body composition for their overweight subjects. In support of this, the authors also reported that peak BP (systolic BP < 250 mmHg) and heart rate (< 90% MHR) were within normal limits for exercise, and the protocol was well tolerated by participants with no adverse events, which may question the specific exercise prescriptive variables adopted. Obesity is also characterized in many cases by a reduction in insulin sensitivity.²⁵ Here this has been associated with an increase in levels of TNF- α , this increase in TNF- α is thought to interfere with insulin related glucose signaling in the muscle via the IRS-1/P13K pathways (25). Interestingly chronic exercise has been shown to significantly ($P < 0.01$) lower the circulating levels of TNF- α .²⁶ Hence, while the recent interest in HIIT has led to the notion that it may be more effective than MICT as a means of reducing body fat in obese populations, there is currently a paucity of quality evidence available to support this, and so, the use of HIIT should not be emphasized over MICT in the current clinical environment for effective management of obesity. Nevertheless, HIIT still seems a very promising, time-efficient modality for the management of body fat in obese individuals. Possible mechanisms underlying the HIIT-induced fat loss effect have been reviewed elsewhere¹¹ but, briefly, relate to increased exercise and post-exercise fat oxidation²⁷ and decreased post-exercise appetite.²⁸

Type 2 diabetes

Type 2 diabetes is a worldwide epidemic associated with obesity and a sedentary lifestyle, and characterized by the inability to maintain normal blood glucose levels, due to impaired glycemic control involving a lack of insulin production, reduced insulin sensitivity or insulin resistance.²⁹⁻³⁴ The number of patients with type 2 diabetes is also rapidly increasing with an estimated 439 million people diagnosed by 2030.³³ Given that type 2 diabetes increases metabolic disease-related morbidity and mortality²⁹ and has a significant impact on quality of life,³² it is of significant importance to develop and/or determine optimal treatment strategies for the effective management of the condition. In healthy individuals, blood glucose is normally maintained between very narrow margins (fasting levels 70-100 mg/dl). This stable level of blood glucose is a balance between the rate of appearance (food intake and hepatic production) and disappearance (uptake by tissue - muscle, adipocytes, brain). This euglycaemic condition is controlled by pancreatic hormones (insulin β cells and glucagon α cells), whereby insulin 'drives' glucose into the tissues and glucagon promotes release of glucose from the liver into the blood. With type 2 diabetes the main issue is the lack of sensitivity of the tissues to insulin. More specifically, skeletal muscle which account for up to 80% of the glucose disposal for oxidation or storage,³⁵ does not respond to the same degree in individuals with type 2 diabetes as that in normal healthy individuals. Thus any intervention which may increase the sensitivity of skeletal muscle to the action of insulin, or indeed an increase in the muscle mass thereby increasing the demand for glucose, may help ameliorate the onset of diseases such as type 2 diabetes.

Insulin sensitivity

A reduced expression of the insulin-regulated glucose transporter type-4 (GLUT4) isoform, which in itself plays an essential role in blood glucose regulation by transporting and mediating glucose uptake,³⁶ is purported to be a causative factor leading to insulin resistance and subsequent diabetic complications.³⁷ As the effect of physical activity on glycemic control and body composition is well documented,^{34,38} exercise training could be used as a first line of

treatment for type 2 diabetes, and numerous studies have also showed the efficacy of HIIT³⁹⁻⁴¹ and MICT^{42,43} with regards to the effective management of the condition. For instance, decreases in average 24h blood glucose concentrations (~1 mmol/l), postprandial excursions for breakfast, lunch and dinner, the prevalence of hyperglycemia (~33%), and increases in GLUT4 activity as well as reduced body fat levels, have previously been reported by studies examining the use of either HIIT or MICT in patients with type 2 diabetes.³⁹⁻⁴³ This enhanced GLUT4 activity and/or glycogen synthesis/utilisation may be in part due to the up regulation of the transcription factor E3 (TFE3), which in mice has been shown to increase glycogen storage and is associated with up regulation of genes related to proteins related to glucose metabolism (glycogen synthase, GLUT4, Hexokinase II).⁴⁴ The lack of 'action' of insulin in type 2 diabetics has been linked to defects in the ability of insulin to phosphorylate the insulin receptor IRS-1, a molecule responsible for downstream regulation of insulin action in skeletal muscle.⁴⁵ Indeed it has been shown that regular exercise leads to up regulation of IRS-1 in humans.²⁵ However, the specific training modality that would be most beneficial for the prevention/management of type 2 diabetes has not yet been determined as comparative studies on HIIT vs. MICT in improving health outcomes among type 2 diabetics are scarce. Mitranun et al.⁴⁶ reported blood glucose and body fat levels in type 2 diabetics to reduce similarly with HIIT and MICT, but glycated haemoglobin (HbA1c) levels (marker of blood plasma glucose) were found to reduce significantly ($P < 0.05$) more with HIIT, relative to MICT. Similarly, Karstoft et al.⁴⁷ found HIIT to significantly decrease blood glucose (continuous glucose monitoring) and body fat levels to a considerably greater extent ($P < 0.05$) than MICT in type 2 diabetic patients, although the MICT protocol (continuous walk training at 55% energy expenditure rate) used in this study may have been insufficient to improve health-related parameters. In addition, Terada et al.⁴⁸ reported no changes in HbA1c levels but significant reductions in body fat following a period of HIIT ($P = 0.007$) and but not MICT ($P = 0.085$) in a cohort with type 2 diabetes. These preliminary studies may suggest that, in the type 2 diabetic population, HIIT is somewhat more effective than MICT with regards to reducing blood glucose and similar to MICT in reducing body fat, which, given the implications of elevated blood glucose concentrations and associated obesity in the development and progression of type 2 diabetes-related co morbidities such as cardiovascular disease,^{31,49,50} could have many clinical benefits. It must be noted, however, that there is currently a lack of quality evidence available to support the potential superior effects of HIIT with respect to improving glycemic control in type 2 diabetics, since the markers used by previous studies (blood glucose, HbA1c) have not consistently improved to a greater magnitude with HIIT relative to MICT, both within and between studies.⁴⁶⁻⁵⁰ Thus, more studies are required to determine the dominant training modality for improving glycemic control in type 2 diabetes patients.

Individuals with insulin resistance and type 2 diabetes typically have reduced mitochondrial content,⁵¹ impaired mitochondrial function,⁵² and/or reduced markers of mitochondrial biogenesis⁵³ in skeletal muscle. These findings have led to the hypothesis that reduced mitochondrial capacity or impaired regulation of mitochondrial biogenesis in skeletal muscle plays a role in the pathogenesis of type 2 diabetes.⁵¹⁻⁵³ Although the cause-effect relationship has not yet been well documented,⁵⁴ interventions that increase muscle mitochondrial content and function may in fact still prove to be effective in the prevention and treatment of type 2 diabetes.^{55,56} Interestingly, the ability of HIIT to increase skeletal muscle mitochondrial capacity in patients with type 2 diabetes has also been demonstrated, with increases in maximal citrate synthase activity (~20%) as well as the

protein content of several subunits from complexes in the electron transport chain (complex II 70 kDa subunit, ~37%; complex III core 2 protein, ~51%; complex IV subunit IV, ~68%).⁴¹ Thus, HIIT could potentially be used to increase the mitochondrial capacity of type 2 diabetics, which may in fact translate to increased cardio respiratory fitness levels and associated improvements in morbidity and mortality among the population.^{57,58} However, whether HIIT is superior to MICT with respect to increasing the mitochondrial capacity of type 2 diabetics is currently unknown and requires further research. Though, given that VO₂peak has previously been shown to improve to a greater extent with HIIT relative to MICT in type 2 diabetic patients,^{46,47} one may speculate that HIIT is the superior modality for the improvement of mitochondrial function in this cohort. Furthermore, there is currently a dearth of evidence concerning HIIT vs. MICT with regards to endothelial adaptations in patients with type 2 diabetes, but the one study by Mitranun et al.⁴⁶ did report a greater magnitude of increases in flow-mediated dilation and cutaneous reactive hyperemia with the use of HIIT compared to MICT, thus suggesting greater improvements in endothelial function with HIIT. More research is required to validate and extend this notion.

Metabolic syndrome

The metabolic syndrome is a multigenic disorder that comprises of a cluster of cardio-metabolic risk factors including hypertension, dislipidemia, visceral obesity, and impaired glycemic control.⁵⁹ Individuals with metabolic syndrome are three times more likely to die from CAD than healthy counterparts, after adjusting for conventional cardiovascular risk factors.⁶⁰ With at least 1.1 billion people overweight people worldwide, the incidence of the metabolic syndrome is expected to continue rising,¹ thus warranting a thorough mechanistic understanding of optimal treatment strategies at a socioeconomic scale. Previous research suggests that impaired aerobic fitness and endothelial function play a role in the development and progression of the cardio-metabolic risk factors that constitute to the metabolic syndrome.⁶¹ Thus, aerobic exercise training could effectively be utilized to reverse the risk factors associated with the pathology, and there is some evidence to suggest that HIIT may be more effective than MICT with regards to metabolic syndrome management.^{9,62,63} Tjønnå et al.⁹ examined HIIT vs. MICT with respect to treating patients with metabolic syndrome and reported the use of HIIT to be more effective at reducing numerous risk factors associated with the condition. In particular, greater improvements were seen with HIIT relative to MICT in terms of VO₂peak (~35% vs. ~16%, P<0.01) via PGC-1 α (~138%) and SERCA (~50%) mechanisms and endothelial function as reflected by increased flow-mediated dilation (~9% vs. ~5%, P<0.001) with respect to increased NO bioavailability (~36%) and reduced oxidized low density lipoprotein (LDL) levels (negative regulator of NO bioavailability) (~17%). Additionally, insulin action (insulin receptor phosphorylation) in skeletal muscle and fat tissue, fasting blood glucose levels, and lipogenesis in adipose tissue (fatty acid transporter protein-1 (FATP-1) and fatty acid synthase (FAS)) were also found to improve more with HIIT in comparison to MICT. These superior effects of HIIT have also been corroborated by Haram et al. in metabolic syndrome rats.⁶³ Here, HIIT produced a larger stimulus than MICT with respect to increasing VO₂peak (~45% vs. ~10%, P=0.01) through greater increases in PGC-1 α (12-fold vs. 6-fold) and SERCA-1 and 2 (~50%). Systolic BP (~20mmHg vs. ~6mmHg, P<0.01), high density lipoprotein (HDL) cholesterol (~25% vs. ~0%, P<0.05), insulin action in skeletal muscle, fat, and liver tissue, and lipogenesis (FATP-1 and FAS) were also found to significantly (P<0.05) improve to a greater extent with HIIT. Moreover, HIIT

had a greater beneficial effect than MICT in improving endothelial function (2.7-fold vs. 2.0-fold) as indicated by improved sensitivity of aorta ring segments to acetylcholine, perhaps due to intensity-dependent effects on expression levels of NO synthase and density of the endothelial luminal caveolae (~65% vs. ~27%). Thus, based on these findings, the use of HIIT appears to be considerably more effective than MICT with regards to reversing the risk factors and adverse effects associated with metabolic syndrome.

Furthermore, one such risk factor in metabolic syndrome patients that has received little attention is QT dispersion (i.e., difference between the longest and the shortest QT intervals on a 12-lead ECG), a marker of myocardial electrical instability that predicts ventricular arrhythmias^{64,65} and sudden cardiac death.⁶⁶ QT dispersion is thought to reflect higher sympathetic and lower parasympathetic inputs to the heart.⁶⁷ Metabolic syndrome is associated with hyper activation of the sympathetic nervous system⁶⁸ and thus increased QT dispersion.⁶⁹ However, exercise training has been shown to reduce QT dispersion⁶⁵ and one study has also examined HIIT vs. MICT with respect to QT dispersion parameters in metabolic syndrome patients.⁶² Drigny et al.⁶² reported similar decreases in ventricular depolarization indices (QT dispersion, standard deviation of QT, relative dispersion of QT, QT corrected dispersion) following HIIT and MICT in patients with metabolic syndrome. Thus, HIIT may also elicit significant improvements in QT dispersion that are comparable to MICT. Taken together, the use of HIIT appears to be very promising in the prevention/management of metabolic syndrome and for the most part could perhaps even lend itself to being considered ahead of MICT in the current clinical environment for the effective management of the condition.

Practical perspectives and applications safety issues/ clinical perspectives

The classic, most widely employed HIIT protocol is the Wingate test, with subjects performing 4-6 bouts of a 30-second "all out" supramaximal effort against a standardized resistance on a cycle ergo meter, interspersed with 4 minutes of rest, for a total of 2-3 minutes of maximal exercise spread over 15-30 minutes.⁷⁰⁻⁷² This "all out" cycle ergo meter form of HIIT is also referred to as sprint interval training (SIT), since most of the power generated represents anaerobic as opposed to aerobic power.⁷³⁻⁷⁵ The primary energy source is glucose derived from muscle glycogen, and as aerobic capacity is exceeded, most of this is converted to lactate to provide anaerobic ATP. The initial 30 second Wingate test can use almost a quarter of the stored muscle glycogen, and although the rate of glycogenolysis is reduced in subsequent bouts, significant amounts of lactate accumulate.^{76,77} Such explosive exercise is extremely stressful, associated with very high perceived exertion, large spikes in plasma adrenalin and great increases in heart rate that could potentially remain within 80% and 90% of maximum for the entire duration of the exercise session.^{16,64} Thus, although SIT may be suitable for healthy, younger populations, it may in fact not be safe, tolerable or appealing for those with metabolic disease, due to the greater risks associated with high workloads.⁷⁸ This has prompted many researchers to develop more practical models of HIIT that involve less risk but still promote significant benefits in a time-efficient manner that are comparable or even superior to MICT for wider application to clinical populations.^{20,41,79-84} These "low-risk" HIIT protocols are usually characterized by a lower absolute intensity of the work bout but with longer duration of work, and shorter rest periods compared to SIT protocols,^{79,80} and have been shown to be effective in the treatment of the above reviewed metabolic diseases.^{20,22,41,47,62}

Conclusion

Moreover, evidence suggests that HIIT is perceived to be more enjoyable than traditional,⁸⁵ which may have certain important clinical implications in terms of exercise adherence. Thus, the use of HIIT could perhaps be considered ahead of traditional MICT in the clinical environment given its similar/superior potency in the treatment of those at risk of, or afflicted with metabolic disease, and enjoyable, and time-efficient nature.

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Conflict of interest

Author declares that there is no conflict of interest.

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