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Cardiorespiratory fitness and sedentary time in subjects with the metabolic syndrome

A randomized controlled trial

Master`s Thesis in Exercise Physiology and Sport Sciences

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The present Master`s thesis is a part of my Master`s degree in Exercise Physiology and Sport Sciences at the Norwegian University of Science and Technology (NTNU) in Trondheim. The study was carried out at the Faculty of Medicine, Department of Circulation and Medical Imaging (ISB), NTNU.

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ABSTRACT

Background: Metabolic syndrome (MetS) is an increasing health concern worldwide. Low cardiorespiratory fitness (CRF) and high amount of sedentary behaviors are strongly associated with the MetS and cardiovascular disease (CVD). Aerobic interval training (AIT) has been found to improve CRF more than continuous moderate exercise (CME) for subjects with MetS, and other groups of patients. However, strategies for decreasing sedentary behaviors are inconclusive and it is unclear whether CRF can be connected with sedentary time. **Objective:** The purpose of this study was to compare the effect of CME, low-volume AIT (1-AIT) and high-volume AIT (4-AIT) on total daily sedentary time (TDST), peak oxygen uptake (VO_{2peak}) and the components of MetS, in subjects with the MetS. **Method:** 32 subjects with MetS were randomized into three groups: CME (n=11), 1-AIT (n=9) and 4-AIT (n=12). All groups underwent 16 weeks of exercise. **Results:** No significant within or between groups differences ($p>0.05$) of TDST or VO_{2peak} were found. The components of MetS showed no significant difference ($p>0.05$) between the groups. Within the groups, only HDL in 1-AIT improved significantly ($p<0.05$). The findings indicated no correlation between VO_{2peak} and TDST. **Conclusion:** After 16 weeks of exercise, no significant differences in TDST, VO_{2peak} or components of MetS were found between the groups. The results suggest that there is no connection between CRF and sedentary time. However, the findings may be biased on several levels and must therefore be interpreted with caution.

Key words: Metabolic syndrome, cardiorespiratory fitness, sedentary time, peak oxygen uptake, aerobic interval training, continuous moderate exercise

ABBREVIATIONS

AIT - aerobic interval training

1-AIT - one aerobic interval training

4-AIT - four aerobic intervals training

BL - baseline

CAD - coronary artery disease

CME - continuous moderate exercise

CRF - cardiorespiratory fitness

CVD - cardiovascular disease

FG - fasting glucose

FU - follow-up

HDL-C - high density lipoprotein cholesterol

IDF - international diabetes federation

LDL - low density lipoprotein

MET - metabolic equivalent of task

MetS - metabolic syndrome

MVPA - moderate-to-vigorous physical activity

TG - triglycerides

VO_{2max} - maximal oxygen uptake

VO_{2peak} - peak oxygen uptake

WC - waist circumferenc

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1. INTRODUCTION

The pandemic of overweight and obesity is a growing health problem worldwide. According to World Health Organization (WHO), obesity has been doubled in most parts of the world between 1980 and 2008 [1]. Currently, about 500 million people are classified as obese, and 1.1 billion as overweight [2]. Data from Norway indicates a similar trend. The population based Health Survey of Nord Trøndelag county (HUNT-survey) showed an increase of 25 % in overweight men from the mid-80`s up to two decades later [3]. The prevalence of metabolic syndrome (MetS) is closely linked with overweight and obesity, and is also expected to increase at alarming rate [2]. The MetS is defined as a clustering of risk factors for cardiovascular disease. Among these are central fat obesity, hypertension, low HDL - cholesterol and glucose- and lipid irregularities [4]. In Europe, frequency of the MetS is reported from 7 to 36 % for men and between 5 to 22 % in women aged 40 to 55 years [5]. While in the U.S, about 34 % of the adult population is classified as having the MetS [6]. Recent studies have also shown a high prevalence of the MetS in states in the Gulf Cooperative Council (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia and the United Arab Emirates), demonstrating that MetS is not only a health problem in western countries [7, 8].

There is well established evidence that the MetS is strongly related to cardiovascular disease (CVD). MetS has been associated with an increase in both CVD and all-cause mortality [9-11]. In a meta-analysis by Motillo et al. [12], including more than 950 000 patients from 87 studies, the MetS was associated with a major increase in risk for cardiovascular disease (CVD), CVD mortality and all-cause mortality.

Cardiorespiratory fitness (CRF) and sedentary time may be determining factors in prevention and treatment of the MetS. Having poor CRF can truly be associated with an increased risk of developing MetS [13, 14]. Furthermore, the risk factors of mortality in men with MetS has been found to be largely explained by CRF [9]. Sedentary time is also associated with metabolic risk factors, and this association seems to be independent of physical activity [15, 16]. Increasing CRF and decreasing sedentary time should consequently be key factors in the development of treatment strategies for MetS patients.

2. THEORETICAL BACKGROUND

2.1 DEFINTION OF METS

The clustering of metabolic irregularities as a health concern was first described in the 1920s [17]. Reaven [18] suggested in 1988 that insulin resistance could be involved in the causation of type 2 diabetes, coronary artery disease (CAD) and hypertension. Today there exist various diagnostic criteria of the MetS, and recently the most used are definitions from the International Diabetes Federation (IDF) and the American Heart Association/National Heart, Lung, and Blood Institute. Even though the diagnostic criteria are similar, measures of waist circumference vary between the two definitions [19]. The IDF version [4] is used in this text and the different features of the diagnosis are presented in Table 1. Waist circumference (WC) values are absolute and vary with ethnicity.

Table 1. Components in the International Diabetes Federation`s definition of metabolic syndrome [4].

Waste circumference	≥ 94 cm in European males ≥ 80 cm in European females
+ 2 of the following:	
Raised triglycerides	≥ 1.7 mmol·L^{-1}, or specific treatment for this lipid abnormality
Reduced HDL cholesterol	< 1.03 mmol·L^{-1}in males < 1.29 mmol·L^{-1}in females, or specific treatment for this lipid abnormality
Raised blood pressure	Systolic BP ≥ 130 mmHg, or diastolic BP ≥ 85 mmHg, or treatment of previously diagnosed hypertension
Raised fasting plasma glucose	≥ 5.6 mmol·L^{-1}, or previously diagnosed type 2 diabetes

HDL, high density lipoprotein; BP, blood pressure.

2.1.1 COMPONENTS OF METS

Although the MetS is a constellation of risk factors for CVD, each individual component represents a risk. The components will be described briefly.

Waist circumference

WC is the primary component in the IDF definition of MetS [4]. This variable is the most prevalent of all indicators of MetS [20] and represent an accurate estimation of abdominal fat [21]. It is well established that central obesity plays an essential role in the development of the MetS [22, 23], and abdominal fat is strongly correlated with different cardiovascular risk factors [24, 25]. Therefore it is not surprising that WC serve as a stronger indicator of CVD risk than body mass index (BMI) [26].

Raised triglycerides

Triglycerides (TG) are a subgroup of lipids (fats) and serve as the main source of fat in our food [27]. In addition, fat stored in fat cells (adipocytes) primarily consist of TG [27]. An elevated concentration of TG, known as hypertriglyceridemia, is connected with several implications. A mild to moderate state of hypertriglyceridemia can be associated with CVDs, whereas higher levels of the condition also can increase the risk of pancreatitis [28].

Reduced HDL cholesterol

Cholesterol is transported in the blood attached to lipoproteins, such as low-density lipoproteins (LDL) and high-density lipoproteins (HDL) [29]. In healthy people, most of the cholesterol attached to LDL is removed in the liver. But for individuals with high cholesterol intake or heredity related high values of cholesterol (hypercholesteremia), the liver have fewer LDL receptors and is therefore less capable of removing LDL from the blood. Consequently, more cholesterol, attached to the LDL, will be available to enter the endothelial cells in the arteries [29]. This process can result in the development of atherosclerosis, which is the accumulation process of plaque in the artery walls [27]. This condition can lead to narrowing, or even occlusion, of the arteries [27].

In contrast to LDL, HDL protects against atherosclerosis [30]. HDL carries cholesterol away from the arterial wall and to the liver, where it is synthesized into bile. For this reason, the amount of HDL is a more precise indicator of cardiovascular risk than total cholesterol itself [27].

Raised blood pressure

Raised blood pressure (BP), also known as hypertension, provides additional strain for the heart due to increased resistance in the vessels [31]. Hypertension can lead to ventricular hypertrophy, stroke, atherosclerosis, artery stiffness, myocardial infarction and other organ damages [31, 32]. A systolic BP of 120-139 mmHg or a diastolic BP of 80-89 mmHg is classified as a prehypertensive stage, whereas pressures of 140-159 mmHg (systolic) or 90-99 mmHg (diastolic) is defined as stage 1 hypertension. At this stage, lifestyle modifications and antihypertensive drugs are recommended [33].

Raised fasting plasma glucose

Insulin is produced in the pancreas and it regulates the absorption of glucose into muscle and adipose tissue [27] Insulin resistance occurs when cells in the tissues become less sensitive, and finally resistant, to insulin. This consequently impairs the absorption of glucose [4]. Raised fasting plasma glucose (FG) is a sign of insulin resistance and prolonged elevated levels can lead to a diagnosis of type 2 diabetes [4]. Type 2 diabetes is considered an independent risk factor for CVD [34]. In addition, the degree of raised glucose in patients with type 2 diabetes is associated with different complications such as retinopathy, nerve system impairment, myocardial infarction or all-cause mortality [35].

2.2 METS AND EXERCISE

Exercise is a well-accepted method for improving health, and provides an effective and inexpensive treatment for patients with the MetS and other inactivity related disorders. Potentially, all components of MetS can improve after prolonged periods of exercise [36-41]. The number of subjects diagnosed with MetS has also been found to decrease considerably after interventions of aerobic exercise [40, 41]. Nevertheless, the mechanisms behind exercise-induced improvements are complex and not fully understood. This topic will be addressed briefly.

The features of MetS are interconnected and probably influence each other. Insulin resistance is highly prevalent in persons having the MetS and this condition is strongly connected with most of the components of MetS [42]. Insulin sensitivity is known to improve after exercise [43], and this can contribute to a lowering of FG per se. Moreover, central obesity is associated with insulin resistance and also probably connected with the accumulation-process of fat [44], which suggests that abdominal obesity, measured as WC, may also decrease as a result of improved insulin sensitivity.

Furthermore, exercise can provide beneficial alterations of fat metabolism, which may be vital for patients with the MetS. First of all, aerobic exercise is known to increase fat oxidation during rest and exercise [27]. Exercise will also rise the total energy expenditure, including the oxidation of excess carbohydrates, and thus prevent these from being converted into stored fat. In addition, intramuscular TG breakdown is improved by exercise and can be connected with improved insulin sensitivity [45].

In respect of BP, endothelial function and HDL-C probably play an important role. The endothelial cells in the blood vessel`s walls produce substances which make the smooth muscle cells dilate or constrict [31]. Nitric oxide is a central dilating-substance [31], and different studies have shown that exercise improve endothelial function, mainly because of an increase in nitric oxide release [46]. Furthermore, endothelial dysfunction can serve as an early predictor of atherosclerosis [47] and exercise may also increase HDL-C [48], which has a positive effect on atherosclerosis [30]. Therefore, the changes found in endothelial function and HDL-C may, at least partly, explain why BP appears to decline after interventions of exercise.

Potential benefits from exercise related with the MetS are illustrated in Figure 1.

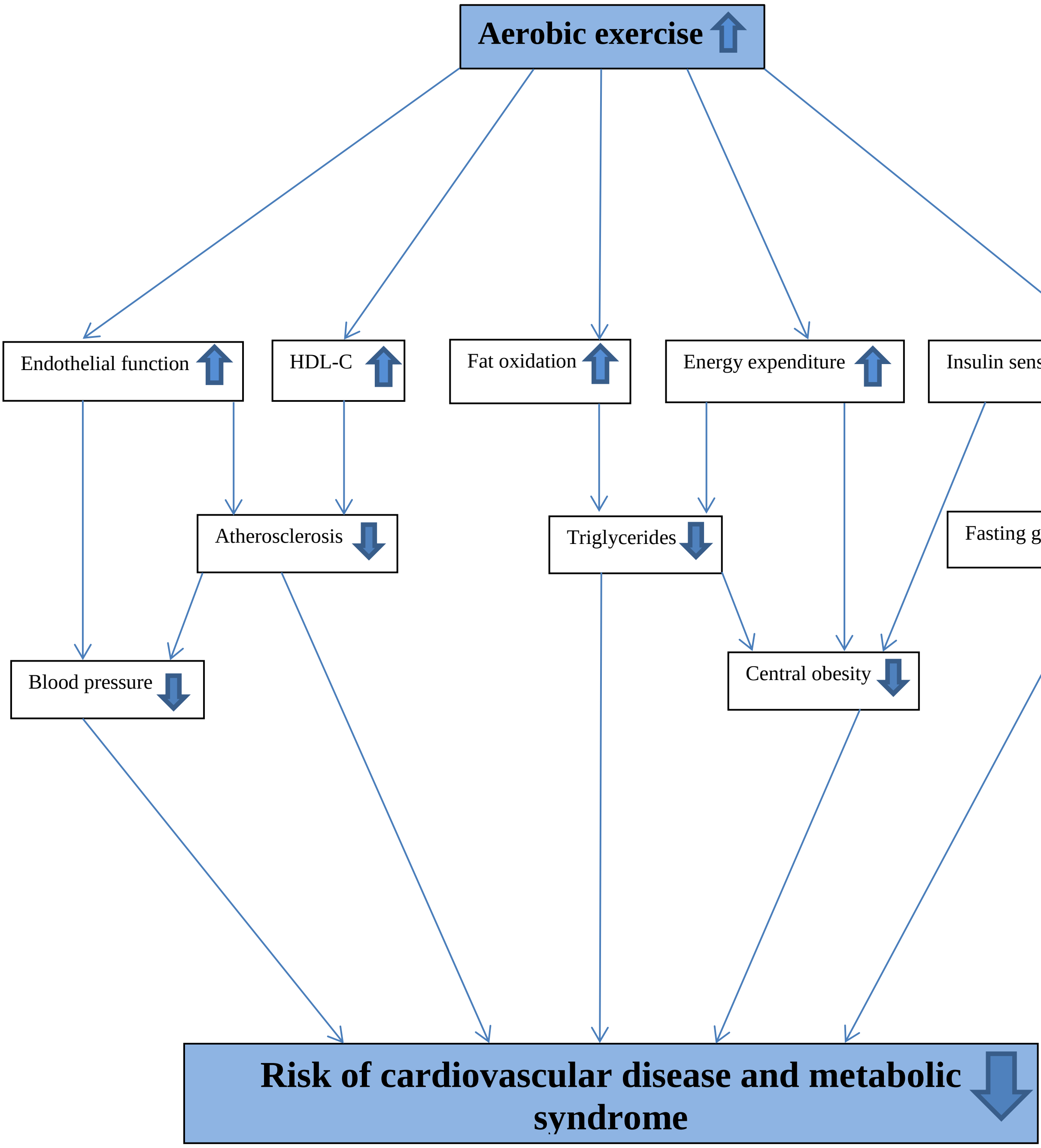

Figure 1. Possible benefits of aerobic exercise in context with the metabolic syndrome.

2.3 CARDIORESPIRATORY FITNESS

CRF is accepted as a strong predictor of mortality and longevity. The well-known study from Myers et al. [49] have demonstrated that exercise capacity is a powerful predictor of mortality for both healthy men and men with CVD. Similar findings have also been reported in healthy women [50], as well as MetS patients [9, 51]. Along with the different risk factors which define the MetS, patients with MetS are associated with having poor CRF [52]. In addition, individuals with MetS are at higher risk of cardiovascular and overall death [11], and different studies have suggested that high CRF is protective against MetS. Findings from Laaksonen et al. [13] showed that men in the upper third of VO_{2max} were 75 % less likely than unfit men to develop MetS. In line with this, Katzmarzyk et al. [9] found that risk factors of mortality for obese men and men with MetS can be largely explained by CRF. Similar results have been found in women [14].

2.3.1 VO_{2MAX}

Maximum oxygen uptake (VO_{2max}) provides an accurate and reproducible measure of cardiorespiratory fitness (CRF) [53], and can be defined as the highest rate at which oxygen can be taken up and utilized by the body during vigorous exercise [54]. The mechanisms behind VO_{2max} can be explained by the Fick equation: Cardiac output (Q) times the arteriovenous oxygen difference (a-vO2 diff) equals the oxygen uptake:

$VO_{2max}\,(ml \times min^{-1}) = Q\,(L \times min^{-1}) \times a\text{-}vO_2\,diff$ [27].

In the equation, cardiac output represent the volume of blood pumped by the heart during one minute, where the quantity is a product of heart rate (HR) and stroke volume of the heart [27]. Because differences in HR_{max} are small, it is mainly the stroke volume that determines the cardiac output at maximum. Next, the a-vO2 diff is explained as the difference in oxygen content between arterial and mixed-venous blood [27].

Although this is a debated issue, most evidence suggests that central capacity (meaning capacity of the heart and the lungs) is the main limiting factor for VO_{2max} [54-56].Therefore, a VO_{2max} test can provide a meaningful measure of the cardiovascular system`s capacity, which can explain the rationale behind using VO_{2max} as an indicator of health status.

2.3.2 FREQUENCY, DURATION AND INTENSITY

The frequency, duration and intensity of physical activity are key factors concerning CRF. Each of these factors contributes to an incline of energy expenditure, which is related with positive health outcomes [57]. In addition, higher volumes of physical activity are associated with a greater health profit [57]. Current guidelines for physical activity recommend at least 30 minutes of moderate physical activity on 5 days, or 20 minutes of vigorous-intensity activity on 3 days, each week [57]. Slentz et al. [58] concluded that the caloric imbalance in overweight individuals can be reversed by walking 30 minutes every day for most individuals. Moreover, Lee et al. have [59] demonstrated that one to two bouts of exercise per week, that generate 1000 kcal or more, may postpone mortality among elderly men without major risk factors.

In a study by Wisløff et al. [60], intensity was found to be the most important in reducing risk of cardiovascular death. They found that a single weekly bout of high intensity, lasting more than 30 minutes, was associated with 39 % and 51 % reduced risk of cardiovascular death for men and women respectively. Moreover, engagement in moderate-to-vigorous physical activity (MVPA) may reduce the risk of having the MetS [61-63].

Considering the important role of this component of CRF, intensity will be further elaborated.

2.3.3. INTENSITY

The different adaptations between high intensity aerobic interval training (AIT) and continuous moderate exercise (CME) have been widely debated. Current guidelines for physical activity recommend activities of moderate, prolonged manner. Yet, AIT, consisting of intervals lasting several minutes, has been reported to yield greater increase in aerobic capacity [36, 64-67]. Considering the strong connection between aerobic capacity and predictions of mortality, it is plausible to question whether today's guidelines are ideal for promoting health.

Sassen et al. [68] have proposed that exercise at higher intensities produces the greatest effect in preventing MetS. Furthermore, Tjønna and colleagues [36] found a significant increase in aerobic capacity for MetS patients who trained AIT (4x4 minutes at 90 % of HR_{max}) compared to a group who trained CME. This enhancement was associated with reversing the risk factors of the MetS. In addition, endothelial function increased more in the AIT group. The authors speculated that the possible larger amount of shear stress on the vessels in this group could have caused a different molecular response, and therefore explain the increased endothelial function. In contrast to this, however, Johnson et al. [69] have reported that moderate intensity may be better than vigorous intensity for improving MetS features. The higher percentage of energy coming from fat oxidation at lower intensities was discussed as a possible explanation to these findings.

Nevertheless, other studies have also found AIT to improve different health markers more than CME. Schjerve et al. [65] found AIT to be better than CME in improving aerobic capacity and endothelial function in a group of obese adults. Also, Hwang et al. [66] concluded in a meta-analysis that AIT was better than CME concerning exercise capacity and metabolic risk factors, in adults with cardiometabolic disorders. Similar findings have been reported in obese adolescents [67], patients with CAD [64] and healthy subjects [70].

More recently, it has additionally been promoted that shorter exercise sessions can provide beneficial health outcomes. Tjønna et al. [71] showed that only one interval of 4 minutes at 90 % of HR_{max}

induced similar physiological alterations as the 4x4 AIT regimen in overweight men. Furthermore, Gibala [72] have proposed numerous shorter intervals consisting of 60 seconds at 90- 95 of HR_{max} as an effective option for cardiovascular improvement.

2.4 PHYSICAL INACTIVITY AND SEDENTARY BEHAVIOR

Physical inactivity is a leading cause of mortality in the world [73]. A follow-up study of the classic Dallas Bed Rest and Training study from 1968 demonstrates the potential influence of inactivity; three weeks of bed rest had a more profound impact on physical work capacity than 30 years of aging [74]. In a paper published in 2012, Lee et al. [75] disturbingly shows how physical inactivity influence worldwide health conditions. It was estimated that physical inactivity causes 6-10% of non-communicable diseases such as coronary heart disease, type 2 diabetes, and breast and colon cancers worldwide If physical inactivity was eliminated, life expectancy would be expected to increase by 0,68 years for the world`s population as a whole, these numbers also including active people and thus appear unexpectedly low. Such numbers are similar to the established risk factors of smoking and obesity.

2.4.1 DEFINITION AND GUIDELINES

The Metabolic Equivalent of Task (METs) is an established estimation of physical activity [76, 77]. One MET represent the energy expenditure at rest, which equals an oxygen consumption of approximately 3.5 $mL \cdot kg^{-1} \cdot min^{-1}$. The values of MET are expressed as multiples of the resting energy cost [27]. Typical values can be walking 3 METs, aerobics 8.5 METs, vacuuming 3.5 METs, and so on [78].

METs are a metric used to distinguish levels of physical activity from another. Sedentary behavior is defined as activities with energy expenditure of 1.5 METs or below [79]. This includes sleeping, lying down, watching television etc.[79]. Associations of sedentary behaviors and deprived metabolic outcomes have been shown to be independent of physical activity [15, 80, 81]. Sedentary behavior should therefore be considered separate from the term inactivity, which refers to *lack* of behaviors above 3 METs [79].

Recently, guidelines for sedentary time have been incorporated in public health recommendations. Based on a united Nordic report, the Norwegian directorate of health recommends a “reduction of sedentary time” for children, adolescents, adults and elderly [82]. In the U.S, the American College of Sports Medicine (ACSM) recommends a reduction of sedentary time and an increase of sedentary breaks, regardless of exercise routines [57].

2.4.2 MEASUREMENT

Self-reported data of physical activity have been common in larger, epidemiological studies. Nevertheless, recent developed accelerometers and armbands, which can measure individual physical activity in detail, will probably give more accurate measures than self- reported data [83]. Today there exists a variety of validated activity monitors [84]. Atienza et al. [85] have showed that objectively measured MVPA had a stronger association with physiological biomarkers than self-reported MVPA. Harris et al. [86] have found comparable results.

2.4.3 METS AND SEDENTARY LIFESTYLE

Physical inactivity is associated with the MetS [13, 87]. However, more recent studies indicate a relationship between sedentary time and metabolic risk, independent of physical activity. Data from Bankoski and colleagues [15] demonstrates that people with MetS spent more time, and a higher percentage of time, as sedentary. Also, sedentary time was associated with MetS after adjusting for physical activity. Healy et al. [16] have found comparable results. Clustered metabolic risks and WC was associated with sedentary time, light-intensity time and mean activity intensity, independent of time spent in MVPA. Also the findings indicated that WC is more influenced by sedentary time than MVPA.

Moreover, Thorp et al. [81] reviewed longitudinal studies published up to January 2011 that had examined relationships of sedentary behavior with mortality and health indicators. Their findings add to the line of evidence that sedentary behavior can lead to poor health outcomes and this may be independent of physical activity.

TV viewing time and sitting time are common sedentary activities. Siting time has been reported as a risk factor for all-cause mortality in both healthy individuals and those with CVD, diabetes and overweight [88]. Not unexpectedly, the MetS is connected with prolonged sitting. Longer TV viewing time has been associated with an increased frequency of the MetS in Australian adults [89]. Furthermore, Healy et al. [90] have found associations between TV time and several metabolic risk factors, even though public health guidelines were met. Consequently, the authors suggested a public recommendation for sedentary behavior in addition to the existing guidelines for physical activity. Studies from Europe have reported corresponding results, where the need of including guidelines for sedentary behavior into public health programs also has been emphasized [62, 91].

2.4.4 CONNECTION BETWEEN CRF AND SEDENTARY TIME

To our knowledge, no studies have been conducted on this exact topic. However, it is reasonable to speculate that CRF can be connected with sedentary time. One could assume that a higher aerobic capacity would make it “easier” to avoid sedentary behaviors. In physiological terms, the level of strain during a specific activity varies considerably dependent on the level of VO_{2max} [92]. Hence, a higher capacity should make light intensity activities, such as walking the stairs or housekeeping, less demanding because their relative energy requirements would be lower. Also, one could suspect that this would have a psychological influence, and that the motivation for decreasing sedentary time would be greater amongst more fit individuals.

2.5 PURPOSE OF THE STUDY

In summary, CRF is accepted as a strong predictor of mortality. Poor CRF and high sedentary time are strongly related to the MetS and cardiovascular risk factors. Current guidelines recommend 30 minutes of moderate activity on most days of the week. However, AIT has been reported to produce a higher increase in CRF than moderate training. Furthermore, sedentary time is associated with negative health outcomes and this may be independent of physical activity. To our knowledge, no study has so far examined whether sedentary time and CRF can be connected.

The primary aim of this study was to measure the effect of CME, low-volume AIT and high-volume AIT on total daily sedentary time (TDST), in subjects with the MetS.

The secondary aim was to measure the effect of CME, low-volume AIT and high-volume AIT, on CRF, assessed as peak oxygen consumption (VO_{2peak}), and, on the components of the MetS.

Primarily, we hypothesized that TDST, CRF, and components of Mets would improve more in AIT than in CME.

In addition, we hypothesized that changes in CRF and TDST would be correlated.

3. METHODS

3.1 SUBJECTS

A total of 54 subjects were screened, whereas 38 were included in the study. Inclusion criteria were having the MetS defined after IDF criteria [4]. Exclusion criteria were unstable angina, recently cardiac infarction (last 4 weeks), uncompensated heart failure, severe valvular illness, pulmonary disease, uncontrolled hypertension, kidney failure, orthopedic/neurological limitations, cardiomyopathy, planned operations during the research period, reluctant to sign the consent form, drug or alcohol abuse or participating in a parallel study.

The included participants were stratified by age and gender, and randomized into three groups: continuous moderate exercise (CME) (n= 11), one aerobic interval training (1-AIT) (n= 9) and four aerobic intervals training (4-AIT) (n= 10). Before the intervention period started, 6 subjects (CME: n=3, 4-AIT: n=1, 1- AIT: n=2) had to be excluded due to lack of activity monitors at the time. During the intervention period, 8 participants (CME: n=3, 1- AIT: n=2, 4-AIT: n=3) withdrew from the study out of personal reasons. Also, two subjects (CME and 1- AIT) was excluded due to poor activity measurements, one (1-AIT) to compliance below 70 %, and one (4-AIT) to long term sickness. In total, 21 subjects (CME: n=7, 1- AIT: n=5, 4-AIT: n=9) completed all tests.

3.2 STUDY DESIGN

The current study was designed as a randomized controlled trial. The subjects were an array of participants from the multicenter-study of the MetS, Met-Ex, lead from St. Olavs University Hospital in Trondheim. The stratification of age and gender were based on the total population of Met-Ex, and is therefore not completely correct for the sample in the present study. The subjects were recruited using web site posters and local newspaper ads, and screening of subjects was done from August to November 2013.

If inclusion criteria were met, the subject was invited to take part in the study. Within a timeframe of approximately 2 weeks after the screening, a VO_{2max} test was carried out and a SenseWear activity monitor worn for 5 days. After this, the 16 weeks intervention period started. The CME group exercised in accordance with today`s guidelines for physical activity, and served as a control group The groups 1-AIT and 4-AIT represented exercise of low volume and high volume AIT. The study progress is explained in Figure 2.

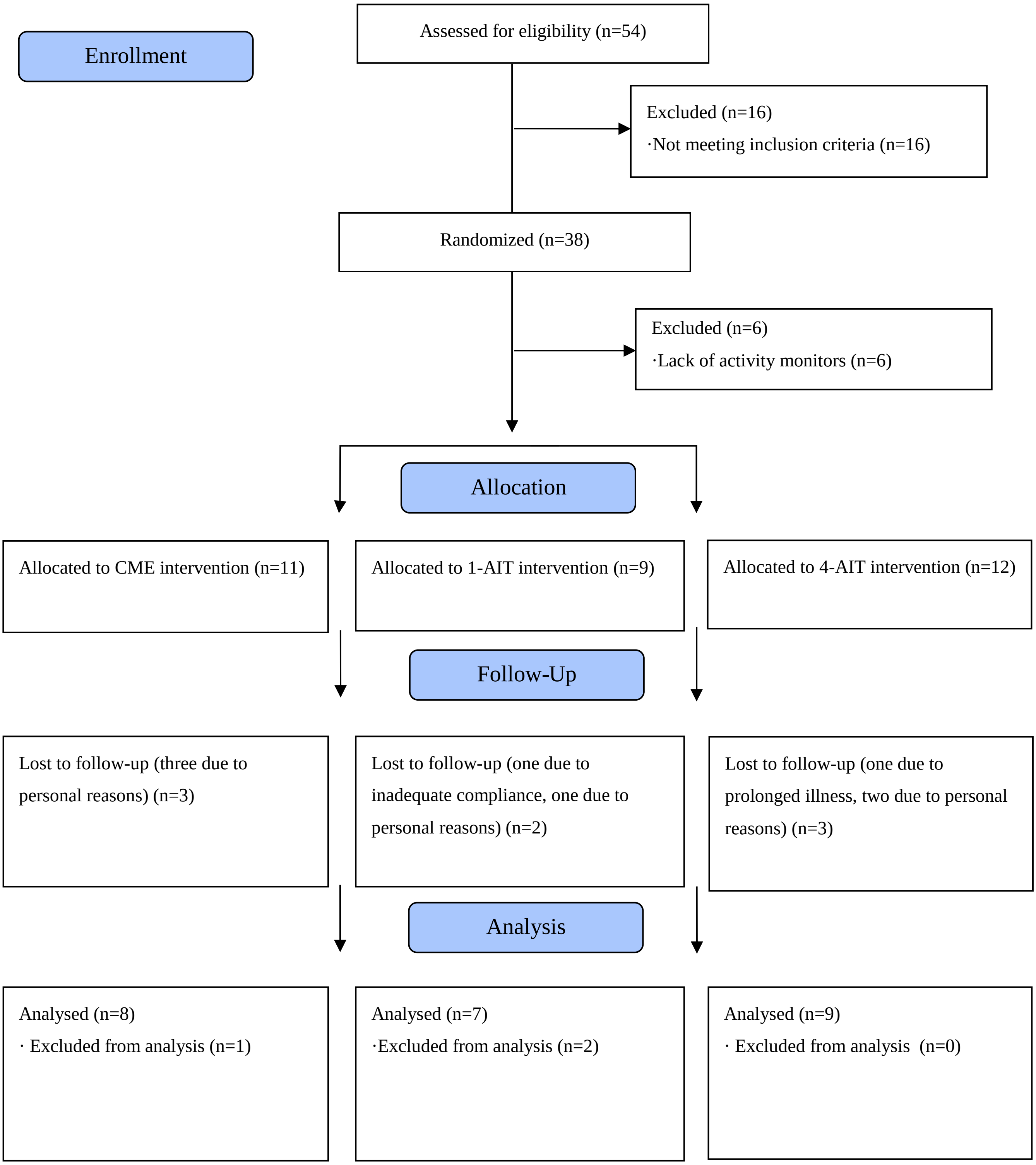

Figure 2. Flow chart of the study progress. CME, continuous moderate exercise; 1-AIT, one aerobic interval training; 4-AIT, four aerobic intervals training.

3.3 TESTING AND MEASUREMENTS

3.3.1 SCREENING

On the first visit, following variables were measured: WC (measured at the mid-point between lowest rib and the hip-ridge, Figure 3), weight, height, BP and blood samples.

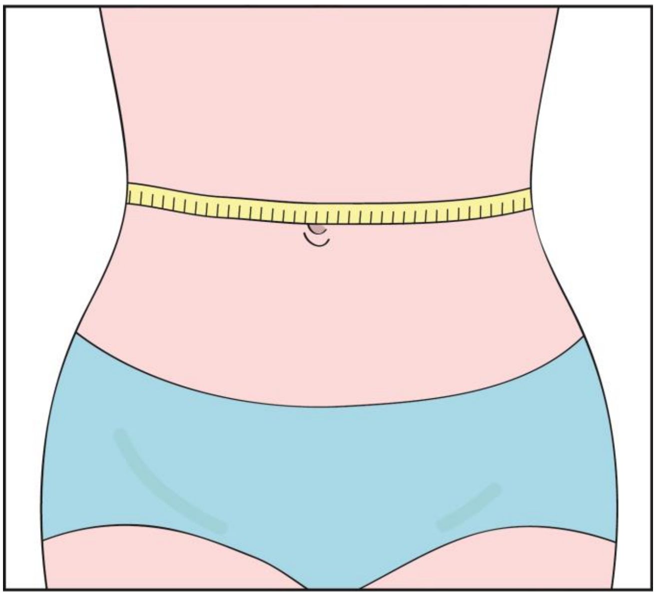

Figure 3. Measurement of waist circumference.

3.3.2 BLOOD PRESSURE

BP was measured noninvasively with an automated device (Criticare 506N-2, Criticare Systems Inc., Waukesha, WI, USA). The subject was instructed to sit still and relax a few minutes before, and during measurement. The dominant arm was measured 3 times with one minute of resting between each measurement. The mean of the last two measurements were calculated and used for analysis. If there was a difference of more than 15 % in either diastolic or systolic pressure between the last two measurements, a new measurement was taken.

3.3.3 BLOOD SAMPLES

Blood samples were obtained after an overnight fast in the morning (≥12 h). Plasma TG, HDL-C and FG were analyzed using standard local procedures at St. Olav's University Hospital, Trondheim. 1x3ml lithium heparin and 1x6ml serum were collected from each participant to perform the abovementioned analysis. The lithium heparin tube was centrifuged instantly after collection and stored on ice before it was sent for analysis. The serum vacutainer was kept in room temperature for 30min before it was centrifuged at 1500g for 10 minutes, and sent for analysis.

3.3.4 VO_{2MAX}

The VO_{2max} -testing was carried out on a treadmill (Woodway USA Inc., Waukesha, WI, USA), and VO_2 was measured using a Jaeger ergospirometry system with a mixing chamber (Oxycon Pro, Erich Jaeger GmbH, Hoechberg, Germany). The Jaeger system has been validated against the Douglas bag method, which is considered to be the gold standard for measuring oxygen uptake [93]. HR was registered by a Polar T31 HR transmitter (Polar Electro, Kempele, Finland) that was compatible with the treadmill. Ambient conditions, gas and volume were calibrated regularly. Gas calibration was performed with and a high precision gas (16.00±0.04% O_2 and 5.00±0.1% CO_2, Riessner-Gase GmbH & Co, Lichtenfels, Germany). At last, the inspiratory flowmeter was calibrated with a 3 liters volume syringe (Hans Rudolph Inc., Kansas City, MO, USA).

Before measurements of VO_{2max}, patients were informed about the test and familiarized with the Borg RPE scale [94]. The testing followed a standardized warm-up protocol starting with 2-3 minutes of rest while breathing in the ergospirometry. HR was noted at the last minute of rest period. Warm- up continued with 4 minutes at 4 km/h and 0% inclination followed by 4 minutes at 4 km/h and 4 %. HR and Borg were noted at the last minute of each stage. The VO_{2max} test was performed using an individual protocol increasing inclination and/ or speed each minute till exhaustion. Criteria for VO_{2max} were levelling off in oxygen uptake, respiratory exchange ratio above 1. 05 and Borg scale 18 or above. If the criteria were not met, VO_{2peak} was used. VO_{2max} was set to be the mean of the three continuously highest 10 second measurements. The highest heart rate and Borg was noted at termination, together with HR after 1 minute. 5 beats were added to HR_{peak} to estimate the HR_{max}. This was used to calculate the intensity zones of the exercise training.

3.3.5 PHYSCIAL ACTIVITY MEASURMENTS

Sensewear Armband, Model MF-SW (BodyMedia, Pittsburgh, PA, USA), activity monitors were delivered to the participants after the VO_{2max} test. SenseWear armbands, including Model MF-SW, have been validated against the gold-standard doubly labeled water (DLW) method of measuring energy expenditure [95]. The armband was placed on the dominant upper arm according to manufacturer`s instructions and worn both day and night for 5 continuous days including a week-end (Figure 4). The monitor was only taken off when showering or bathing. Handedness, height, body weight, age and smoking status (smoker or nonsmoker) for each participant was plotted into the software (SenseWear Professional software, version 7.0, BodyMedia, Pittsburgh, PA, USA) to make calculations of energy expenditure. Sleep time was included in the analyzed data. Measurement of partial days and days with less than 90 % wear time were excluded from calculations in the software. When data from baseline (BL) and follow-up (FU) did not match in number of days (for example due to less total wear time), or respective days of the week, the measurement period was changed to get comparable data for BL and FU. 1.5 MET was set as cut off point for sedentary time as recommended in previous studies [78, 79].

Figure 4. Placement of the SenseWear activity monitor.

3.4 TRAINING PROTOCOL

1-AIT and 4-AIT were performed as endurance training walking or running “uphill” 3 times/week for 16 weeks (two supervised sessions (treadmill) and one at home each week). A warm-up of 10 min at 70% of HR_{max} was done before performing 1x4 or 4x4 minutes intervals at 85- 95% of HR_{max}. 4-AIT used a 3 min active break between each interval, while 1-AIT went directly to the 5 minute cool-down period after the interval. The CME group exercised at moderate intensity for (60-70% of HR_{max}) for a minimum of 30 minutes, 5-7 times a week for 16 weeks (two supervised sessions (treadmill) and 3 or more home). HR was continuously monitored during the supervised exercise to ensure that the subjects exercised at the intended intensity. 70 % compliance was set as minimum requirement for the final analyses.

3.5 FOLLOW-UP

After the 16 weeks of intervention, the participants were scheduled for FU-testing within approximately one week. Some participants needed to extend their training period due to sickness or low compliance. These were tested after getting well, or sufficient training sessions were completed. Blood samples and BP were taken in the morning, followed by a lunch break of approximately one hour before the VO_{2max} test was carried out. A SenseWear monitor was delivered after the test and worn for 5 days. A few participants had to postpone their activity monitoring due to lack of monitors at the time.

3.6 STATISTICAL ANALYSES

Statistical analyses were performed using SPSS® version 21 (SPSS Inc. Chicago, IL, USA). For graphical illustrations, GraphPad Prism version 6 (GraphPad Software Inc., San Diego, CA, USA) was used. Extreme outliers, detected with boxplot, were removed from the dataset. All variables were considered to be normally distributed as assessed by visual inspection of Normal Q-Q plots and Shapiro-Wilk tests. Paired samples t-test was used to calculate differences within subjects from BL to FU. One-way ANOVA was used to analyze, based on delta-values, the differences between groups from BL to FU. If the F-ratios were significant, a post-hoc analysis with least significant difference (LSD) was used to determine where the specific difference was found. Test for homogeneity of variances was assessed by Levene's Test of Homogeneity of Variance. If the assumption of homogeneity was violated, a one-way Welch ANOVA was used to calculate the difference between groups. A McNemar`s test was assessed to analyze within-group changes of MetS components. The 25^{th} and 75^{th} percentile of VO_{2peak} delta-values were used to calculate the alternative groups *high*ΔVO_{2peak}, *moderate*ΔVO_{2peak} and *low*ΔVO_{2peak}. Linear relationship was checked using visually inspection of scatterplots. Data are presented as mean ± SD. A p value of $p<0.05$ was set as level of significance for all tests.

4. RESULTS

4.1 SUBJECT CHARACTERISTICS

At BL, subject characteristics were similar in all groups for most variables. However, mean age in 1-AIT was significantly lower than the other groups ($p<0.05$). Also, systolic BP was significantly lower in CME than 4-AIT ($p<0.05$). These differences were observed in spite of randomization. Subject characteristics are presented in Table 2.

Out of the planned training sessions, the subjects completed 91.6 %, 84.2 % and 85 % for CME, 1-AIT and 4-AIT respectively. There was no significant difference between groups ($p>0.05$).

Table 2. Subject characteristics.

	CME	1-AIT	4-AIT
	Baseline	Baseline	Baseline
N (males/females)	5/2	3/2	4/5
Age (years)	49.6 ± 5.1#	38.2 ± 7.0*	48.4 ± 7.5
Physical characteristics			
Height (cm)	179.6 ± 9.5	177.6 ± 9.7	170. 9 ± 10.0
Weight (kg)	99.9 ± 18.0	101.7 ± 9.4	91.3 ± 10.9
BMI ($kg \cdot m^{-2}$)	30.8 ± 3.4	32.2 ± 1.2	31.3 ± 2.8
WC (cm)	105.0 ± 9.4	105.1 ± 5.1	103.8 ± 8.2
Blood variables			
TG ($mmol \cdot L^{-1}$)	1.68 ± 0.62	1.89 ± 0.97	1.40 ± 0.74
HDL-C ($mmol \cdot L^{-1}$)	1.10 ± 0.21	1.17 ± 0.28	1.35 ± 0.28
FG ($mmol \cdot L^{-1}$)	5.70 ± 0.59	5.70 ± 0.45	5.90 ± 0.75
Blood pressure			
Systolic (mmHg)	129 ± 14§	134 ± 13	148 ± 10
Diastolic (mmHg)	87 ± 4	83 ± 13	86 ± 5
CRF			
VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$)	33.2 ± 6.1	33.3 ± 3.2	31.2 ± 2.8
VO_{2peak} ($L \cdot min^{-1}$)	3.3 ± 0.9	3.4 ± 0.5	2.9 ± 0.5
HR rest (bpm)	64 ± 10	72 ± 11	69 ± 11
Sedentary time			
TDST (hours)	17.9 ± 1.8	18.0 ± 2.1	18.8 ± 1.8
Medications			
Angiotensin II blockers	3	0	1
Beta-blockers	0	0	0
Calsium antagonists	0	0	1
α-blockers	0	0	0
Statin	0	0	1
Acetylsalicylic acid	0	0	0
Metformin	0	0	0
Insulin	0	0	0

Data are presented as mean ± SD or number of patients. CME; continuous moderate exercise; 1-AIT, one aerobic interval training; 4-AIT, four aerobic intervals training; BMI, body mass index; WC, waist circumference; TG, triglycerides; HDL, high density lipoprotein cholesterol; CRF, cardiorespiratory fitness; FG, fasting glucose; HR, heart rate; TDST, total daily sedentary time. * Difference between 1-AIT and 4-AIT ($p<0.05$). § Difference between CME and 4-AIT ($p<0.05$). # Difference between CME and 1-AIT ($p<0.05$).

4.2 TOTAL DAILY SEDENTARY TIME

After 16 weeks of exercise, TDST decreased 5.5 %, 0.1 % and 1.1 % for CME, 1-AIT and 4-AIT respectively. These changes were not significant within the groups, or between the groups ($p > 0.05$, Figure 5).

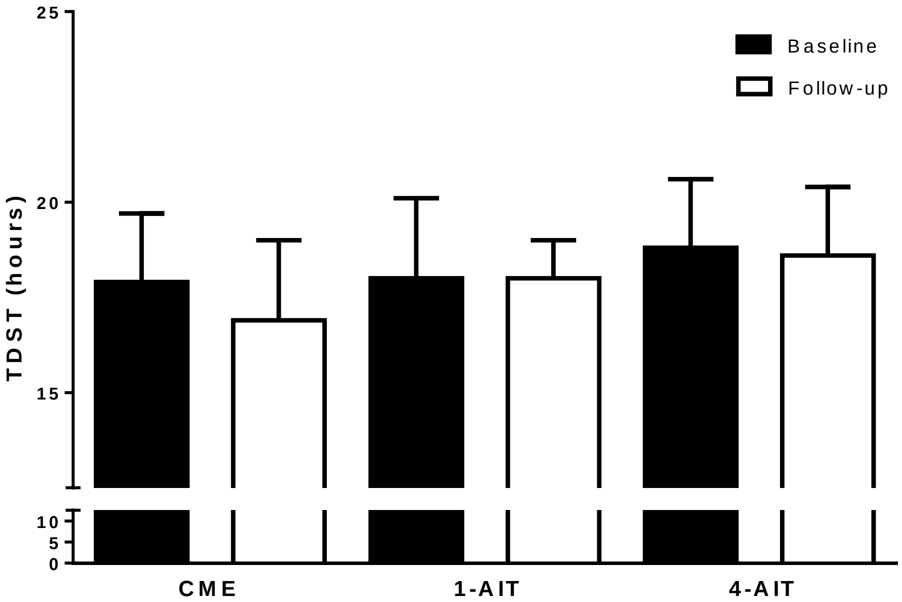

Figure 5. Total daily sedentary time (TDST) at baseline and follow-up. No significant differences were found. Vertical lines represent standard deviation (SD). CME, continuous moderate exercise; 1-AIT, one aerobic interval training; 4-AIT, four aerobic intervals training.

There was no linear relationship between TDST and VO_{2peak} in BL-data, FU-data or delta values, thus correlation analyses were not be applied for these variables (Figure 6).

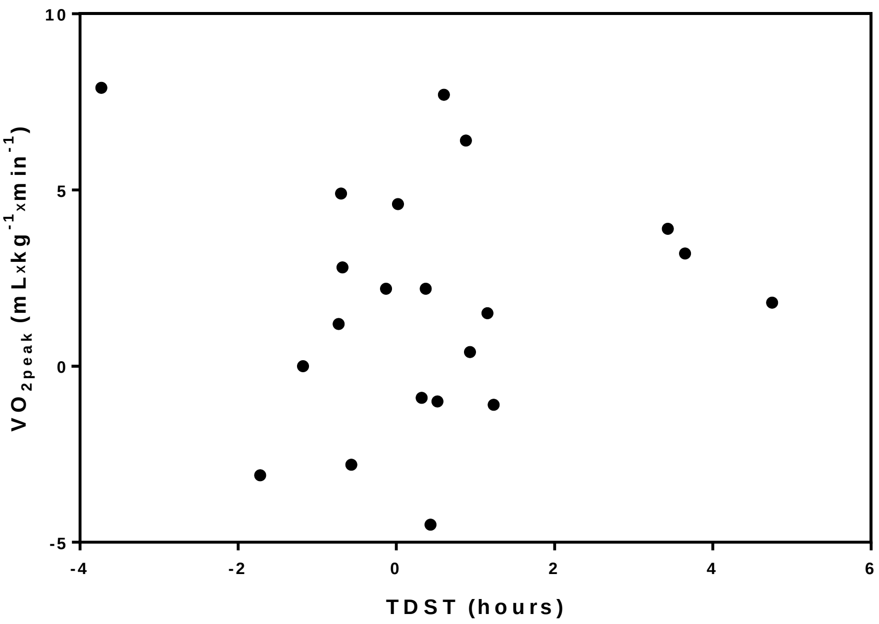

Figure 6. Distribution of individual values for decrease in total daily sedentary time (x-axis), and increase in VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$, y-axis). No linear relationship was found.

4.3 VO_{2PEAK}

VO_{2peak} increased 9.4 %, 0.1 % and 5.4 % for CME, 1-AIT and 4-AIT respectively. These changes were not significant within groups, or between groups ($p > 0.05$, Figure 7).

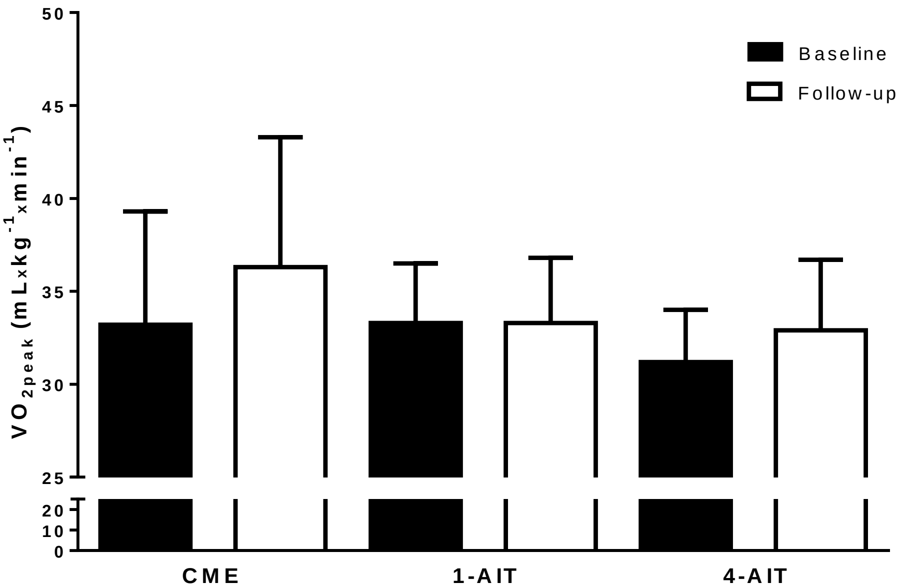

Figure 7. VO_{2peak} at baseline and follow-up. No significant differences were found. Vertical lines represent standard deviation (SD). CME, continuous moderate exercise; 1-AIT, one aerobic interval training; 4-AIT, four aerobic intervals training.

4.4 COMPONENTS OF METS

HDL-C increased 6.8 % in 1-AIT ($p < 0.05$). No other significant changes were observed among the components of MetS. However, we found minor improvements in most variables for all groups. Results are presented in Table 4.

Despite few significant changes in MetS components, we observed a small, insignificant ($p > 0.05$) decrease in the individual distribution of components from BL to FU within the groups. Results are presented in Table 3.

Table 3. Distribution of specific components of the metabolic syndrome

	CME		**1-AIT**		**4-AIT**	
	Baseline	**Follow-up**	**Baseline**	**Follow-up**	**Baseline**	**Follow-up**
N	7	7	5	5	9	9
WC	7/7	7/7	5/5	5/5	9/9	9/9
TG	4/7	3/7	2/5	2/5	2/9	3/9
HDL-C	4/7	3/7	2/5	1/5	2/9	3/9
FG	4/7	4/7	3/5	3/5	6/9	3/9
BP	6/7	5/7	4/5	3/5	9/9	9/9
Defined with MetS	7/7	5/7	5/5	4/5	9/9	6/9

Data are presented as number of subjects. No significant differences were found. CME; continuous moderate exercise; 1-AIT, one aerobic interval training; 4-AIT, four aerobic intervals training; BMI, body mass index; WC, waist circumference; TG, triglycerides; HDL-C, high density lipoprotein cholesterol; FG, fasting glucose; BP, blood pressure

4.5 BODY COMPOSITION

Both weight and BMI decreased 3.1 % in CME ($p < 0.05$). The change of weight and BMI was significant different between CME and 4-AIT ($p < 0.05$). No other significant changes were observed in body composition. Results are presented in Table 4.

Table 4. Subject baseline values, and mean group change post exercise

	CME		1-AIT		4-AIT	
	Baseline	**Follow-up**	**Baseline**	**Follow-up**	**Baseline**	**Follow-up**
N (males/females)	5/2		3/2		4/5	
Age (years)	49.6 ± 5.1		38.2 ± 7.0		48.4 ± 7.5	
Physical characteristics						
Height (cm)	179.6 ± 9.5		177.6 ± 9.7		170. 9 ± 10.0	
Weight (kg)	99.9 ± 18.0	-3.1 ± 2.3*§	101.7 ±9.4	-1.2 ± 1.7	91.3 ± 10.9	0.4 ± 2.4
BMI ($kg\cdot m^{-2}$)	30.8 ± 3.4	-1.0 ± 0.7*§	32.2 ± 1.2	-0.3 ± 0.4	31.3 ± 2.8	0.1 ± 0.9
WC (cm)	105.0 ± 9.4	-2.4 ± 3.1	105.1 ± 5.1	1.0 ± 3.5	103.8 ± 8.2	-1.3 ± 3.9
Blood variables						
TG ($mmol\cdot L^{-1}$)	1.68 ± 0.62	-0.18 ± 0.29	1.89 ± 0.97	-0.22 ± 0.82	1.40 ± 0.74	0.06 ± 0.69
HDL-C ($mmol\cdot L^{-1}$)	1.10 ± 0.21	0.04 ± 0.13	1.17 ± 0.28	0.08 ± 0.05*	1.35 ± 0.28	0.03 ± 0.11
FG ($mmol\cdot L^{-1}$)	5.70 ± 0.59	-0.14 ± 0.44	5.70 ± 0.45	-0.24 ± 0.23	5.90 ± 0.75	-0.33 ± 0.44
Blood pressure						
Systolic (mmHg)	129 ± 14	-3 ± 10	134 ± 13	-4 ± 5	148 ± 10	-3 ± 10
Diastolic (mmHg)	87 ± 4	-5 ± 6	83 ± 13	-2 ± 3	86 ± 5	-1 ± 4
CRF						
VO_{2peak} ($L\cdot min^{-1}$)	3.3 ± 0.9	0.2 ± 0.3	3.4 ± 0.5	-0.0 ± 0.3	2.9 ± 0.5	0.2 ± 0.2
HR (bpm)	64 ± 10	-2 ± 8	72 ± 11	-12 ± 8*	69 ± 11	-4 ± 8

Data are presented as mean ± SD or number of patients. CME; continuous moderate exercise; 1-AIT, one aerobic interval training; 4-AIT, four aerobic intervals training; BMI, body mass index; WC, waist circumference; TG, triglycerides; HDL-C, high density lipoprotein cholesterol; CRF, cardiorespiratory fitness; FG, fasting glucose; HR, heart rate; TDST, total daily sedentary time. * Difference from baseline within group ($p < 0.05$). § Difference between CME and 4-AIT ($p < 0.05$).

4.6 ALTERNATIVE GROUPS

From whole sample data, meaning all groups combined, we observed an increase in VO_{2peak} of 5.5 % (from 32.4 ± 5.0 to 34.1 ± 4.2 mL·kg^{-1}·min^{-1}) ($p<0.05$). Furthermore, HDL-C increased 4.9 % (from 1.22 ± 0.27 to 1.29 ± 0.34 mmol·L^{-1}) ($p< 0.05$), diastolic BP decreased 3.1 % (from 85 ± 7 to 83 ± 7 mmHg) ($p< 0.05$) and FG decreased 4.3 % (from 1.61 ± 0.75 to 1.52 ± 0.50 mmol·L^{-1}) ($p< 0.01$).

In regard of whole sample changes, we created three alternative groups from the percentiles of VO_{2peak} values (*high*Δ*VO_{2peak}*: >75th percentile, *moderate*Δ*VO_{2peak}*: 75th to 25th percentile and *low*Δ*VO_{2peak}*: <25th percentile). In the *high*Δ*VO_{2peak}* group weight decreased 4.0 % and BMI decreased 3.8 %. VO_{2peak} (mL·kg^{-1}·min^{-1}) increased 19.8 % and absolute VO_{2peak} (L·min^{-1}) increased 14.6 %. These changes were significantly different between the groups *high*Δ*VO_{2peak}* and *low*Δ*VO_{2peak}* ($p< 0.05$). In addition, WC decreased 2.9 % in *high*Δ*VO_{2peak}*. Although not significant, this change was better than *low*Δ*VO_{2peak}* where WC increased 1.7 %. ($p= 0.09$). Results are presented in Table 5.

Table 5. Alternative groups divided after level of increased VO_{2peak}. Results are presented as mean baseline values and mean group change post exercise.

	HIGH*Δ*VO_{2peak}		***MODERATE*Δ*VO_{2peak}***		***LOW*Δ*VO_{2peak}***	
	Baseline	**Follow-up**	**Baseline**	**Follow-up**	**Baseline**	**Follow-up**
N	5		11		5	
Body composition						
WC (cm)	102.0 ± 8.6	-3.0 ± 3.1	106.1 ± 8.7	-1.5 ±3.5	103.4 ± 3.7	1.8 ± 3.3
Weight (kg)	96.8 ± 21.5	-3.9 ± 1.7*$^{\#}$	96.0 ± 12.9	-0.9 ± 1.7	98.0 ± 6.6	1.2 ± 2.7
BMI (kg·m^{-2})	31.4 ± 3.2	-1.2 ± 0.4*$^{\#}$	31.4 ± 3.1	-0.3 ± 0.5	31.1 ± 1.2	0.4 ± 0.9
Blood variables						
TG (mmol·L^{-1})	1.69 ± 0.37	-0.37 ± 0.34	1.63 ± 0.70	-0.02 ± 0.62	1.49 ± 1.21	0.04 ± 0.78
HDL-C (mmol·L^{-1})	1.14 ± 0.24	0.03 ± 0.10	1.29 ± 0.29	0.05 ± 0.11	1.16 ± 0.29	0.05 ± 0.11
FG (mmol·L^{-1})	5.94 ± 0.99	-0.34 ± 0.27*	5.72 ± 0.56	-0.17 ± 0.46	5.76 ± 0.27	-0.32 ± 0.37
Blood pressure						
Systolic BP (mmHg)	135 ± 19	-5 ± 7	141 ± 13	-5 ± 10	134 ± 13	1 ± 4
Diastolic BP (mmHg)	84 ± 3	-5 ± 4	86 ± 5	-4 ± 5*	86 ± 13	1 ± 4
CRF						
VO_{2peak} (mL·kg^{-1}·min^{-1})	31.8 ± 4.5	6.3 ± 1.5*$^{\#}$	31.8 ± 3.9	1.6 ± 1.4*	34.2 ± 4.8	-2.5 ± 1.5*
VO_{2peak} (L·min $^{-1}$)	3.1 ± 1.1	0.5 ± 0.2*$^{\#}$	3.0 ± 0.5	0.1 ± 0.1*	3.4 ± 0.7	-0.2 ± 0.1*
HR (bpm)	61 ± 7	-8 ± 8	70 ± 13	-2 ± 7	71 ± 8	-10 ± 10
Sedentary time						
TDST (hours)	17.3 ± 1.3	0.6 ± 1.9	18.5 ± 1.5	-1.1 ± 2.0	18.8 ± 2.7	0.1 ± 1.2

Data are presented as mean ± SD or number of patients. BMI, body mass index; WC, waist circumference; TG, triglycerides; HDL-C, high density lipoprotein cholesterol; CRF, cardiorespiratory fitness; FG, fasting glucose; HR, heart rate; TDST, total daily sedentary time. *Difference between baseline and follow-up ($p<0.05$) $^{\#}$ Difference between the other two groups $p< 0.05$).

5. DISCUSSION

The main findings of the present study were: 1) changes in TDST, VO_{2peak} or the components of MetS did not differ between the groups, 2) TDST did not correlate with VO_{2peak}, 3) HDL-C in 1-AIT was the only component of MetS that improved significantly within the groups.

5.1 TOTAL DAILY SEDENTARY TIME

It was hypothesized that TDST would improve more in the AIT groups than in CME, and that change in TDST and VO_{2peak} would correlate.

Findings from the present study showed no significant difference in change of TDST between CME and the other two groups. Furthermore, none of the groups showed a correlation between TDST and VO_{2peak} concerning either delta values between BL and FU, or BL and FU data isolated. As discussed later, we observed no significant improvements of VO_{2peak} in any group. Therefore, testing the hypothesis that change in TDST will correlate with change in CRF can be problematic. However, when we re-arranged our data into groups based on level of increased $VO_{2peak,}$ where VO_{2peak} significantly improved by 18% in the highest group ($p<0.05$), we still found no correlation between TDST and VO_{2peak}. In fact, although not significant, a minor increase of TDST was observed in this group. Taken together, these findings can suggest that TDST and CRF do not correlate and therefore our hypothesis must be rejected.

None of the groups changed their level of TDST significantly from BL to FU. To our knowledge no studies have investigated TDST, and compared it against CRF, before and after an exercise intervention. Consequently it is difficult to say whether our delta values between BL and FU are representative for this type of population.

At BL, we observed an average of 17.9, 18.0, and 18.8 hours of TDST for CME, 1-AIT and 4-AIT respectively. In comparison, Scheers et. al [63] found a TDST of 16.7 hours in a study including 370 Belgian men and women with varying health status. In this study, only 10.2 % of the men, and 5.2 % of the women were classified with the MetS. Also, WC values were considerably lower than in our subjects. However, sedentary time is associated with the MetS [16] and thus one could speculate that our TDST data would be higher. This makes it likely to assume that our findings are comparable to those in the study of Scheers et. al [63].

Another study, by Bankoski et al. [15], reported a TDST of 9.7 hours in subjects with MetS. These data did not include sleep time and therefore our findings probably correspond in some degree. In the same study, TDST was found 0.5 hours lower in subjects not classified as having the MetS compared to those having the MetS.

Altogether, the level of sedentary time seems to be somewhat higher in our BL-data compared to previous findings of subjects without the MetS. Taken in consideration that the MetS and sedentary time have been associated [15, 89], this finding was expected. However, TDST did not change after the intervention and also, very few improvements were found in the components of MetS, as discussed later. Therefore, one may speculate that a decrease in TDST in our study would have contributed to a larger improvement in the components of MetS, due to the previous found associations of sedentary time and the MetS.

5.2 CARDIORESPIRATORY FITNESS

We hypothesized that the AIT-groups would improve CRF more than CME.

Data from the present study showed no significant difference between improvements of VO_{2peak}. In addition, none of the groups increased VO_{2peak} significantly from BL to FU. Nevertheless, we observed some dissimilarity between the groups. VO_{2peak} was improved 9.4 %, 0.1 % and 5.4 % for CME, 1-AIT and 4-AIT respectively. These findings are rather unexpected and not in line with former studies of subjects with the MetS [36, 37], obesity [65], CAD [64] or with healthy subjects [70].

Tjønna et al. [36] studied the effect of CME and 4-AIT in MetS subjects after an intervention lasting 16 weeks. The CME group trained three times a week, but each session lasted 47 minutes in order to equalize the 4-AIT group in terms of kcal spent per session. It was found VO_{2max} values around 36 $mL \cdot kg^{-1} \cdot min^{-1}$ in the CME group at BL, which is somewhat higher than our findings of 33.2 $mL \cdot kg^{-1} \cdot min^{-1}$. Furthermore, in the 4-AIT group they reported a BL value of 33.6 $mL \cdot kg^{-1} \cdot min^{-1}$, and this is also slightly higher than our results of 31.2 $mL \cdot kg^{-1} \cdot min^{-1}$. After the intervention, VO_{2max} increased significantly by 35 % and 16 % for 4-AIT and CME respectively. Compared to our study, improvements within the 4-AIT group are substantially higher (35 % versus 5.2 %). However, results from the CME groups are more alike (16 % and 9.2 % improvement).

A recent published study by Mora-Rodriguez et al. [37] utilized a similar intervention protocol as the abovementioned study and our own. Although this study did not include a CME or a 1-AIT group, the 4-AIT group improved VO_{2peak} significantly by 21 % after 16 weeks, from 21.5 $mL \cdot kg^{-1} \cdot min^{-1}$ to 26.1 $mL \cdot kg^{-1} \cdot min^{-1}$. Findings from Schjerve et al. [65] also demonstrate a difference from our results. They studied obese patients who trained CME, strength training or 4-AIT for 12 weeks. Regarding BL values, findings from this study showed a fairly higher $VO2_{max}$ than our results. Still, the 4-AIT group improved 33 %, while the CME group improved 16 %. Similar enhancements were found in CAD patients, where the CME and 4-AIT groups increased VO_{2max} 7.9 % and 17.9 %, respectively [64]. Moreover, in a study of healthy, fit subjects, Helgerud et al. [70] showed an increase of 7.9 % in VO_{2max} within the 4-AIT group. The CME group showed no change. However, the lower levels of improvements could be explained by the initial much higher level of VO_{2max} in this study (CME: 53.4 $mL·kg^{-1}·min^{-1}$ and 4-AIT: 51.8 $mL·kg^{-1}·min^{-1}$).

None of the mentioned studies [36, 37, 64, 65, 70] included a 1-AIT group. In general, this is a less investigated exercise regimen and thus it is difficult to compare our findings. Anyhow, data from Tjønna and colleagues [71] suggest that 1-AIT should induce improvements in line with those in 4-AIT. Our results from the 1-AIT group are consequently lower than anticipated.

As stated, the results from our CME group are to some extent comparable with the abovementioned studies. In subjects with MetS [36], obesity [65] or CAD [64] it seems to be likely to increase $VO2_{max}$ 8- 16 % after an exercise intervention of CME lasting 10-16 weeks. Therefore, the main difference between previous findings and our study is the level of VO_{2max} -incline seen in the 4-AIT groups, nonetheless also the significant variance between these groups and the CME groups.

If trying to explain these dissimilarities, one can speculate about different aspects within our study. First of all, the groups in the mentioned studies [36, 64, 65, 70] were matched in regard of energy expenditure per exercise session. In our study, the CME group exercised 30 minutes 5-7 days a week, which means that two of the key factors of CRF, volume and frequency, have extended the AIT groups. Although we observed no statistical differences between the groups, CME showed the largest improvement in VO_{2peak}. Therefore, one may assume that the higher volume and frequency in this group can have contributed to the better results.

Furthermore, the compliance in the AIT groups was lower in our study (84.2 % and 85 % for 1-AIT and 4-AIT respectively). In the study by Scjerve et al. [65], compliance was not reported. However, in the other discussed studies [36, 64, 70], the compliance was over 90 % for the 4-AIT groups. Although the difference from our study is minor, this may have had an influence.

Compliance may also be an aspect concerning the differences we found between CME and the AIT groups in our own study. CME completed 91.6 % of their scheduled sessions. This is not significantly higher than the other groups ($p>0.05$), still a difference worth mentioning. Besides, when we calculated the compliance, 5 sessions per week were set as 100 %, although this group was instructed to exercise “at least” 5 times a week in accordance with today`s guidelines. Some subjects reported more than 5 sessions per week throughout the intervention. Hence, the compliance of CME is underestimated.

We also noticed some factors within the subjects which could have influenced our data. Primarily, two of the subjects in the CME group reported HR values above their target zones in several sessions throughout the intervention. Furthermore, one subject in the 1-AIT group claimed that he took part in prolonged strenuous exercise three times a week before he joined the study. This continued during the intervention and hence, 4 minutes three times a week in addition may not have been sufficient to induce improvements in oxygen uptake. This could explain why this particular subject showed no improvement in $VO_{2peak.}$ Finally, two subjects in the 4-AIT group increased body mass by 1.7 and 5.7 kg, and decreased VO_{2peak} by 1.0 and 4.5 $mL \cdot kg^{-1} \cdot min^{-1}$, respectively. The absolute values of VO_{2peak} for the respective subjects did not decrease correspondingly (43 and 267 ml, respectively), which suggests that the weight gain in some degree have contributed to the decline seen in $VO_{2peak.}$

5.3 COMPONENTS OF METS AND BODY COMPOSITION

Except from HDL-C in the 1-AIT group ($p<0.05$), our findings showed no significant change in the components of MetS from BL to FU, even though FG showed a strong trend of decrease in 4-AIT ($p=0.051$). Significant alterations in the variables between groups were not observed. These findings are in contrast with former research. In the study by Tjønna et al. [36], it was found significant improvements within the 4-AIT group in all components except TG, and FG improved significantly more in the AIT group than the CME group. Furthermore, Mora-Rodriguez et al. [37] reported significant improvements of WC, HDL-C and BP after 16 weeks of 4-AIT.

In a study of healthy, young women, Stasiulis and colleagues [38] also found improvements in various variables related to the MetS. In addition VO_{2max} improved by 16 %. In this study, however, the participants trained 60 minutes continuously at an intensity set to the ventilatory threshold three times a week for 8 weeks. By this, the findings from Stasiulis and colleagues [38] cannot entirely be compared with ours, or with the studies discussed earlier [36, 37, 64, 65, 70]. Still, the improvements seen in both VO_{2max}, and components related to the MetS in this study, are noteworthy.

Concerning body composition, both weight and BMI decreased 3.1 % in CME. This change was significant within the group and also between the other groups ($p<0.05$). In the other groups, no significant difference was observed. Alterations in body composition show varying outcomes in the previously mentioned studies, however it seems that weight and BMI in CME decrease similar to, or even slightly more than the 4-AIT groups [36, 64, 65, 70]. In these studies the CME group and 4-AIT group exercised with matched energy expenditure, as mentioned. Thus, the weekly amount of exercise equaled approximately 135 minutes for the CME groups. In our study, CME exercised at least 150 minutes of per week. This indicates that CME spent more energy than 4-AIT during a week. Along with the somewhat higher compliance found in CME, it is likely to assume that this group would lose more weight than 4-AIT.

5.4 VO_{2PEAK} AND ALTERNATIVE GROUPS

Although the present study showed no significant change in VO_{2peak} within the groups, we observed a significant improvement for the sample as a whole ($p<0.05$). In regard of former studies [36-38], where improvement in VO_{2peak} seems to be connected with a decrease in the occurrence of MetS features, we re-arranged our data into percentile-groups after level of increased VO_{2peak}. Data from the $high\Delta VO_{2peak}$ group showed an improvement of 19.8 % in $V0_{2peak}$, whereas the $low\Delta VO_{2peak}$ group decreased by 7.3 %. By this, all the components of MetS, except HDL-C, improved more in $high\Delta VO_{2peak}$ than in $low\Delta VO_{2peak}$. None of these differences were significant between groups, yet, by observing the all variables (see Table 5), one may speculate that there is a connection in our findings between the increase of VO_{2peak} and the improvements in MetS components.

Taken together, the alterations of the individual features of MetS seen in the $high\Delta VO_{2peak}$ group can be related with several beneficial health outcomes. For example, both systolic and diastolic BP was reduced by 5 mmHg in this group. Alterations of this extent can, in the long term, be associated with a major reduction in the risk of death from cardiovascular causes [96]. Along with this, the improvements seen in WC and the blood variables, and those seen in VO_{2peak}, imply that the subjects in this group may have considerably reduced their risk of death [49], and CVDs [97-99].

5.5 STUDY LIMITATIONS

We experienced an unexpected high number of dropouts and excluded subjects due to resource limitations and technical problems with the activity monitoring. The sample size is therefore rather small, especially in the 1-AIT group (n=5), and group differences have possibly been hard to detect. Furthermore, many of our subjects were recruited through ads on the local fitness center`s website. Some subjects were also engaged in systematic aerobic exercise before they joined the study. Even though each subject was defined with MetS at BL, an active lifestyle prior to the intervention may have decreased the probability of improvement within the variables.

The subjects carried out at least one training session at home without supervision. Other than self-reported data, we had no assurance that the target HR zones was reached at all time. Especially in the interval groups, where the physical strain is hard, one could suspect that the intensity has been too low in some of the home based sessions.

Furthermore, the measurements of physical activity was carried out during five days, and for many subjects we had to reduce the measurement period due to wear time less than 90 % on some days, or to lack of congruence between BL and FU- data. Thus, a longer period of wear time could have been beneficial. Lastly, a food diary and nutritional follow-up could have provided useful information. For reasons unknown, some subjects gained weight during the intervention period and this may have influenced some of the variables.

5.6 CONCLUSION

Between groups of CME and AIT, the present study showed no significant difference in change of TDST or VO_{2peak} after 16 weeks of exercise. Also, no components of MetS differed between the groups, and only HDL-C within the 1-AIT group improved significantly after the intervention. These findings are not in line with previous studies and should therefore be interpreted with caution. Nevertheless, there seems to be a connection in our data between increased VO_{2peak} and improvements in the components of MetS.

Secondly, the present study implies that TDST and CRF do not correlate. However, in regard of a low sample size and possible sources of bias, this topic should be further investigated in order to draw conclusions for other populations.

5.7 PERSPECTIVES

Physical inactivity and sedentary time are key factors in the development of the MetS, hence knowledge about possible methods for decreasing these behaviors is of importance. Larger scaled exercise studies are necessary to determine whether there exist a correlation between CRF and sedentary time. Furthermore, improving CRF and decreasing sedentary time can yield several positive health outcomes and should be emphasized in the treatment and prevention for subjects with the MetS.

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