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**Comparing the Effects of High-Intensity Interval Training Versus Moderate Intensity
Continuous Training on VO₂max/peak, Blood Pressure, and Weight Loss in Patients with
Cardiovascular Disease or Risk Factors**

By

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Introduction

Cardiovascular disease (CVD) kills 17.9 million Americans each year.¹ It will affect 40% of Americans by the time they are 60 years old; it increases to 70% by 75 years old.² Coronary heart disease is the leading cause of death in the United States of America.³ In fact, about 735,000 Americans have a heart attack each year.³ Major risk factors of cardiovascular disease are hypertension, obesity, cholesterol disorders, smoking, and type II diabetes, which are all common in the general population.⁴

CVD manifests in four major areas⁵:

1. Coronary heart disease complicated by angina pectoris, heart failure, a fatal or nonfatal myocardial infarction
2. Cerebrovascular disease complicated by a fatal or nonfatal stroke and transient ischemic attack
3. Peripheral artery disease complicated by intermittent claudication and critical limb ischemia
4. Aortic atherosclerosis complicated by a thoracic/abdominal aortic aneurysm, aortic dissection, and arterial thromboembolism

Prevention of these disorders by modifying their risk factors is preferable to treating established disease. One of the first steps in preventing CVD is starting physical exercise. Although exercise history is not uniformly assessed, the presence or absence of regular exercise is one of the most important indicators of overall health and CVD risk.² Some researchers would

say physical fitness is the strongest predictor of cardiovascular disease and total mortality.⁶ The current guidelines published by American Heart Association⁴ require at least 150 minutes of moderate-intensity aerobic exercise a week or 75 minutes of vigorous exercise per week or a combination of the two. Moderate intensity is defined as being able to hold a conversation during the activity whereas vigorous intensity would only allow a few words to be said before stopping to take a breath.⁴

Of the many different types of physical exercise, two are of particular interest with respect to CVD risk factors – moderate-intensity continuous training (MICT) and high-intensity interval training (HIIT). MICT is a well-studied form of physical activity and includes exercise regimens such as jogging, cycling, swimming, and walking. On the other hand, HIIT is described by the American College of Sports Medicine⁷ as a type of training that combines intense work periods ranging from 5 seconds to 8 minutes and performed between 80-95% of a person's estimated maximal heart rate, which is 220 beats per minute minus the person's age.⁸ After one intense interval, a recovery period of shorter, equal, or longer duration exercise follows at 40-50% of a person's estimated maximal heart rate. These recovery periods allow for the brief periods of high-intensity exercise that could not be maintained continuously.⁹ Initially, HIIT was utilized by coaches to improve exercise performance in their athletes. It was popularized in the early 1950s when Olympic champion long-distance runner, Emil Zátopek, won the 1952 Helsinki Olympic 10,000-meter race by using HIIT.⁹ Today, the HIIT model is focused on improving overall health in non-athletes because it allows training to be personalized to accommodate almost any exercise setting.

With increasing numbers of persons affected by CVD, it is important to examine innovative forms of exercise to find regimens that may fit individual lifestyles. A common barrier for adults meeting the minimum-recommended level of physical activity is lack of time.¹⁰ Decreasing the time required for effective exercise would surmount this barrier. Current guidelines suggest that 1 minute of vigorous activity equates to 2 minutes of moderate intensity activity. Thus, HIIT may provide a novel way to incorporate vigorous exercise for people who are limited on time or those not fit enough to perform continuous high-intensity exercise.¹¹ Current research comparing actual CVD events occurring after either HIIT or MICT is not yet available. However, comparing the effects of HIIT with MICT on surrogate markers for CVD risk in patients with established CVD or its risk factors could answer this question. Examining changes in these surrogates (VO₂ max/peak, blood pressure, and weight loss) within 6 months could predict CVD clinical outcomes.

Discussion

Studies examining these surrogate outcomes for CVD risk found evidence of their improvement with both of these types of exercise. Defining the meaning of these terms is integral to making valid comparisons.

VO₂ max/peak

VO₂max/peak is a strong predictor of both cardiac and all-cause deaths among patients with established coronary vascular disease.¹² Naturally, it declines with aging. Hill, Long, and Lupton¹³ were the first to introduce VO₂maximum uptake. VO₂max is a value that indicates the

highest rate of oxygen uptake the body uses during an intense exercise and does not change with intensification in work. The VO_2 max/peak is a marker of the body's efficiency at producing work and considered the "gold standard" for aerobic fitness.¹⁴ The difference between VO_2 peak and VO_2 max is that VO_2 peak is the highest value of VO_2 attained upon an incremental or high-intensity exercise.¹³ It is expressed in milliliters of oxygen consumed per minute and adjusted for body weight in kilograms: ml/kg/min.¹⁵

To test for VO_2 max/peak, the participant starts by exercising on a treadmill or bike breathing into a mouthpiece that collects information on inspired and expired air.¹⁵ The test starts off with a light workload and gradually increases to heavier workloads. The workload is changed by increasing resistance on a bike or speed on a treadmill.¹⁵ The test is completed once the patient has reached the maximum level of tolerable workload or when the maximal heart rate is reached or when oxygen consumption has peaked.¹⁵

The effect of exercise intensity on VO_2 peak has been extensively studied. The increase in VO_2 peak depends on numerous factors: intensity, frequency, duration of each session, initial fitness level of a subject, and length of a training program.¹⁴ In a randomized controlled trial (RCT), Rognmo et al¹⁶ placed patients with heart disease into either a HIIT or MICT groups for 10 weeks to evaluate the VO_2 peak. Both groups showed results of statistical significance in VO_2 peak. From their baseline, the HIIT group improved 17.9% and the MICT group by 7.9%. Wisloff, Stylen, and Loennechen¹⁷ conducted an RCT for post infarction and heart failure patients in a 12-week program with 3 groups: HIIT, MICT, and control. The HIIT group also had a larger increase in VO_2

peak at 46% compared to a 14% increase in MICT. The results were statistically significant and showed that HIIT was superior to MICT. The weaknesses of this trial were the small sample size and predominance of male participants. The researchers suggested this study be viewed as a "proof of concept" study and proposed that a larger, multicenter study be done using the same training technique. Molmen-Hansen, et al¹⁸ conducted a 12-week study with 88 hypertensive patients assigned to one of three groups, HIIT, MICT, and a control group. VO₂max was analyzed and revealed statistically significant differences among these groups. The HIIT group improved by 15% and the MICT group by 5%. Kessler et al performed a meta-analysis of HIIT vs MICT and HIIT elicited the same or greater improvements in VO₂ max even when the exercise time was less, which may indicate that HIIT requires less time to achieve the same results as MICT.¹¹ Moholdt et al¹⁴ analyzed VO₂ peak at 3 different levels of high intensity in patients with coronary heart disease. The three groups were separated into maximal heart rate ranges, <88%, 88-92%, and >92% of maximal heart rate. Results showed that the increase in VO₂ peak was highest in the >92% intensity zone subjects. This study was the first of its kind to evaluate training within a high-intensity zone in patients with coronary heart disease.

Findings from these trials consistently showed that improvement in VO₂ max or VO₂peak was greater in HIIT groups than the MICT groups. Moholdt et al¹⁴ evaluated the different levels of high intensity. His results revealed the highest intensity exercise had the largest increase in VO₂ peak. The studies described above were statistically significant results and had adequate sample sizes, aside from one trial¹⁷ that had a small sample size.

Blood pressure

Hypertension is a modifiable risk factor in CVD. Roughly 75 million people in the United States are affected by it; it is the cause of about 7.5 million deaths (12.8%) of all total deaths.^{19,20} The Molmen-Hansen et al¹⁸ RCT compared the effects of HIIT and MICT on hypertension. The systolic and diastolic blood pressures were analyzed and revealed statistically significant differences between the HIIT and MICT group. Results showed the HIIT group's systolic blood pressures were reduced by 12.0 mmHg and the MICT reduced by 4.5 mmHg. Both groups had improvements in diastolic blood pressure, but the HIIT group showed a larger decrease. After the completion of the study, 24% of the subjects in HIIT became normotensive and only one person in the MICT and control group became normotensive. These results demonstrated that blood pressure reduction is intensity dependent. The reduction in the systolic blood pressure seen in the HIIT group is comparable to a patient taking one antihypertensive medication to reduce blood pressure.²¹ Unfortunately, during this study, one patient in the MICT group sustained a myocardial infarction at home. As a result of this event, researchers suggest a larger sample size to determine the safety of exercise in high-risk patients.

Grace et al²² evaluated two groups of men: sedentary men who had not participated in any form of exercise and the control group of master athletes. The sedentary men engaged in 6 weeks of a pre-conditioning followed by 6 weeks of HIIT. Blood pressure improved significantly in the sedentary group after 6 weeks of HIIT; decreases in systolic, diastolic, and mean arterial blood pressure of 7.7, 4.6 mmHg and 5.5 mmHg, respectively, were found. The study demonstrated that the combination of preconditioning and HIIT could be an ideal method for

improving health in sedentary men. However, the combination training in this study may have confounded the results because researchers could not rule out how much the preconditioning contributed to the overall results.

Eicher et al²³ investigated low, moderate, and high-intensity exercise in white men with stage 1 and 2 hypertension. Data was taken 9 hours after each exercise. Results revealed statistically significant differences between high, moderate, and low intensity. The results showed lower blood pressure readings after a high-intensity exercise compared to blood pressure readings after a low or moderate exercise. This study confirmed a direct relationship with blood pressure and high-intensity exercise.²³

Given that HIIT provides post-exercise hypotension for 12-24 hours after exercise, Holloway and Spriet²⁴ argue that this is the very reason why frequent exercise in the practice of chronic endurance training or moderate continuous training for most days of the week is an appropriate exercise prescription to maintain the benefit from exercising. In addition, the Kessler et al¹¹ meta-analysis review on blood pressure showed that there were only measurable improvements in blood pressure if treatment was at least 12 weeks in duration using HIIT. HIIT had no effect on blood pressure if the patient was already on hypertensive medication or if training was less than 12 weeks. Strengthening these observations was the inclusion of many years of studies dating as far back as 1984. In addition, they included people who were healthy, had CVD, and metabolic syndrome were included. On the other hand, researchers could not perform a formal review because of the limited number of articles and the inadequate lengths of

follow-up in some studies; thus, their inclusion and exclusion criteria were suboptimal. Nonetheless, the findings from these studies were helpful in evaluating the effects of HIIT versus MICT on blood pressure. The evidence for HIIT having greater beneficial effect on blood pressure appears to be of good quality.

Weight loss

Being overweight or obese is a major risk factor for cardiovascular disease and increases the risk of all-cause mortality. Of the total population, 39.8% were obese in 2015-2016, per the Center of Disease and Control.²⁵ The highest percentage of obesity, 42.8%, was within the 40-59-year-old group, 41% of persons 60 years and older were obese, and 35.9% in the 20-39 years old population were obese.²⁵ Sedentary men have a 56% chance of sustaining a cardiac arrest during or after exercise compared to the 5% of men who exercise at a high level.¹⁰

A meta-analysis by Weweger, Berg, Ward, and Keech²⁶ reviewed HIIT versus MICT. The study examined changes in body composition of overweight and obese individuals exercising on a treadmill versus cycling. The results revealed statistically significant improvements in whole body fat mass and waist circumference of both groups, but insignificant weight loss. Despite similar results in each group, HIIT groups exercised ~40% less than the MICT groups. However, the type of training program made a difference in body composition; running, compared to cycling, produced more favorable outcomes. Although both high dropout rates and lack of blinding limited this study, it was the first to directly compare HIIT and MICT regimens by

examining body composition changes. Based on these findings, specific exercise prescriptions that include running can decrease whole body fat mass in patients with elevated BMI.

A 12-week study done by Cheema, Davies, Stewart, and Atlantis²⁷ compared HIIT versus MICT and the effects of weight loss on overweight or obese adults. The HIIT group performed boxing as their exercise and the MICT group walked. Results showed that there was a reduction in body fat percentage by 13.2% and waist circumference by 5.3% in the boxing group and no change in the walking group. These results were not statistically significant given the small sample size and the short duration of the study. Researchers are confident that improving the limitations in a future study will provide statistical significance and help change clinical guidelines and practice for the treatment of obesity.

Keating et al²⁸ compared MICT and HIIT exercise regimens to a control group. Overweight and inactive individuals were randomly assigned to 12 weeks of either MICT or HIIT or were placed in the control group. Body fat reductions were measured by a dual-energy X-ray absorptiometry. No noteworthy changes in body mass or lean body mass were found in either group compared to the controls. The MICT group showed reduced total percent body fat, android fat, and trunk fat, whereas the HIIT group did not. Both HIIT and MICT had reduced gynoid fat, but there were no significant differences between the two. Among the three groups, no significant differences in the waist and hip circumference were found. The evidence in this study suggests that overweight adults seeking to achieve fat loss would not benefit from HIIT. Of note, the HIIT group was using cycling as their form of exercise, which may have contributed to the lack

of evidence supporting HIIT as a regimen for weight loss. Weweger et al²⁶ suggested that HIIT should incorporate running on a treadmill instead of cycling because cycling did not reduce body fat in the body composition trials. This study was the first to examine the efficacy of HIIT versus MICT on body fat levels in obese and overweight participants. This strength was offset by the small sample size and predominance of female Caucasian participants. The researchers urged a larger study with more diverse participants. Another limitation of the study was the failure to assess lifestyle changes, such as diet, that could have impacted body fat. A meta-analysis done by Chin, Kahathudawa, & Binks²⁹ assessed caloric restriction, exercise, and the combination of the two. Results revealed statistically significant outcomes for weight loss when diet and exercise were combined. This meta-analysis compared a prescribed aerobic exercise and walking intervention, resistance training, and habitual activity (counting steps throughout the day). It did not specifically look at HIIT and MICT combined with diet, but it did reveal that higher levels of exercise with diet had the best outcome for weight loss. It also suggested that participants were more likely to maintain weight loss long-term if they were eating a healthy diet and maintaining physical activity. The strengths of this review were its intention to treat analyses and its selection of studies with similar designs, thus avoiding heterogeneity of exercise protocols. All trials were limited by the lack of reporting on energy intakes and expenditures.

Overall, these findings are helpful in assessing the impact of HIIT and MICT on weight loss and fat distribution. Good quality evidence suggests that HIIT is not the ideal form of exercise for losing weight although when it includes running, whole body fat decreases. Currently, the most effective way to lose weight is by combining a healthy diet with MICT.

Summary

The effects of HIIT versus MICT on surrogates for CVD risk (VO₂max/peak, blood pressure, and weight loss) were examined. Evidence showed that HIIT can improve VO₂max/peak, the gold standard for aerobic fitness¹⁴, substantially more than MICT. Improvement in blood pressure was found with both HIIT and MICT, but was greater in HIIT groups. Molmen-Hansen et al¹¹ showed that HIIT reduced blood pressure as effectively as one anti-hypertensive medication²¹ and more than MICT. Eicher et al²² showed that blood pressure improvements were intensity dependent. Kessler et al¹¹ argued BP could only be reduced by HIIT if exercise was sustained for at least 12 weeks and the patient was not already on an antihypertensive. However, not all evidence favored HIIT for reducing CVD risks. HIIT was not superior to MICT for promoting weight loss, despite the finding that HIIT running resulted in greater whole-body fat reduction. In fact, MICT was more effective for inducing weight loss. Nonetheless, the best weight loss was observed when a healthy diet was incorporated as part of an exercise regimen.²⁹

These studies revealed new information and exposed knowledge gaps. An incidental finding in the Molmen-Hansen, et al trial was the improvements in social functioning in the HIIT group.¹⁸ Whether this improvement in social function/quality of life independently improves cardiovascular function is unknown.

Knowledge gaps concerning the use of HIIT to reduce CVD events and risks include variations on HIIT and the practicality of HIIT. HIIT has been performed as sprint interval training (SIT). Kessler et al¹¹ suggest more studies to determine the true efficacy of SIT on cardiometabolic

risk, clinical outcomes, safety, and feasibility. HIIT is very structured and requires guidance in inexperienced and untrained individuals. Whether the complexity of HIIT will hinder its use is unknown. Furthermore, adherence to HIIT versus MICT has yet to be determined.

Another area of concern from the critics of HIIT is safety, especially in patients that are not able to tolerate the intensity.²⁴ The safety is still being established but increasing data shows HIIT improves physiological measures, functional capacity, and quality of life.³⁰ Molholdt et al¹⁴ ensured that all patients were on optimal medical treatment and/or underwent cardiac revascularization, and passed cardiopulmonary exercise testing prior to participation. Significantly, no one suffered from any cardiac events despite having coronary artery disease. Wisloff et al¹⁷ showed that HIIT can also be safe and beneficial in patients with chronic heart failure. Rognmo et al¹⁶ examined over 175,000 exercise training hours where patients performed both HIIT and MICT and found that there was only 1 fatal cardiac arrest during MICT and 2 non-fatal cardiac arrests in HIIT. Guiraud et al³¹ monitored troponin T in his individuals with CHD, which showed no elevated serum concentration in either HIIT or MICT groups thus excluding myocardial injury in the participants.

In addition to the safety concerns, the feasibility of incorporating HIIT as part of an exercise prescription needs elucidation. The practicality of an exercise regimen includes its desirability or enjoyment in addition to its accessibility, training, equipment, and time requirement. Measuring participants' affect during exercise can predict future exercise behavior and adherence.³² Jung et al³² used the activation-deactivation adjective checklist to compare

affective responses in HIIT vs MICT. Results showed HIIT was more pleasurable than continuous vigorous exercise, but less pleasurable than MICT. Despite the discrepancy between how pleasurable HIIT and MICT were perceived, participants preferred HIIT over MICT and continuous vigorous exercise. Participants felt confident in performing HIIT and MICT on their own. Rognmo et al¹⁶ had each participant rate the HIIT and MICT exercises on the Borg Scale of Perceived Exertion after every training session. Results revealed HIIT averaged around 14.4 compared to the MCT at 13.5. Guiraud et al¹⁷ also gave his participants the BORG scale and the outcome exhibited those whom did HIIT preferred it over MICT. The HIIT group's perceived exertion measure was lower than that of MICT. Kessler et al¹¹ noted the HIIT group liked the exercise because the varying intensities were motivating compared to the MICT which was perceived a boring. So despite HIIT's complexity, adherence to HIIT would likely be good in view of both the perceived enjoyment of it and its shorter time commitment compared to MICT.

Conclusion

The effects of HIIT versus MICT on surrogate outcomes for CVD and CVD risk factors were compared in multiple studies. Specifically, changes in these surrogates, VO₂peak/max, blood pressure, and weight loss were examined within 6 months of training in patients with CVD or its risk factors. Good quality evidence from currently available literature showed that HIIT was superior to MICT for improving VO₂max/peak and reducing blood pressure. However, for the purpose of losing weight, the evidence showed that HIIT was inferior to MICT.

The safety of HIIT is still being investigated. It cannot be safely recommended as an exercise prescription across all populations due to the lack of data. However, current evidence suggests that HIIT is safe. Some researchers suggest sedentary individuals start moderate-intensity physical activity consistently before trying HIIT. In addition, patients with chronic disease should be cleared to exercise prior to HIIT.¹⁰

Presently, HIIT's long-term effects on morbidity and mortality are unknown but a study is in progress to evaluate these outcomes. This RCT called Generation 100³³, is comparing the effects of high versus moderate intensity exercise training on risk factors for CVD in the elderly population. It is the first large RTC that will evaluate risk factors for CVD. This study will determine if exercise can be used as a preventive intervention for disease and improve overall morbidity and mortality in this population. Ultimately, information from this study may change the way providers recommend exercise.

Current clinical practice suggests that 75 minutes of vigorous intensity workout is just as efficient as 150 minutes of moderate intensity workout a week. Compared to MICT, HIIT may offer a safe and time efficient solution because the necessary exercise can be achieved in about half the time required for an MICT workout. As of now, the evidence is adequate for recommending HIIT as an alternative to MICT for persons with established CVD or CVD risk factors. However, further research is necessary to establish the overall benefit and safety of HIIT compared to MICT.

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