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# Effects of Individualized Exercise Prescription vs. General Guidelines on Low-grade Inflammation and, Glucose and Lipid Metabolism in Overweight and Obese Subjects

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Master's Thesis

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**Abstract**

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**Background and objective**. This study investigates the impact of a three-month exercise prescription on inflammation markers, glucose and lipid profiles, and body composition among overweight and obese individuals. Additionally, it explores the effects of individualized versus general exercise guidelines and their influence on the parameters.

**Methods**. In a randomized controlled trial, 89 participants aged 18-40 with a BMI over 27.5 were assigned to three intervention groups: Group 1 (n=14) adhered to standard exercise and nutrition guidelines, Group 2 (n=22) received a personalized intervention, and Group 3 (n=20) underwent a highly personalized intervention. Baseline and post-intervention assessments were conducted over a 12-week period, with additional follow-ups at 12 months. 56 participants attended the post-intervention measurements. Blood samples were analyzed for glucose, lipid profiles, and inflammatory markers, including CRP, TNF-α, and interleukins IL-1β, IL-6, IL-8, IL-10, IL-15, and IL-17A. Oxygen consumption (VO2) and exercise performance (W) at ventilatory thresholds (VT1 and VT2) and maximum capacity were measured during a step-incremental cycle-ergometer exercise test. Anthropometric values, encompassing weight (kg), Body Mass Index (BMI), Body Fat percentage (BF%), and Fat-Free Mass (FFM), were also assessed.

**Results.**

Significant negative changes were only observed in Group 3 for Weight, Body Fat Percentage, Visceral Fat, and BMI ($p<0.05$), with no significant changes in Group 1 and Group 2. All groups showed significant positive changes in power at both ventilatory thresholds (VT1 and VT2). Group 3 exhibited significant changes in all parameters. Significant differences between groups were observed in $VO_{2max}$, VT1, and VT2. Changes in inflammatory marker levels, glucose profiles, or lipid profiles showed no statistically significant differences in all participants combined or among different groups. Significant positive correlations were found between anthropometric markers and $VO_{2max}$, power, insulin, and HOMA-ir. Glucose and lipid profiles showed significant positive correlations with weight, visceral fat, and BMI, while no significant correlations were found in glucose profiles with cardiorespiratory and fitness markers. Of the lipid profiles, cholesterol and LDL correlated negatively with some cardiorespiratory and exercise performance markers, most notably VT1 and Power at VT1 and VT2. TNF-α and IL-8 correlated significantly negatively with Weight, BMI, Fat %, and Visceral Fat. IL-8 also correlated with all power parameters and $VO_{2max}$ but not when scaled to Fat Free Mass.

**Conclusions.** The study's findings support the efficacy of individualized exercise prescriptions in promoting favorable changes in health markers, offering insights for future interventions in obesity management. Consideration of the challenges in implementing highly individualized programs in broader populations is discussed, highlighting the need for innovative frameworks and tools for personalized exercise prescriptions.

**Keywords** obesity, exercise intervention, randomized trial, physical activity, cytokines, myokines, low-grade inflammation, glucose profile, lipid profile, maximal oxygen uptake, anthropometry

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# 1 INTRODUCTION

Obesity, a prevalent global health concern, serves as a significant inflammatory factor associated with changes in insulin resistance, hypertension, atherosclerosis, and certain cancers (Hotamisligil, 2006). This condition is marked by altered levels of inflammatory markers like TNF-α, CRP, and interleukins in the blood, contributing to chronic low-grade inflammation. These cytokines play a role in adipose tissue inflammation, which may be the case of the before-mentioned complications such as insulin resistance, cardiovascular issues, and metabolic syndrome. (Festa et al., 2001; Hotamisligil, 2006; Park et al., 2005.)

Both dietary interventions, particularly caloric restriction, and regular exercise have demonstrated their effectiveness in reducing inflammation in obesity, along with associated metabolic dysfunctions (Donnelly et al., 2009; Klein et al., 2004). Even though there is more knowledge than ever of the link between lifestyle and an individual's health, many still fall into a sedentary lifestyle that ends up being detrimental to their health. The notion of "exercise more and eat healthier" appears straightforward, yet its implementation proves challenging for many in their daily routines.

Low-grade inflammation markers and glucose and lipid profiles are useful tools for measuring the effects of an intervention on the individual's overall health and can predict the onset of diseases such as cardiovascular disease and diabetes.

## *1.1 Low-grade Inflammation and Inflammatory Markers*

A sedentary lifestyle is linked to an elevated risk of obesity, metabolic syndrome, diabetes, cardiovascular disease, mental and cognitive disturbances, musculoskeletal issues, and increased cardiovascular and all-cause mortality. The development of these health problems is associated with low-grade inflammation, triggered by physical inactivity leading to the accumulation of visceral fat and the activation of the inflammation cascade. Chronic low-grade inflammation has been recognized as a hallmark feature of obesity, further exacerbating the associated health risks. This low-grade inflammatory state is characterized by a chronic production of various inflammatory factors, such as interleukins and acute-phase proteins, albeit at a lower level than in acute inflammation. Click or tap here to enter text. It is usually

associated with an increased disease risk and even mortality. (Minihane et al., 2015¸ Chung et al., 2019.)

Research indicates that the combination of work-related stress, reduced physical activity, and weight gain in individuals contributes to the persistence of low-grade inflammation (Physical Activity Guidelines Advisory Committee, 2018). This cycle, with detrimental health effects such as depression, musculoskeletal disorders, and metabolic/cardiovascular diseases, may also diminish work capacity and curtail careers. Chronic low-grade inflammation is a characteristic feature in various chronic conditions, including non-alcoholic fatty liver disease, type 2 diabetes mellitus, and cardiovascular disease. (Hotamisligil, 2006; Libby, 2002.)

Obesity, according to the World Health Organization, is a condition characterized by the abnormal or excessive accumulation of fat in adipose tissue to the extent that it can adversely affect health. In Western populations, an individual is classified as obese when their Body Mass Index (BMI) exceeds 30 $kg/m^2$. Disturbing statistics indicate that the occurrence of obesity has more than doubled in the last four decades, presenting a substantial global public health concern. (WHO Regional Office for Europe, 2022.)

Obesity has been shown to increase the number of inflammation markers in the bloodstream. Systemic concentrations of pro-inflammatory mediators are higher in obese (BMI>30 $kg/m^2$) than in normal-weight individuals (Herder et al., 2006). Adipocytes, also known as fat cells, produce several factors that are linked to low-grade inflammation, such as proinflammatory cytokines IL-1b, IL-6, IL-8, and IL-10 and acute-phase proteins like CRP, and TNF-α (Calder et al., 2011; Hotamisligil et al., 1993). This and increased macrophage numbers due to enlarging adipocytes contribute to a higher expression of pro-inflammatory cytokines (Greenberg & Obin, 2006).

The aforementioned markers of inflammation are thought to contribute to the development of insulin resistance and other metabolic disruptions, including alterations in glucose and lipid metabolism. Hotamisligil et al. (1993) discovered that the levels of TNF-a expression are increased in the adipocytes of obese and insulin-resistant mice, and insulin sensitivity improved when anti-TNF-a antibodies were administered. These findings suggest that adipose tissue plays a crucial role in the immune system and may serve as a significant contributor to the development of chronic inflammation, insulin resistance, and atherosclerosis. These characteristics are commonly associated with metabolic dysregulation linked to obesity. (Hotamisligil et al., 1993.)

### 1.1.1 C-Reactive Protein (CRP)

C-reactive protein (CRP) is an acute-phase inflammatory protein that plays an active regulatory role in the inflammation process. When the body is in a non-inflammatory state, CRP is released slowly from the endoplasmic reticulum. However, during inflammation or tissue damage, there is a rapid increase in CRP secretion (Ciubotaru et al., 2005). CRP is mainly produced in the hepatocytes of the liver in response to pro-inflammatory cytokines, with the main inducer being interleukin-6 (IL-6) with interleukin-1(IL-1) and tumor necrosis factor alpha (TNF-α) enhancing the reaction (Boras et al., 2014; Zhang et al., 1996). CRP is a commonly used plasma marker for overall inflammation and general illness, even though proven not specific enough to influence treatment plans (Clyne & Olshaker, 1999). Among individuals with obesity, an increased baseline CRP level has been linked to a heightened risk of developing type 2 diabetes and other metabolic disorders. Obesity stands out as a significant factor influencing baseline CRP levels (Laaksonen et al., 2004). Regular exercise has been shown to reduce baseline CRP concentrations, suggesting its potential as a lifestyle intervention for mitigating inflammation in obesity (Lakka et al., 2005).

### 1.1.2 Interleukins

Within the intricate network of inflammatory markers, interleukins assume a pivotal role in the context of obesity-induced inflammation. Interleukin 1 beta (IL-1β), a potent pro-inflammatory cytokine, is primarily produced by innate immune cells, such as monocytes and macrophages (Dinarello, 1996). It plays a crucial role in inducing the acute-phase response and fever during local inflammatory events (Fattori et al., 1994). The production is downregulated by other cytokines, most notably IL-10 (Howard et al., 1993).

Similarly, interleukin 6 (IL-6), known for its multifaceted role as both a pro-inflammatory cytokine and an immunomodulatory agent, is produced in various cells, including contracting skeletal muscle, adipose tissue, and endothelial cells. While IL-6 was initially classified as pro-inflammatory, it exerts an anti-inflammatory effect in the context of exercise, which is thought to be mediated by the exercise-induced secretion of IL-10 and IL-1Ra (Steensberg et al., 2003). Chronically elevated levels of IL-6 in obese individuals are linked to various diseases associated with obesity and sedentary lifestyles, such as cardiovascular disease (Bastard et al., 2000; Hejazi & Wong, 2023).

Another inflammatory marker associated with obesity is interleukin 8 (IL-8), also known as the neutrophil chemotactic factor. IL-8 plays a crucial role in inducing chemotaxis and stimulating

phagocytosis, and its increased production at the site of inflammation recruits and activates inflammatory cells by forming a concentration gradient (Baggiolini & Clark-Lewis, 1992; Moore et al., 2000). Many kinds of stimulants can induce the production of IL-8 in cells, including proinflammatory cytokines such as TNF-α and IL-1 (Standiford et al., 1990). Elevated plasma levels of IL-8 might have an anti-inflammatory effect, as they reduce the recruitment of neutrophils away from the site of inflammation (Moore et al., 2000). Adipose tissue has been identified as a significant source of IL-8 production, with its secretion positively correlated with the amount of adipose tissue in an individual (Calder et al., 2011).

Interleukin 10 (IL-10) is a critical player in the regulation of both immune responses and inflammation. IL-10 has anti-inflammatory effects, and its most crucial role lies in limiting and terminating both adaptive and innate immune responses by inhibiting the function of T cells, monocytes, and macrophages. Moreover, IL-10 assumes a crucial role in the differentiation of diverse cell types, encompassing B cells, NK cells, cytotoxic T cells, and helper T cells (Moore et al., 2001). IL-10 levels have been shown to increase during systemic inflammatory responses caused by severe trauma, infectious events, or burns (Howard et al., 1993). The suppressive impact of IL-10 on the production of proinflammatory cytokines and the physiology of specific cell types suggests its potential as a robust in vivo anti-inflammatory agent. Studies have demonstrated its correlation with diminished levels of TNF and IL-1 (Howard et al., 1993).

Interleukin 15 (IL-15) holds a significant position in the inflammatory process, acting as a connector between the innate and adaptive immune systems (Pagliari et al., 2013). It plays a critical role in the development, homeostasis, and function of T cells, NK cells, and NK-T cells (Waldmann & Tagaya, 1999). Exercise has been demonstrated to increase IL-15 levels in the blood post-exercise, and regular physical activity has been found to lower the base levels of IL-15 over time, demonstrating its potential impact on inflammation in both obese and lean individuals (Pérez-López et al., 2018).

Interleukin 17a (IL-17a), a pro-inflammatory cytokine predominantly produced by activated T cells, serves as a regulator of neutrophil response during inflammation (Schwarzenberger et al., 2000). Its elevated production has been associated with the activation of cytokines, chemokines, and adhesion molecules in different cell types, suggesting its involvement in the development of various inflammatory diseases, including rheumatoid arthritis (Csiszar & Ungvari, 2004). IL-17A-induced chemokines have also been shown to recruit IL-1-producing innate immune cells (McGinley et al., 2020).

Tumor necrosis factor alpha (TNF-α) represents one of the pivotal factors in acute inflammation within the human body (Csiszar & Ungvari, 2004). Moreover, TNF-α has been shown to partially regulate cell apoptosis and necrosis (Idriss & Naismith, 2000). It is of particular significance that white adipose tissue synthesizes and produces TNF-α, thereby contributing to higher plasma levels of TNF-α in obese individuals (Hotamisligil et al., 1993).

Obesity-induced inflammation arises from the expanded mass of adipose tissue, leading to profound changes in its distribution within the body. Adipocytes and skeletal muscle, in this context, play a central role by secreting multiple factors associated with low-grade inflammation, such as pro-inflammatory cytokines (e.g., IL-1β, IL-6, IL-8, IL-15, and IL-17A), the anti-inflammatory IL-10, and acute-phase proteins like CRP and TNF-α. Moreover, an increased number of macrophages in adipose tissue contributes to higher expression of pro-inflammatory cytokines. The interplay between these factors in response to the lack of exercise contributes to the development of chronic inflammation, insulin resistance, atherosclerosis, and metabolic dysregulation, which are often observed in the context of obesity.

## *1.2 Effects of Obesity on Macronutrient Metabolism*

Insulin plays a crucial physiological role by regulating the metabolism of all three major macronutrients: carbohydrates, lipids, and proteins, in addition to promoting cellular growth. Its actions in lipid metabolism are akin to its role in glucose metabolism, as it primarily supports anabolic processes while inhibiting catabolic ones. Insulin facilitates glucose transport and triglyceride synthesis (lipogenesis) while also inhibiting lipolysis (Boden, 2001). Specifically, insulin enhances the activity of lipoprotein lipase and promotes the gene expression of intracellular lipogenic enzymes, including acetyl-CoA carboxylase (ACC) and fatty acid synthase (FAS), consequently promoting lipogenesis. Additionally, insulin hinders adipocyte hormone-sensitive lipase, thereby suppressing lipolysis (Eckel, 1992). Insulin has also been shown to impact the release of proteins from mature adipocytes, potentially by elevating the production of enzymes essential for processing precursor proteins before secretion (Wang et al., 2006).

### 1.2.1 Effect of Obesity on Carbohydrate Metabolism

After the intake of glucose, plasma glucose concentration increases. This prompts the secretion of insulin by the beta cells. The resulting hyperinsulinemia, in conjunction with hyperglycemia, triggers four key actions: the suppression of hepatic glucose production, the promotion of glucose uptake by muscle, liver, and adipocytes through GLUT4, the inhibition of lipolysis leading to a decrease in plasma free fatty acid concentration, contributing to the suppression of hepatic glucose production, and the enhancement of muscle glucose uptake and vasodilation in muscle, contributing to improved muscle glucose disposal. Despite alternating periods of feeding and fasting, the plasma glucose in normal individuals consistently stays within a narrow range of 4 to 7 mM. (Saltiel & Kahn, 2001, Norton et al., 2022.)

GLUT4 (Glucose Transporter 4) is a protein that plays a crucial role in the regulation of glucose uptake into cells, primarily in muscle cells and adipose tissue. It is one of several glucose transporter proteins found in the human body. Increased expression of GLUT4 specifically within adipose tissue has been shown to improve overall insulin sensitivity and glucose tolerance in the entire body. On the other hand, selectively removing GLUT4 from adipose tissue has been found to induce insulin resistance comparable to that observed in muscle-specific GLUT4 knockout models. In the context of obesity, the downregulation of GLUT4 is a significant contributing factor to the compromised insulin-mediated glucose transport in adipocytes. (Shepherd et al., 1993; Shepherd & Khan, 1999.)

Beyond regulating glucose, insulin plays a crucial role in controlling lipid metabolism. It accomplishes this by stimulating lipid synthesis in the liver and fat cells, while simultaneously suppressing lipolysis, the breakdown process of fatty acids (Roberts et al., 2013). Insulin resistance and susceptibility to type 2 diabetes are outcomes associated with both obesity and lipoatrophy (Gavrilova et al., 2000). The skeletal muscle of obese individuals has been shown to exhibit defects in the insulin signal transduction pathway (Goodyear et al., 1994). Adipose tissue hypertrophy is associated with immune cell infiltration and crucial cytokines like TNF-a, IL-6, and IL-1b that mediate the insulin signaling cascade, fostering insulin resistance. This culminates in disrupted glucose and lipid metabolism in adipose tissue, skeletal muscle, and liver. This, combined with the role of skeletal muscle in insulin-stimulated glucose uptake, emphasizes the potential benefits of a body composition characterized by high muscle mass and low body fat for enhanced insulin sensitivity. (Weisberg et al., 2003; Wildman et al., 2008.)

Another pivotal mechanism fueling insulin resistance in obesity involves heightened whole-body lipolytic rates and the consequent excessive supply of fatty acids to tissues like skeletal muscle and liver (Ryan et al., 2020). Impaired suppression of fatty acid release from adipose tissue by insulin seems foundational to most metabolic dysfunctions accompanying obesity (Schleh et al., 2023).

Obesity is associated with decreased glucose utilization within adipose tissue, potentially leading to the onset of conditions such as hyperglycemia, hyperlipidemia, hyperinsulinemia, and insulin resistance (Colditz GA et al., 1990; Kraegen et al., 1985; G. Reaven, 1995; P. Shepherd & Khan, 1999). Various molecules, such as free fatty acids (FFA), leptin, or tumor necrosis factor-alpha (TNF-α), which are released from adipose tissue, are known to indirectly influence glucose regulation. Moreover, it is possible that undiscovered molecules originating from adipose tissue also exert an influence on systemic metabolism (Greenberg & Obin, 2006). Resistance to the hormones leads to hyperglycemia and hyperlipidemia, while a lack of insulin results in protein-wasting, ketoacidosis, and eventually death (Saltiel & Kahn, 2001). The link between insulin resistance and significant cardiometabolic anomalies, including metabolic syndrome, type 2 diabetes, and cardiovascular disease (CVD), has been firmly established (Bloomgarden, 2007).

### 1.2.2 Effect of Obesity on Lipid Metabolism

Obesity is linked to heightened basal lipolysis within adipose tissue and an increase in circulating free fatty acids (FFAs) (Welle S et al., 1994). Serum amyloid A (SAA), an acute phase protein and adipokine with lipolytic properties in humans has been associated with the stimulation of basal lipolysis. This lipolytic activity is hypothesized to function as an autocrine feedback mechanism, potentially contributing to insulin resistance as enlarged adipocytes produce more SAA, which subsequently enters the bloodstream. SAA mediates its effects through the CLA-1 receptor and the extracellular signal-regulated kinase signaling pathway, directly promoting lipolysis (Jejeebhoy et al., 1976). Alternatively, the increased lipolysis induced by SAA may be mediated through the activation of lipolytic cytokines such as IL-6 and TNF-α (Van Lenten et al., 1995).

In addition, SAA has a direct influence on cholesterol metabolism as it inherently functions as an apolipoprotein, specifically associated with high-density lipoprotein (HDL) (Van Lenten et al., 1995). The interaction between SAA and HDL has been studied for its effects on inflammation. Reduced circulating HDL levels correlate positively with the severity of the

uncontrolled inflammatory response in diseases such as sepsis, ischemia-reperfusion injury, and hemorrhagic shock (Wu et al., 2004). The elevation of SAA caused by excess adipose tissue in obesity might serve as a crucial link between obesity, reduced HDL levels, and an increased risk of diseases such as coronary artery disease, atherosclerosis, and inflammation.

Another significant metabolic alteration observed in obesity pertains to plasma triglyceride concentrations. It together with tissue resistance to insulin-mediated glucose uptake, which can lead to an accelerated production rate of very low-density lipoprotein (VLDL), has been shown to lead to endogenous hypertriglyceridemia (Barter & Nestel, 1973; Kissebah et al., 1976; Lewis et al., 1993; G. M. Reaven et al., 1967). Within the context of obesity, there is a decrease in lipoprotein lipase-mediated chylomicron-TG hydrolysis and ineffective inhibition of hormone-sensitive lipase-mediated lipolysis in adipose tissue (Lewis et al., 1993). Obesity is also characterized by postprandial lipemia and elevated plasma-free fatty acid and triglyceride levels. The presence of excess fatty acids during the early postprandial period, when insulin typically suppresses them, can significantly impact glucose uptake, potentially reducing it by as much as 50% (C-W Yu & Cooper, 2001).

### 1.2.3 Role of Different Fat Deposits in Metabolism

Several studies have shown that excess fat in the upper part of the body correlates more with increased mortality and risk for disorders than with lower-body fat deposits. These disorders include diabetes, hyperlipidemia, hypertension, and atherosclerosis of coronary, cerebral, and peripheral vessels (Chow et al., 2007; Ohlson et al., 1985). Abdominal fat comprises abdominal subcutaneous fat and intra-abdominal fat, consisting of visceral and intraperitoneal fat. Visceral fat is linked to disruptions in insulin-glucose regulation and alterations in plasma lipoprotein-lipid levels, notably characterized by elevated plasma triglycerides and reduced concentrations of HDL cholesterol (Jensen, 2008). These changes in the lipid profile could be ascribed to the connection between insulin resistance and disturbances in the transport of plasma lipids, as well as variations in the levels of lipoproteins. (Laakso et al., 1990). Free fatty acids (FFAs) are released more swiftly from visceral fat cells compared to subcutaneous ones, largely due to the heightened lipolytic activity within visceral adipocytes. This discrepancy could be attributed to the amplified presence and operation of β-adrenoreceptors, alongside a diminished affinity of insulin receptors and signal transduction in visceral adipocytes. Consequently, this variance leads to fluctuations in the function of hormones that regulate lipolysis, such as catecholamines and insulin (Laakso et al., 1990).

## *1.3 Physical Activity*

Physical activity is defined by The Physical Activity Guidelines Advisory Committee (2018) as "bodily movement produced by skeletal muscles that results in energy expenditure". Exercise on the other hand is defined as physical activity that is planned, repetitive, structured, and has an aim to improve the fitness, performance, or health of an individual. It is recommended that to avoid any misunderstandings descriptive words such as sedentary behavior, vigorous, moderate, moderate-vigorous, etc. should be used to describe different intensities of physical activity and exercise (Physical Activity Guidelines Advisory Committee, 2018). Moderate intensity refers to 64 % - 76 % of maximal heart rate (46 % - 63 % $VO_{2max}$) and vigorous intensity refers to 77 % - 95 % maximal heart rate (64 % - 90 % $VO_{2max}$) (Garber et al., 2011).

Lack of physical activity has been identified as a primary factor contributing to overweight and obesity (Booth et al., 2012). Certain interventions promoting healthy physical activity habits among overweight individuals have shown positive outcomes. However, there are also inconsistent results regarding the expected outcomes of these interventions (Bonomi & Westerterp, 2012).

Carbohydrates, specifically glucose, and lipids are key substrates during exercise. While amino acids are involved in energy provision during exercise, their overall contribution to fueling working muscles is typically limited under normal circumstances (Lemon & Nagle, 1981). The metabolism of substrates during exercise is influenced by the exercise's intensity, duration, and the individual's training status. As exercise intensity escalates, the importance of muscle and liver glycogen for energy provision rises, while the relative contribution of plasma free fatty acids decreases (Romijn et al., 1993).

### 1.3.1 Effects of Physical Activity on Glucose Metabolism

During extended exercise sessions lasting beyond 60 minutes, the depletion of muscle glycogen stores occurs. As a result, there is a necessity for an increased contribution of plasma substrates to the overall energy expenditure to sustain power output. Despite this, plasma glucose concentration remains relatively stable during moderate-duration exercise. This stability is maintained as hepatic glucose output increases in proportion to the heightened muscle glucose uptake, ensuring a consistent supply of glucose to the bloodstream. (Romijn et al., 1993.)

Apart from skeletal muscle, insulin-stimulated glucose uptake is observed in adipose tissue and the liver. Nonetheless, adipose tissue plays a minor role in post-exercise glucose uptake, contributing only 1-2% of glucose clearance after an intravenous glucose load in normal individuals and approximately 3-4% in obese subjects (Marin et al., 1987). Trained individuals exhibit higher insulin sensitivity compared to untrained counterparts (Hardin et al., 1995; King et al., 1987; Li & Mcneil1, 1997). Yet, recent research suggests that exercise's impact on insulin action might arise from acute responses to exercise sessions rather than long-term adaptations (Ryan et al., 2020).

### 1.3.2 Effects of Physical Activity on Lipid Metabolism

Studies suggest that physical activity lowers plasma LDL concentrations and triglycerides while increasing HDL levels in healthy and obese individuals (Doewes et al., 2022). Different exercise interventions, ranging from short-term and long-term training to high-intensity interval training (HIIT) and moderate-intensity interval training (MIIT), have shown positive impacts on lipid profiles (Sabaka et al., 2015). However, it has been observed that longer durations of physical activity and higher intensity exercises tend to result in more pronounced improvements in lipid profile (Kannan et al., 2014; Ribeiro et al., 2015).

Right after starting to exercise, there's a brief drop in free fatty acid (FFA) concentration due to an increase in the muscle’s uptake. The initial discrepancy between FFA mobilization and uptake undergoes gradual correction through the stimulation of lipolysis, and as exercise continues for an extended period, notably increased FFA concentrations become apparent. The extent of fat oxidation during exercise is primarily influenced by exercise intensity rather than duration, given that human lipid stores are theoretically adequate for several days of exercise. Absolute rates of fat oxidation start to decline at exercise intensities exceeding approximately 70% of V̇O2max, coinciding with a rapid decrease in turnover and plasma levels of free fatty acids (FFA). (Romijn et al., 1993.)

### 1.3.3 Effects of Physical Activity on Low-Grade Inflammation

The concept of skeletal muscle functioning as a "secretory organ" through cytokine production in response to contraction has garnered increasing attention (Keller et al., 2001; Schnyder & Handschin, 2015). Myocytes contribute to this process by releasing a diverse array of cytokines, collectively known as "myokines," which include interleukin-6 (IL-6), IL-7, IL-15, and myostatin (Coletti et al., 2019; Schnyder & Handschin, 2015). Operationally, myokines predominantly engage in autocrine and paracrine signaling pathways within the skeletal muscle

microenvironment. Nevertheless, a noteworthy subset demonstrates endocrine characteristics, participating in inter-tissue communication (Schnyder & Handschin, 2015). This refined perspective underscores the intricate regulatory role of myokines, influencing not only local skeletal muscle processes but also orchestrating systemic responses through interactions with various tissue types.

A suggested mechanism for the observed changes in cytokines is that regular exercise results in a decrease in body fat. Accumulation of fat mass especially in the visceral area triggers the activation of innate immunity, initiating a local response to cellular damage characterized by heightened blood flow, immune cell infiltration (particularly macrophages), and the production of inflammatory mediators to facilitate tissue repair and neutralization any toxic agents generated (Poburski et al., 2016). Adipocytes contribute significantly to the production of pro-inflammatory cytokines, such as TNF-α, CRP, and IL-6. (Hotamisligil, 2006; Laaksonen et al., 2004). The continual presence of these pro-inflammatory cytokines in the circulation leads to low-grade systemic inflammation, contributing to an inflammatory cascade that adversely affects various tissues and heightens the risk of developing non-communicable diseases (Booth et al., 2012; Klein et al., 2004; Pedersen, 2011; Tikkanen et al., 2018).

On the flip side, regular exercise has been shown to increase the circulating concentration of anti-inflammatory cytokines such as interleukin-6 (IL-6) or interleukin-10 (IL-10), which play a pivotal role in propagating these anti-inflammatory signals, effectively hindering the onset of low-grade systemic inflammation (Docherty et al., 2022; Ouyang et al., 2011; Pedersen, 2009, 2011; Tanaka et al., 2014).

The link between exercise, low-grade inflammation, and obesity is however still not fully clear. This anti-inflammatory effect has been demonstrated to occur due to chronic exercise even without changes in weight or body composition. This suggests that there are likely other mechanisms in play, possibly involving direct anti-inflammatory effects on immune cells (Laaksonen et al., 2004; Nicklas et al., 2008). This is thought to be achieved by diminishing the expression of Toll-like receptors (TLR2 and TLR4) in immune cells, mitigating the activity of M1 macrophages and CD8+ T-cells, reducing macrophage infiltration in adipose tissue, and enhancing the blood and nutrient supply to fat mass (Frisbee et al., 2006; Kawanishi et al., 2013). On the other hand, systematic reviews indicate that exercise-induced modifications in inflammation markers, such as CRP, are more significant when accompanied by BMI reduction (Fedewa et al., 2017). However, endurance, resistance, and high-intensity interval training have

also been found to reduce pro-inflammatory cytokines and stimulate anti-inflammatory cytokines, independent of fat mass loss (Gonzalo-Encabo et al., 2021).

Shortly after the onset of exercise, there is typically a slight decrease in free fatty acid (FFA) concentration due to increased muscle uptake. This initial mismatch between FFA uptake and mobilization is gradually corrected by the stimulation of lipolysis. With prolonged exercise, significantly elevated FFA concentrations become evident. The extent of fat oxidation during exercise is primarily influenced by exercise intensity rather than duration, given that human lipid stores are theoretically adequate for several days of exercise. Absolute rates of fat oxidation start to decline at exercise intensities exceeding approximately 70% of V̇O2max, coinciding with a rapid decrease in turnover and plasma levels of free fatty acids (FFA). (Romijn et al., 1993.)

### 1.3.4 Effects of Physical Activity on Fitness

Chronic training results in an increase in maximal exercise capacity. Maximal exercise capacity is influenced by various factors, including the ability to transport oxygen maximally to the muscle mitochondria and utilize this oxygen for ATP generation (VO2peak) (Wagner, 2011). A sedentary lifestyle and overall lack of physical activity result in a lower $VO_{2peak}$. Individuals who engage in a greater amount of moderate- and vigorous-intensity physical activity display higher $VO_{2peak}$ levels. The duration of physical activity performed at light, moderate, and vigorous intensities, in addition to age and sex, accounts for 67% of the variation in $VO_{2peak}$ values (ml/kg/min) (Wagner et al., 2021). The transport pathway for $VO_{2peak}$ involves four essential steps (ventilation, alveolar/capillary diffusion, circulation, and muscle diffusion), with each step collectively influencing the overall capacity without any single step acting as the exclusive limiting factor. Alterations in any of these steps can impact the functioning of others, illustrating their interconnected nature and mutual influence. (Wagner, 2022.)

In unfit individuals with low peak VO2 values, metabolic limits appear to be the primary factor, as providing additional oxygen does not enhance VO2, and moderately reducing the fraction of inspired oxygen (FIO2) does not diminish $VO_{2peak}$. On the other hand, in fit subjects, oxygen transport limits play a more significant role, as extra oxygen supplementation does not lead to improvements in VO2. In such cases, all components of the oxygen transport pathway work together to restrict $VO_{2peak}$ in an integrated manner. (Wagner, 2011.)

Cells retain a limited amount of ATP close to the contractile proteins. The utilization of this ATP is independent of oxygen supply, making the energy promptly available as needed by the muscle. To sustain exercise beyond a few seconds, cells must synthesize ATP through one of two metabolic pathways: anaerobic (glycolytic) or aerobic (oxidative) (Rivera-Brown & Frontera, 2012). Chronic inactivity can result in a decrease in VO2max and impaired exercise performance by hindering one or more of the mechanisms related to either oxygen transport (stroke volume and/or heart rate) or oxygen utilization in cells (CaO2 or CVO2) (Ledhill et al., 1994).

Current exercise guidelines advise adults to engage in 150 to 300 minutes of moderate-intensity aerobic physical activity, 75 to 150 minutes of vigorous-intensity, or an equivalent combination of both every week (Piercy et al., 2018). Adults with chronic conditions or disabilities should follow the guidelines to the best of their abilities. The recommendations stress that increasing physical activity and reducing sedentary behavior will be advantageous for almost everyone (Piercy et al., 2018).

## *1.4 Aims of the Study*

This thesis is a part of the Motivation Makes the Move! (MoMaMo!) study. MoMaMo! aims to decrease sedentary lifestyles by creating and validating enduring and personalized IT- and mHealth-supported strategies for behavior change, along with identifying best practices for engaging citizens in health, well-being, and disease prevention. It focuses especially on physically inactive overweight individuals who are at risk for chronic diseases and complications due to their current habits. Despite their awareness of unhealthy lifestyles and perceived susceptibility to disease, overweight individuals are less likely to pick up new habits, and very little is known about how to best go about changing sedentary behavior in adults. This thesis aims to see what type of effects the three different exercise programs had on markers of low-grade inflammation, glucose, and lipids in obese subjects.

Specified study questions and hypotheses are:

1. Is a three-month exercise intervention effective in reducing low-grade inflammation markers? Are personalized and highly personalized exercise interventions (Groups 2 and 3) more effective at this than general guidelines (Group 1)?

*Hypothesis*: A three-month exercise intervention reduces low-grade inflammation markers in all groups, and the most significant change will be seen with highly personalized exercise interventions.

2. Is a three-month exercise intervention effective in improving lipid and glucose profiles? Are personalized and highly personalized exercise interventions (Groups 2 and 3) more effective at this than general guidelines (Group 1)?

*Hypothesis*: A three-month exercise intervention improves the lipid and glucose profiles of all groups, and the most significant change will be seen with highly personalized exercise interventions.

3. Do the changes in low-grade inflammation markers and glucose and lipid profiles occur simultaneously?

*Hypothesis*: Low-grade inflammation markers and glucose and lipid profiles will improve simultaneously due to having similar reactions to similar stimulants; however, the changes in the values are independent of each other.

4. Does a positive change in low-grade inflammation markers and glucose and lipid profiles require an improvement in anthropometry, fitness, or both?

*Hypothesis*: Positive change will require a change in both body composition and fitness.

# 2 MATERIALS AND METHODS

## *2.1 Test Subjects, Eligibility Criteria, and Interventions*

The voluntary test subjects were obese individuals (ages 18-40) with a BMI of over 27.5 and they had been given a referral from a physician to consult a lifestyle clinic due to physical inactivity and obesity. The subjects were recruited from the Helsinki metropolitan area through the local occupational health clinics and the local University of Applied Sciences. A total of 89 people were included in the study (n=89) and of those 34 (38%) were male and 55 (62%) were female. The data was collected between 2016 and 2019.

56 volunteers (n=56) were excluded from the study. Exclusion criteria included for example neurological or psychiatric disorders, any medical treatment influencing glucose homeostasis (excluding insulin) or autonomic nervous system function such as regular β-blockers or SSRIs, pregnancy, physical disability, substance abuse, smoking, severe anemia, and significant co-operation difficulties. A total of 56 participants took part in the postintervention measurements, 14 from Group 1, 22 from Group 2, and 20 from Group 3 (Figure 1).

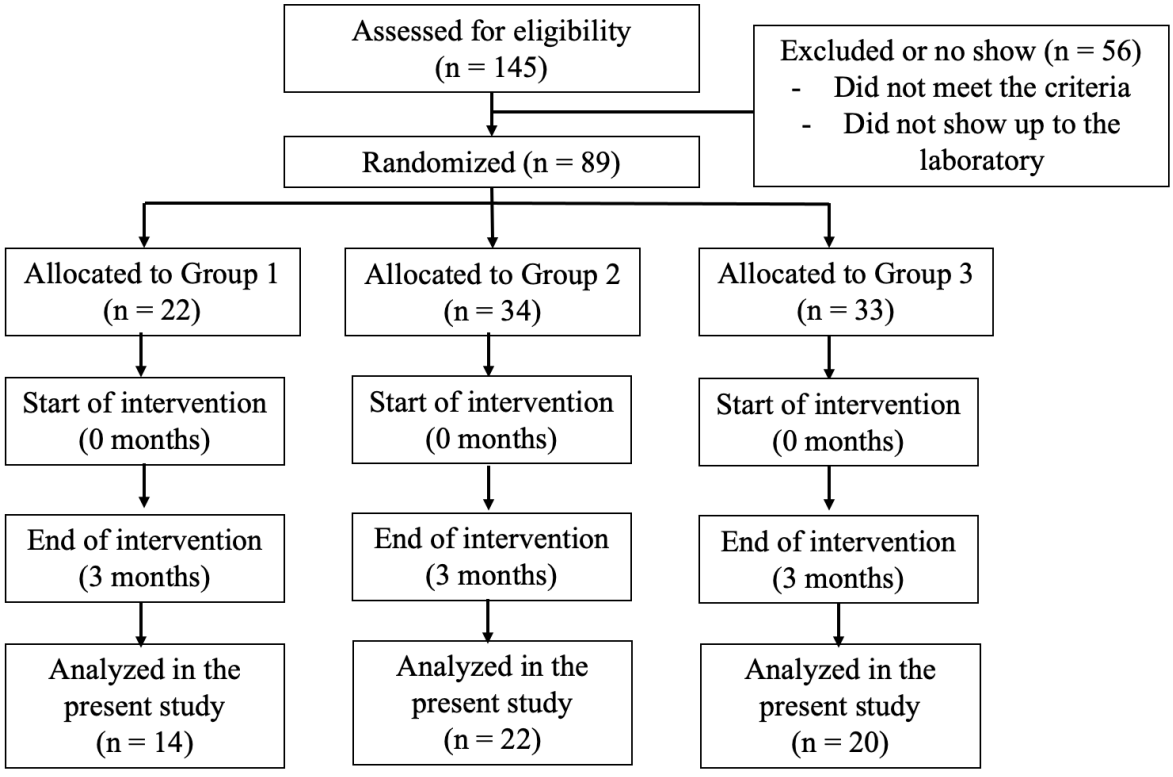


Figure 1. Flow diagram of enrollment, intervention length, and participant flow. Total number of samples analyzed in the study is 56 (n = 56).

The test subjects were assigned randomly to three groups using a random allocation sequence generated by the Principal Investigator (PI) of the study. The research nurses responsible for scheduling laboratory visit times performed the random allocation by conducting a blind draw of a piece of paper containing a number, either 1, 2, or 2b, for each participant. Number 1 corresponded with Group 1, number 2 corresponded with Group 2, and number 2b corresponded with Group 3. The difference between the groups was the individualization level of the training interventions. This intervention presents a dose-response setting (Table 1).

Group 1, the general guidelines group's subjects (n=14) received general guidelines based on recommendations for a healthy diet and physical activity and did not receive individually tailored programs.

Group 2, the individualized intervention group, (n = 22) subjects received support from a multi-professional team and wellness technology. The multi-professional team worked alongside the subject to tailor the intervention based on their expertise in physical exercise, nutrition, and utilizing music to enhance exercise and relaxation. They created a multimedia guide for Group 2 and Group 3, which offered peer support and encouraged participants to stay committed to the intervention. In Group 2, the exercise intervention was individualized by taking into account the participant's clinical status, personal goals, preferences, and estimated $VO_{2peak}$.

Group 3, consisting of 20 participants, underwent a highly personalized intervention, taking into account their clinical status, individual goals, preferences, and measured exercise capacity, including VO2peak and ventilatory thresholds. This involved determining optimal intensity zones and volumes tailored to each individual for exercise training. Similar to Group 2, a multidisciplinary team, well-versed in physical exercise, nutrition, and the integration of music for enhanced exercise and relaxation, oversaw the intervention. The utilization of mobile and cloud technologies further enhanced the intervention by collecting subjective feedback, emotional responses, exercise and recovery data, and nutritional information throughout the intervention period. Additionally, those willing to participate in semi-supervised strength training were provided sessions at Unisport.

In contrast to Group 2, the exercise training in Group 3 was refined by incorporating individual heart rate and intensity training zones, determined through ventilatory thresholds in CPET—the timing of measurements and follow-ups aligned with Group 2.

Participants in both Groups 2 and 3 were instructed to utilize specific smartphone apps to plan and monitor their physical activity, exercise routines, and health habits. The Sports Tracker app (Amer Sports Digital Services Oy, Vantaa, Finland) in combination with a Suunto heart rate belt (Suunto Oy, Vantaa, Finland) guided and logged exercise sessions. For tracking daily steps, subjects used the Argus app UAzumio Inc. Redwood City, CA, USA) or similar alternatives. Weight measurement was facilitated by the Weight Diary app (CurlyBrace Apps Ltd, UK) or its equivalents. The study's website provided additional training instructions and support.

Table 1: Interventions of each Group.

| Group | Intervention | Information used for training program |
|---|---|---|
| Group 1 | General Guidelines | General guidelines based on UKK Institutions recommendations for healthy diet and physical activity |
| Group 2 | Individualized | Clinical status, personal goals, preferences and estimated VO2peak |
| Group 3 | Highly Individualized | Clinical status, personal goals, preferences, measured exercise capacity, VO2peak and ventilatory thresholds were used to determine optimal intensity zones and volumes |

## *2.2 Measurements*

All groups went through the same basic measurements before the beginning of the intervention. On their first visit, the participant's height, weight, and body composition were assessed. They filled out self-report questionnaires on physical activity, work productivity, and activity impairment. During the second visit, a thorough medical examination was conducted by a physician for each subject to assess their suitability for exercise testing and training. Subsequently, a step-incremental cardiopulmonary exercise test was performed on a cycle ergometer (Monark Ergomedic 839 E, Monark Exercise AB) until voluntary fatigue. This test involved gathering various data, including measurements of pulmonary ventilation (Triple V, Jaeger Mijnhardt), alveolar gas exchange (Oxycon Pro), electrocardiography (ECG; PowerLab, AD Instruments), and the assessment of perceived exertion (RPE) ratio. 76 subjects of the

original 89 completed this test. On the third visit, blood tests were conducted, and the subjects received concise feedback on their results and measured health outcomes. These measurements including the step-incremental cardiopulmonary exercise test were repeated 3 months into the intervention when 51 of the 76 subjects participated.

In addition to the initial visit, Group 2 underwent a submaximal step-incremental cycle ergometer test with ECG and RPE recordings. After completing all measurements, personalized feedback meetings were organized for participants in Groups 2 and 3. During these sessions, individuals in both groups received tailored advice on adopting healthy lifestyle habits and were presented with an exercise plan customized based on their specific results and preferences.

For Group 2, the exercise plan was crafted using data from the submaximal cycle ergometer test. This involved utilizing estimations of maximal oxygen consumption ($VO_{2\ max}$), work-rate-specific heart rate, and ratings of perceived exertion (RPE) to personalize the exercise volume and intensity. On the other hand, Group 3's exercise prescription was developed using measurements of $VO_{2max}$, ventilatory thresholds, heart rate response, and RPE obtained during a maximal cycle ergometer test.

The decision to employ a simpler exercise test for Group 2 aimed to assess its effectiveness in comparison to the more comprehensive cardiopulmonary exercise test administered to Group 3. Meanwhile, Group 1 received general guidelines for maintaining a healthy diet and engaging in physical activity (Garber et al., 2011; Piercy et al., 2018).

### 2.2.1 Sera Samples

The sera samples were processed by Piia Karisola at the University of Helsinki. The frozen serum samples were thawed, and the possible precipitates were centrifuged down at 10 000 x g at +4 °C for 10 min. The clear supernatants were then transferred to new 1.5 ml tubes and the samples were diluted 1:4 into the Bio-Plex sample diluent (Bio-Rad, CA, USA). Then 50 µl of the dilution was pipetted onto the plate.

The soluble inflammatory markers including IL-1b, IL-6, IL-8, IL-10, IL-15, IL-17A, and TNFα were measured by Bio-Plex Pro Assays (Bio-Rad, CA, USA) in Luminex (Bio-Plex 200, Bio-Rad, CA, USA) system according to the manufacturer's instructions. The observed target concentrations were calculated with the help of 8 standards. The concentration ranges for the targets were 0.07-1114.25 mg/ml for IL-1 b, 0.1-1639.25 mg/ml for IL-6, 0.24-3905.75 mg/ml for IL-8, 0.34-5571 mg/ml for IL-10, 3.18-52091 mg/ml for IL-15, 0.71-11708.5 mg/ml for IL-

17A and 0.79-12963 mg/ml for TNFα. In addition to these standards, three internal standards were used to confirm the quality between different plates.

Fasting serum glucose and fasting plasma insulin, HDL and LDL cholesterol, and triglycerides were obtained from the antecubital vein and analyzed in the local accredited laboratory (HUSLAB, Helsinki). From these values, HOMA-ir was calculated. The Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) is a model for estimating insulin sensitivity. It predicts β-cell response and insulin resistance from fasting insulin and fasting glucose (Antuna-Puente et al., 2011).

HOMA-IR was calculated by using the following equation:

$$\text{HOMA} = \{[\text{fasting insulin (U/mL)}] \times [\text{fasting glucose (mmol/L)}]\} / 22.5.$$

The denominator 22.5 reflects normalization, based on normal fasting values as the result of the product of 5 U/mL insulin levels and 4.5 mmol/L glucose levels.

### 2.2.2 Body Composition Measurements

Body composition was assessed using an InBody720 device (Biospace Co., Ltd., Seoul, South Korea), which utilizes the bioimpedance method to evaluate body composition. These measurements were taken during the participants' initial visit. For this study, relevant variables such as body mass index (kg/m²) (BMI), fat percentage (BF%), and visceral fat cross-section (cm²) were selected for analysis.

BMI was calculated with the following equation:

$$\text{Weight [kg]} / \text{Height m}^2$$

Body Fat Percentage (BF%) was calculated by the following equation:

$$\text{Fat Mass [kg]} / \text{Weight [kg]} \times 100$$

Fat-Free Mass (FFM) was calculated with the following equation:

$$\text{Weight [kg]} \times (1 - (\text{Body Fat Percentage [\%]} / 100)$$

### *2.2.3* Physical Fitness and Maximal Oxygen Consumption

The subjects' physical performance and maximal oxygen uptake were measured using a step-up bicycle ergometer test (cardiopulmonary exercise test, CPET). In the test, subjects cycled

(Monark Ergomedic 839E; Monark Exercise AB, Vansbro, Sweden) until exhaustion. During the test, the body's responses were measured during five minutes of sitting at rest, five minutes of exercise pedaling (0 W), step-by-step exercise every three minutes (load stairs 30 W for women and 40 W for men), and five minutes of sitting recovery. Physical performance was determined based on the maximum work output achieved (W, W/kg).

A clinical cardiopulmonary exercise stress test (CPET) employs a step incremental protocol on a cycle ergometer until voluntary fatigue, serving as a method to monitor exercise responses and assess the determinants of cardiorespiratory fitness. The cycle ergometer is safer, and more appropriate for obese subjects. It also enables the simultaneous monitoring of other parameters such as ECG and RPE (Glaab & Taube, 2022).

*$VO_{2max}$*

A respiratory gas analyzer (Oxycon Pro; CareFusion Corp., Höchberg, Germany) was used to measure ventilated and alveolar gas exchange during the above-mentioned bicycle ergometer test. Maximal oxygen uptake capacity ($VO_{2max}$) was calculated for each subject in liters per minute (L/min), milliliters per kilogram of body weight (ml/kg/min), and milliliters per fat-free body weight (ml/kg·FFM/min). $VO_{2max}$ relative to fat-free body mass considers body composition by excluding the mass of passive adipose tissue in exercise performance in the division calculation: the traditional maximum oxygen uptake capacity calculated with total body weight alone may underestimate the performance of overweight people (Rissanen et al., 2016).

$VO_{2max}$ was calculated with cardiac output (CO) or in other words the amount of blood pumped per minute and the arterial veinous oxygen difference ((a-v) O2diff) using the Fick's equation:

$$VO_{2max}\ [L/min] = CO \times (a\text{-}v)\ O2_{diff}$$

An increase in cardiac output (CO) is however not the only factor of maximal oxygen consumption. For example, both perfusive and diffusive conductances are necessary to calculate a given muscle's O2 uptake. Wagner combined the Fick's principle and Fick's law in a diagram that recognizes the infinite diffusing capacity of the skeletal muscle. This can be better used to determine limitations (Wagner, 2022). Overall, Wagner's diagram provides a visual representation of how the components of Fick's equation interact to determine cardiac output and oxygen delivery to the tissues.

The $VO_{2max}$ relative to fat-free mass (FFM) was calculated by using the following equation:

$$VO_{2max}\ (FFM)\ [mL/kg/min] = VO_{2max}\ [L/min] * 1000 / FFM\ [kg]$$

*Ventilatory Thresholds*

Ventilatory thresholds were determined according to Beaver et al. 1986 and the names ventilatory threshold 1 (VT1) and ventilatory threshold 2 (VT2) were used (Beaver et al., 1986).

## *2.3 Data Analysis*

The aim was to examine if the three different types of exercise programs had different effects on the response variables. The response variables were the test subjects' weight, fat-free mass, muscle mass, interleukins, TNF-α, CRP, lipid- and glucose profiles, BMI, and $VO_{2max}$. The explanatory values were the exercise program, and the time of the measurements (0mo, 3mo, 6mo, 12mo). When available, caloric intake was also used as an explanatory variable.

The data analysis was conducted with the SSPS software (version 29.00). Descriptive statistics were performed to summarize the baseline characteristics of the participants and are presented as means and standard deviations.

The relative changes in values with all the participants were analyzed according to the intervention time (3 months) with a paired samples t-test. Repeated measures general linear model with group and time interaction was used to examine the differences in changes between groups.

To measure if two variables covary linearly, bivariate correlation analysis was done to the delta changes calculated from the 0- and 3-month measurements of the variables. Results were presented as Pearson's correlation coefficients and their two-tailed significances.

For all analyses, the statistical significance was set at $p<0.05$ (two-tailed), meaning that any value below this number was considered significant.

# 3 RESULTS

## *3.1 Baseline Characteristics*

The baseline characteristics at 0 months of all groups and participants are presented in Tables 2-5. The average of all the participants' BMI is 33.8. The average of Body Fat % is 39.3% and the average of Visceral Fat area is over 140 $cm^2$ for all patients. Group 3 had the highest baseline values in all body composition characteristics (Table 2), and Group 1 had the highest inflammation marker levels (Table 5).

Table 2: Baseline body composition characteristics of all participants.

| | Group | | | |
|---|---|---|---|---|
| Variable | 1 | 2 | 3 | All |
| Weight (kg) | 99.8 ± 11.4 | 92.4 ± 15.0 | 109.0 ± 18.2 | 99.7 ± 16.9 |
| Fat Free Mass (kg) | 61.3 ± 8.7 | 56.8 ± 12.2 | 64.1 ± 11.8 | 60.3 ± 11.6 |
| Fat % | 38.4 ± 6.8 | 38.6 ± 8.1 | 40.7 ± 9.3 | 39.3 ± 8.2 |
| Visceral Fat ($cm^2$) | 154.8 ± 31.2 | 140.8 ± 36.1 | 179.6 ± 51.6 | 157.2 ± 44.1 |
| BMI ($kg/m^2$) | 34.4 ± 5.4 | 32.2 ± 3.6 | 35.8 ± 6.6 | 33.8 ± 5.0 |

Data are presented as mean ± standard deviation (SD). Group 1: General guidelines, Group 2: Individualized intervention, Group 3: Highly individualized intervention, BMI: body mass index.

Table 3: Baseline fitness characteristics of all participants.

| | Group | | | |
|---|---|---|---|---|
| | 1 | 2 | 3 | All |
| $VO_{2max}$ (L/min) | 2.83 ± 0.79 | 2.53 ± 0.63 | 2.70 ± 0.54 | 2.67 ± 0.64 |
| $VO_{2max}$ (ml/kg/min) | 27.4 ± 6.7 | 28.6 ± 5.5 | 24.9 ± 5.9 | 26.8 ± 6.1 |
| $VO_{2max}$ (ml/FFM/min) | 45.5 ± 7.9 | 46.1 ± 6.2 | 42.1 ± 4.0 | 44.5 ± 6.2 |
| VT1 | 1.5 ± 0.4 | 1.4 ± 0.4 | 1.5 ± 0.3 | 1.43 ± 0.35 |
| VT1 (ml/FFM/min) | 24.1 ± 4.1 | 25.0 ± 4.7 | 22.7 ± 3.4 | 23.9 ± 4.2 |
| VT2 | 2.3 ± 0.6 | 2.1 ± 0.5 | 2.2 ± 0.5 | 2.2 ± 0.5 |
| VT2 (ml/FFM/min) | 36.9 ± 5.3 | 38.0 ± 5.2 | 34.7 ± 4.3 | 36.5 ± 5.1 |
| Power | 189 ± 52 | 173 ± 46 | 184 ± 32 | 181 ± 43 |
| Power at VT1 | 81 ± 29 | 72 ± 24 | 75 ± 25 | 76 ± 26 |
| Power at VT2 | 145 ± 34 | 134 ± 34 | 142 ± 32 | 139 ± 34 |

Data are presented as mean ± standard deviation (SD). Group 1: General guidelines, Group 2: Individualized intervention, Group 3: Highly individualized intervention.

Table 4: Baseline glucose and lipid profiles of all participants.

| | Group | | | |
|---|---|---|---|---|
| | 1 | 2 | 3 | All |
| Glucose (mmol/L) | 5.8 ± 0.6 | 5.3 ± 0.5 | 6.0 ± 1.2 | 5.6 ± 0.9 |
| Insulin (mmol/L) | 11.5 ± 4.5 | 11.3 ± 5.9 | 16.9 ± 9.9 | 13.4 ± 7.8 |
| HOMA-ir (mmol/L) | 3.0 ± 1.2 | 2.7 ± 1.3 | 4.2 ± 2.7 | 3.3 ± 2.1 |
| Cholesterol (mmol/L) | 4.7 ± 0.7 | 4.7 ± 0.9 | 4.8 ± 0.8 | 4.7 ± 0.8 |
| HDL (mmol/L) | 1.2 ± 0.2 | 1.3 ± 0.3 | 1.2 ± 0.4 | 1.3 ± 0.3 |
| LDL (mmol/L) | 3.1 ± 0.5 | 2.9 ± 0.9 | 3.0 ± 0.7 | 2.8 ± 0.8 |
| Triglycerides (mmol/L) | 1.2 ± 0.8 | 1.4 ± 0.6 | 1.6 ± 0.7 | 1.4 ± 0.7 |

Data are presented as mean ± standard deviation (SD). Group 1: General guidelines, Group 2: Individualized intervention, Group 3: Highly individualized intervention, HOMA-ir: Homeostatic Model Assessment for Insulin Resistance, HDL: High-density lipoprotein, LDL: Low-density lipoprotein.

Table 5. Baseline inflammation markers of all participants.

| | Group | | | |
|---|---|---|---|---|
| | 1 | 2 | 3 | All |
| IL-1b | 0.0 ± 0.0 | 0.0 ± 0.2 | 0.0 ± 0.0 | 0.0 ± 0.0 |
| IL-6 | 1.0 ± 1.0 | 0.5 ± 0.5 | 0.5 ± 0.5 | 0.6 ± 0.6 |
| IL-8 | 2.9 ± 1.3 | 2.3 ± 0.9 | 2.4 ± 1.3 | 2.5 ± 1.1 |
| IL-10 | 11.8 ± 42.3 | 0.1 ± 0.2 | 0.1 ± 0.4 | 2.7 ± 19.9 |
| IL-15 | 1.8 ± 6.6 | 1.7 ± 7.2 | N/D | 1.1 ± 5.7 |
| IL-17A | 0.1 ± 0.3 | 0.1 ± 0.2 | 0.1 ± 0.1 | 0.1 ± 0.2 |
| TNF-α | 8.4 ± 2.8 | 5.0 ± 3.0 | 4.1 ± 2.4 | 5.4 ± 3.2 |
| CRP | 6.7 ± 7.2 | 4.3 ± 5.2 | 5.7 ± 10.0 | 5.3 ± 7.6 |

Data are presented as mean ± standard deviation (SD). Group 1: General guidelines, Group 2: Individualized intervention, Group 3: Highly individualized intervention, TNF-α: Tumor necrosis factor alpha, CRP: C-reactive protein, N/D: No Data.

## *3.2 Body Composition and Exercise Performance*

### 3.2.1 Anthropometric Variables

The anthropometric changes of all participants combined are presented in Table 6. Statistically significant negative changes were observed in Weight (-1.0, $p<0.05$), Body Fat Percentage (-0.8, $p<0.01$), Visceral Fat (-4.7, $p<0.01$), and BMI (-0.9, $p<0.05$) There was no significant change in Fat Free Mass.

Table 6: Anthropometric changes of all participants (0 vs. 3 months).

| | 0 months | 3 months | Change | Sig. |
|---|---|---|---|---|
| Weight (kg) | 99.7 ± 16.9 | 98.8 ± 16.7 | -1.0 | **0.025*** |
| Fat Free Mass (kg) | 60.3 ± 11.6 | 60.5 ± 11.5 | 0.2 | 0.446 |
| Fat % | 39.3 ± 8.2 | 38.4 ± 8.3 | -0.8 | **0.005**** |
| Visceral Fat ($cm^2$) | 157.2 ± 44.1 | 152.6 ± 34.0 | -4.7 | **0.005**** |
| BMI ($kg/m^2$) | 33.8 ± 5.0 | 33.5 ± 5.0 | -0.9 | **0.028*** |

Data are presented as mean ± standard deviation (SD). * $p < 0.05$, **$p < 0.01$: Statistical significance levels.

The anthropometric changes between different groups are presented in Table 7. Significant negative changes were only observed in Group 3 in the variables Weight ($p<0.05$), Body Fat Percentage ($p<0.05$), Visceral Fat ($p<0.05$), and BMI ($p<0.05$), but not in Fat Free Mass. No significant changes were observed in Group 1 and Group 2 (Table 7).

Table 7. Changes in anthropometry in Groups 1, 2, and 3 from 0 to 3 months and the differences between Groups.

| | Group 1 | Group 2 | Group 3 | 1 vs 2 | 2 vs 3 | 1 vs 3 |
|---|---|---|---|---|---|---|
| Outcome Variables | | | | Between Group Differences in Change from 0 to 3 months | | |
| Body Composition | | | | | | |
| Weight (kg) 0kk | 99.8 ± 11.4 | 92.4 ± 15.0 | 109.0 ± 18.2 | | | |
| Weight (kg) 3kk | 99.9 ± 12.5 | 91.7 ± 14.9 | 107.0 ± 18.0 | 0.456 | **0.007**** | 0.152 |
| *Within-group change (p-value)* | 0.958 | 0.125 | **0.041*** | 0.396 | 0.192 | 0.134 |
| Fat Free Mass (kg) 0kk | 61.3 ± 8.7 | 56.8 ± 12.2 | 64.1 ± 11.8 | | | |
| Fat Free Mass (kg) 3kk | 61.4 ± 8.6 | 57.2 ± 12.6 | 64.2 ± 2.4 | 0.481 | 0.492 | 0.841 |
| *Within-group change (p-value)* | 0.878 | 0.354 | 0.886 | 0.602 | 0.690 | 0.955 |
| Fat % 0kk | 38.4 ± 6.8 | 38.6 ± 8.1 | 40.7 ± 9.3 | | | |
| Fat % 3kk | 38.3 ± 7.1 | 37.8 ± 7.9 | 39.4 ± 9.7 | 0.165 | **0.003**** | 0.069 |
| *Within-group change (p-value)* | 0.760 | 0.067 | **0.030** | 0.336 | 0.380 | 0.136 |
| Visceral Fat ($cm^2$) 0kk | 154.8 ± 31.2 | 140.8 ± 36.1 | 179.6 ± 51.6 | | | |
| Visceral Fat ($cm^2$) 3kk | 1.45 | 137.8 ± 33.4 | 170.2 ± 52.9 | 0.342 | **0.001**** | **0.041*** |
| *Within-group change (p-value)* | 0.888 | 0.144 | **0.007**** | 0.481 | 0.077 | 0.062 |
| Body Mass Index ($kg/m^2$) 0kk | 34.4 ± 5.4 | 32.2 ± 3.6 | 35.8 ± 6.6 | | | |
| Body Mass Index ($kg/m^2$) 3kk | 34.4 ± 5.3 | 31.9 ± 3.6 | 35.1 ± 6.6 | 0.547 | **0.009**** | 0.178 |
| *Within-group change (p-value)* | 0.916 | 0.124 | **0.049*** | 0.348 | 0.261 | 0.138 |

Data are presented as mean ± standard deviation (SD). * $p < 0.05$, ** $p < 0.01$, *** $p<0.001$: Statistical significance levels.

The anthropometric changes from pre-trial (0 months) to post-trial (3 months) observed in all subjects are illustrated in Figure 3. Decreases were observed in Weight, BMI, Body Fat % (BF%), and Visceral Fat, and an increase was observed in Fat-Free Mass (FFM). The biggest relative changes were observed in Group 3 in all other variables except Fat-Free Mass, where Group 2 observed the largest relative change (Figure 3).

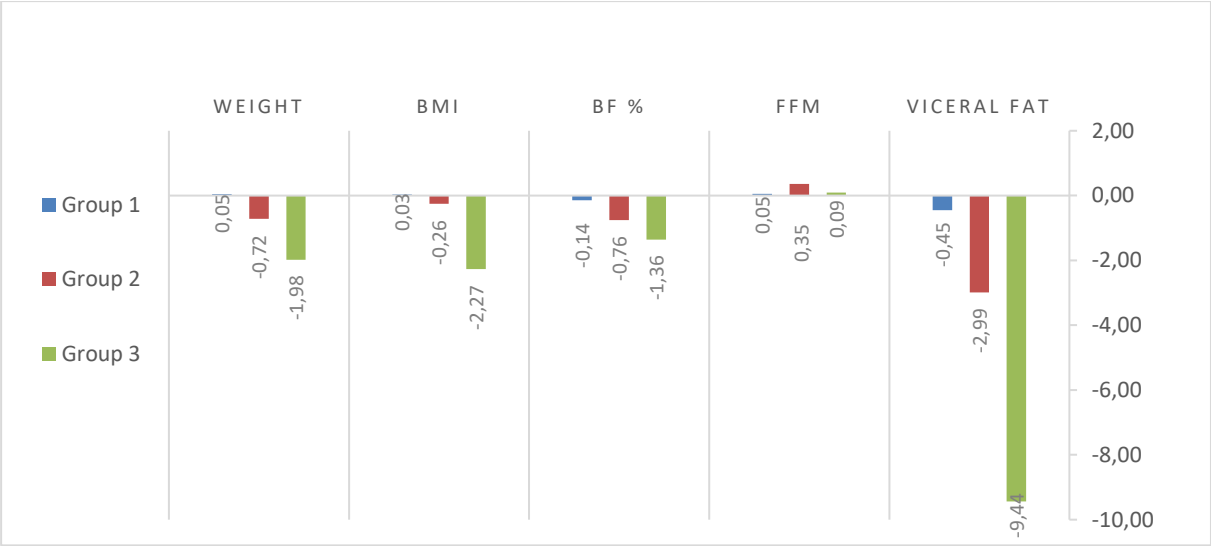


Figure 2: Relative changes from 0 to 3 months in anthropometry of Groups 1, 2, and 3.

### 3.2.2 Cardiorespiratory Fitness and Power

The changes in cardiorespiratory fitness and power output are shown in Table 8. Statistically significant positive changes ($p<0.05$) were observed in $VO_{2max}$ (L/min) ($p<0.05$), both VT1 parameters ($p<0.05$) and all power parameters ($p<0.001$) (Table 8).

Table 8: Changes in cardiorespiratory parameters and exercise performance of all participants (0 vs. 3 months).

| | 0 months | 3 months | Change | Sig |
|---|---|---|---|---|
| $VO_{2max}$ (L/min) | 2.67 ± 0.64 | 2.74 ± 0.68 | +0.07 | **0.046*** |
| $VO_{2max}$ (ml/kg/min) | 26.8 ± 6.1 | 27.8 ± 5.8 | +1.0 | 0.055 |
| $VO_{2max}$ (ml/FFM/min) | 44.3 ± 7.0 | 44.5 ± 9.0 | +0.3 | 0.998 |
| VT1 | 1.4 ± 0.4 | 1.5 ± 0.4 | +0.1 | **0.018*** |
| VT1 (ml/FFM/min) | 23.9 ± 4.2 | 25.1 ± 4.4 | +1.1 | **0.043*** |
| VT2 | 2.2 ± 0.5 | 2.3 ± 0.5 | +0.1 | 0.053 |
| VT2 (ml/FFM/min) | 36.5 ± 5.1 | 37.5 ± 5.2 | +1.0 | 0.134 |
| Power | 181 ± 43 | 194 ± 46 | +13 | **< 0.001***** |
| Power at VT1 | 76 ± 26 | 87 ± 29 | +11 | **< 0.001***** |
| Power at VT2 | 139 ± 34 | 151 ± 35 | +11 | **< 0.001***** |

Data are presented as mean ± standard deviation (SD). * $p < 0.05$, *** $p < 0.001$: Statistical significance levels.

The changes of different groups in cardiorespiratory parameters and exercise performance are presented in Table 9. All Groups showed significant positive changes in power at both ventilatory thresholds, VT1 and VT2 ($p<0.05$). Group 2 had also significant positive changes in power ($p<0.05$), and Group 3 exhibited significant changes in all parameters. Significant differences ($p<0.05$) between groups were observed between Group 1 and Group 3 in $VO_{2max}$ (L/min), $VO_{2max}$ (ml/FFM/min), VT1, VT1 (FFM), VT2 (FFM).

Table 9. Changes in cardiorespiratory fitness and exercise performance in Groups 1, 2, and 3 from 0 to 3 months and the differences between Groups.

| | Group 1 | Group 2 | Group 3 | 1 vs 2 | 2 vs 3 | 1 vs 3 |
|---|---|---|---|---|---|---|
| Variables | | | | Between Group Differences in Change from 0 to 3 months | | |
| Fitness | | | | | | |
| $VO_{2max}$ (L/min) 0kk | 2.83 ± 0.79 | 2.53 ± 0.63 | 2.70 ± 0.54 | | | |
| $VO_{2max}$ (L/min) 3kk | 2.77 ± 0.79 | 2.60 ± 0.68 | 2.88 ± 0.59 | | | |
| *Within-group change (p-value)* | 0.418 | 0.286 | **0.005**** | 0.198 | 0.201 | **0.012*** |
| $VO_{2max}$ (ml/kg/min) 0kk | 27.4 ± 6.7 | 28.6 ± 5.5 | 24.9 ± 5.9 | | | |
| $VO_{2max}$ (ml/kg/min) 3kk | 27.8 ± 8.1 | 28.4 ± 5.1 | 27.1 ± 4.8 | | | |
| *Within-group change (p-value)* | 0.573 | 0.392 | **0.006**** | 0.428 | 0.475 | 0.174 |
| $VO_{2max}$ (ml/FFM/min) 0kk | 45.5 ± 7.9 | 46.1 ± 6.2 | 42.1 ± 4.1 | | | |
| $VO_{2max}$ (ml/FFM/min) 3kk | 44.6 ± 2.4 | 44.4 ± 2.4 | 44.6 ± 5.2 | | | |
| *Within-group change (p-value)* | 0.420 | 0.536 | **0.031*** | 0.820 | 0.172 | **0.037*** |
| VT1 0kk | 1.5 ± 0.4 | 1.4 ± 0.4 | 1.5 ± 0.3 | | | |
| VT1 3kk | 1.5 ± 0.4 | 1.4 ± 0.4 | 1.6 ± 0.4 | | | |
| *Within-group change (p-value)* | 0.929 | 0.462 | **0.001**** | 0.576 | 0.078 | **0.018*** |
| VT1 (ml/FFM/min) 0kk | 24.1± 4.1 | 25.0 ± 4.7 | 22.7 ± 3.4 | | | |
| VT1 (ml/FFM/min) 3kk | 24.1 ± 5.0 | 25.5 ± 4.4 | 25.3 ± 4.0 | | | |
| *Within-group change (p-value)* | 0.988 | 0.659 | **0.002**** | 0.755 | 0.086 | **0.033*** |
| VT2 0kk | 2.3 ± 0.6 | 2.1 ± 0.5 | 2.2 ± 0.5 | | | |
| VT2 3kk | 2.3 ± 0.5 | 2.1 ± 0.5 | 2.4 ± 0.5 | | | |
| *Within-group change (p-value)* | 0.770 | 0.668 | **0.001**** | 0.626 | 0.071 | **0.015*** |
| VT2 (ml/FFM/min) 0kk | 37.0 ± 5.3 | 38.0 ± 5.2 | 34.7 ± 4.3 | | | |
| VT2 (ml/FFM/min) 3kk | 36.7 ± 5.4 | 38.2 ± 5.8 | 37.3 ± 4.5 | | | |
| *Within-group change (p-value)* | 0.837 | 0.832 | **0.010**** | 0.779 | 0.130 | 0.056 |
| Power | | | | | | |
| Power 0kk | 189 ± 52 | 173 ± 46 | 184 ± 32 | | | |
| Power 3kk | 201 ± 54 | 185 ± 48 | 200 ± 39 | | | |
| *Within-group change (p-value)* | 0.058 | **0.005**** | **< 0.001***** | 0.994 | 0.441 | 0.536 |
| Power at VT1 0kk | 81 ± 29 | 72 ± 24 | 75 ± 25 | | | |
| Power at VT1 3kk | 88 ± 34 | 82 ± 25 | 90 ± 31 | | | |
| *Within-group change (p-value)* | **0.003**** | **0.049*** | **0.004**** | 0.730 | 0.449 | 0.314 |
| Power at VT2 0kk | 145 ± 34 | 134 ± 34 | 142 ± 32 | | | |
| Power at VT2 3kk | 153 ± 32 | 144 ± 38 | 157 ± 34 | | | |
| *Within-group change (p-value)* | **< 0.001***** | **0.046*** | **< 0.001***** | 0.892 | 0.321 | 0.277 |

Data are presented as mean ± standard deviation (SD). Differences are displayed as p-values. * $p < 0.05$, ** $p < 0.01$, *** $p<0.001$: Statistical significance levels.

The relative changes in fitness parameters of the intervention groups are expressed as changes from pre-trial (0 months) to post-trial (3 months) in Figure 4. All parameters increased in all groups except for $VO_{2max}$ (L/min), $VO_{2max}$ (ml/kg/min), and $VO_{2max}$ (ml/FFM/min) which decreased in Group 2 (Figure 4 A). The relative changes in power variables of the intervention groups are expressed as changes from pre-trial (0 months) to post-trial (3 months), where all parameters increased and were significant in all groups (Figure 4 B).

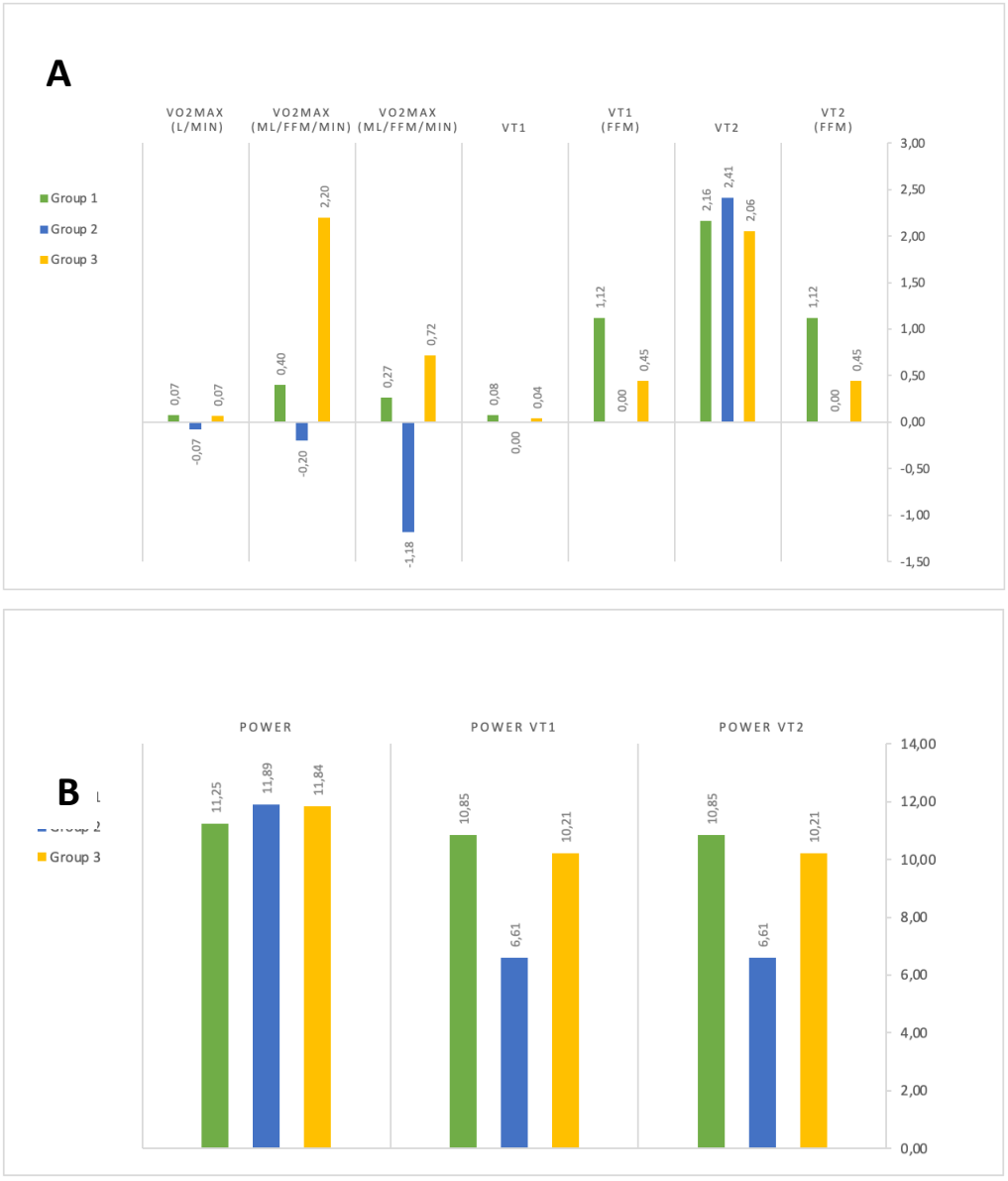


Figure 4. Relative change of cardiorespiratory parameters (A) and power (B) from one to three months in Group 1, Group 2, and Group 3.

## *3.3 Glucose and Lipid Profiles*

The changes in glucose and lipid profiles of all participants combined are presented in Table 10. There were no statistically significant changes observed in any of the variables.

Table 10. Glucose and lipid profiles at baseline and after three-month intervention of all participants.

| | 0 months | 3 months | Change | p-value |
|---|---|---|---|---|
| Glucose (mmol/L) | 5.62 ± 0.88 | 5.36 ± 0.64 | -0.26 | 0.531 |
| Insulin (mmol/L) | 13.41 ± 7.80 | 11.91 ± 5.80 | -1.51 | 0.475 |
| HOMA-ir | 3.32 ± 2.06 | 2.84 ± 1.43 | -0.48 | 0.053 |
| Cholesterol (mmol/L) | 4.67 ± 0.83 | 4.74 ± 0.87 | -0.03 | 0.318 |
| HDL (mmol/L) | 1.26 ± 0.32 | 1.27 ± 0.34 | 0.01 | 0.203 |
| LDL (mmol/L) | 2.80 ± 0.75 | 2.94 ± 0.76 | -0.03 | 0.338 |
| Triglycerides (mmol/L) | 1.43 ± 0.66 | 1.41 ± 0.75 | -0.02 | 0.310 |

Data are presented as mean ± standard deviation (SD).

The glucose and lipid profiles pre- and post-trial are presented in Table 11. No significant changes were observed in any of the groups. Significant differences between group and parameter were also observed in Groups 2 and 3 in Insulin ($p<0.05$) and in Groups 1 and 3 in Cholesterol ($p<0.05$) and HDL ($p<0.05$). No significant differences were observed between Groups 1 and 2 (Table 11).

Table 11. Changes in glucose and lipid profiles in Groups 1, 2, and 3 from 0 to 3 months and the differences between Groups.

| | Group 1 | Group 2 | Group 3 | 1 vs 2 | 2 vs 3 | 1 vs 3 |
|---|---|---|---|---|---|---|
| Outcome Variables | | | | Between Group Differences in Change from 0 to 3 months | | |
| Glucose Profile | | | | p-value | | |
| Glucose (mmol/L) 0kk | 5.76 ± 0.63 | 5.27 ± 0.48 | 5.95 ± 1.17 | | | |
| Glucose (mmol/L) 3kk | 5.63 ± 0.64 | 5.18 ± 0.39 | 5.43 ± 0.82 | | | |
| *Within-group change (p-value)* | 0.310 | 0.286 | 0.134 | 0.816 | 0.189 | 0.452 |
| Insulin (mmol/L) 0kk | 11.51 ± 4.46 | 11.28 ± 5.87 | 16.93 ± 9.86 | | | |
| Insulin (mmol/L) 3kk | 11.44 ± 4.54 | 10.6 ± 5.22 | 13.75 ± 6.69 | | | |
| *Within-group change (p-value)* | 0.972 | 0.430 | 0.188 | 0.731 | **0.046*** | 0.141 |
| HOMA-ir 0kk | 2.96 ± 1.17 | 2.67 ± 1.29 | 4.21 ± 2.71 | | | |
| HOMA-ir 3kk | 2.87 ± 1.20 | 2.51 ± 1.27 | 3.20 ± 1.66 | | | |
| *Within-group change (p-value)* | 0.860 | 0.477 | 0.068 | 0.876 | 0.125 | 0.294 |
| Lipid Profile | | | | | | |
| Cholesterol (mmol/L) 0kk | 4.70 ± 0.68 | 4.740 ± 0.90 | 4.83 ± 0.82 | | | |
| Cholesterol (mmol/L) 3kk | 4.99 ± 0.72 | 4.79 ± 0.96 | 4.56 ± 0.83 | | | |
| *Within-group change (p-value)* | 0.148 | 0.577 | 0.074 | 0.215 | 0.058 | **0.033*** |
| HDL (mmol/L) 0kk | 1.16 ± 0.19 | 1.33 ± 0.31 | 1.22 ± 0.37 | | | |
| HDL (mmol/L) 3kk | 1.26 ± 0.29 | 1.34 ± 0.33 | 1.19 ± 0.37 | | | |
| *Within-group change (p-value)* | 0.126 | 0.761 | 0.350 | 0.148 | 0.379 | **0.040*** |
| LDL (mmol/L) 0kk | 3.12 ± 0.50 | 2.87 ± 0.85 | 3.03 ± 0.74 | | | |
| LDL (mmol/L) 3kk | 3.33 ± 0.53 | 2.88 ± 0.83 | 2.84 ± 0.72 | | | |
| *Within-group change (p-value)* | 0.180 | 0.903 | 0.115 | 0.191 | 0.142 | 0.055 |
| Triglycerides (mmol/L) 0kk | 1.23 ± 0.83 | 1.40 ± 0.58 | 1.55 ± 0.70 | | | |
| Triglycerides (mmol/L) 3kk | 1.20 ± 0.62 | 1.43 ± 0.64 | 1.47 ± 0.91 | | | |
| *Within-group change (p-value)* | 0.700 | 0.663 | 0.491 | 0.631 | 0.402 | 0.809 |

Data are presented as mean ± standard deviation (SD). * $p < 0.05$: Statistical significance levels.

The relative changes of the lipid and glucose profiles intervention groups are shown in Figure 5. None of the changes were statistically significant (Figure 5).

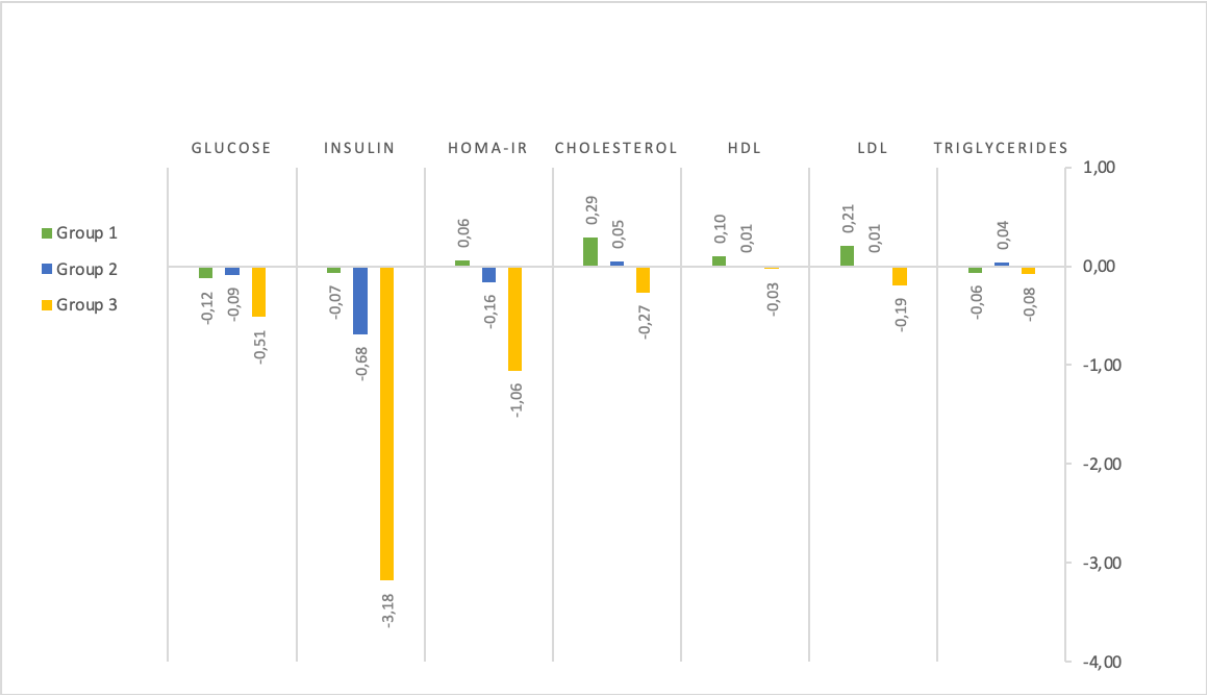


Figure 5. Relative changes from 0 to 3 months in glucose and lipid profiles in Group 1, Group 2, and Group 3.

## *3.4 Inflammatory Markers*

The changes in inflammatory marker levels of all participants combined are presented in Table 12. There were no statistically significant changes observed in any of the variables.

Table 12. Inflammatory markers at baseline and after three-month intervention of all participants.

| | 0 months | 3 months | Change | p-value |
|---|---|---|---|---|
| IL-1b (mmol/L) | 0.01 ± 0.03 | 0.01 ± 0.03 | 0.0 | 0.575 |
| IL-6 (mmol/L) | 0.62 ± 0.64 | 0.50 ± 0.62 | -0.12 | 0.099 |
| IL-8 (mmol/L) | 2.49 ± 1.11 | 2.59 ± 1.39 | +0.10 | 0.612 |
| IL-10 (mmol/L) | 2.66 ± 19.85 | 6.26 ± 47.75 | +3.60 | 0.326 |
| IL-15 (mmol/L) | 1.13 ± 5.66 | 0.92 ± 5.24 | -0.22 | 0.763 |
| IL-17A (mmol/L) | 0.11 ± 0.21 | 0.11 ± 0.26 | 0.0 | 0.903 |
| TNFα (mmol/L) | 5.43 ± 3.15 | 5.68 ± 4.73 | +0.28 | 0.726 |
| CRP (mmol/L) | 5.27 ± 7.61 | 4.74 ± 6.52 | -0.53 | 0.388 |

Data are presented as mean ± standard deviation (SD).

The interleukin, CRP, and TNF-α levels pre- and post-trial and their differences are presented in Table 13. No significant changes were observed in Group 1, Group 2, or Group 3. Due to limitations in the quality and quantity of data of Group 3, there is no data for IL-10 and IL-15 and no standard deviations calculated for IL-1b and IL-17A (Table 13).

Table 13. Changes in inflammatory markers in Groups 1, 2, and 3 from 0 to 3 months and the differences between Groups.

| | Group 1 | Group 2 | Group 3 | 1 vs 2 | 2 vs 3 | 1 vs 3 |
|---|---|---|---|---|---|---|
| Outcome Variables | | | | | | |
| **Inflammatory Markers** | | | | | p-value | |
| IL-1b (mmol/L) 0kk | 0.02 ± 0.05 | 0.01 ± 0.21 | 0.01 ± 0.017 | | | |
| IL-1b (mmol/L) 3kk | 0.03 ± 0.07 | 0.01 ± 0.10 | 0.00 ± 0.00 | | | |
| *Within-group change (p-value)* | 0.213 | 0.307 | 0.118 | 0.866 | 0.776 | **0.044*** |
| IL-6 (mmol/L) 0kk | 1.01 ± 0.97 | 0.50 ± 0.47 | 0.51 ± 0.49 | | | |
| IL-6 (mmol/L) 3kk | 0.74 ± 1.12 | 0.39 ± 0.27 | 0.49 ± 0.47 | | | |
| *Within-group change (p-value)* | 0.169 | 0.289 | 0.854 | 0.057 | 0.518 | 0.188 |
| IL-8 (mmol/L) 0kk | 2.90 ± 1.25 | 2.34 ± 0.91 | 2.43 ± 1.25 | | | |
| IL-8 (mmol/L) 3kk | 2.42 ± 1.31 | 2.49 ± 1.39 | 2.82 ± 1.47 | | | |
| *Within-group change (p-value)* | 0.081 | 0.541 | 0.351 | 0.117 | 0.603 | 0.123 |
| IL-10 (mmol/L) 0kk | 11.81 ± 42.28 | 0.05 ± 0.19 | 0.09 ± 0.41 | | | |
| IL-10 (mmol/L) 3kk | 28.25 ± 101.72 | 0.04 ± 0.17 | 0.05 ± 0.14 | | | |
| *Within-group change (p-value)* | 0.338 | 0.816 | 0.646 | 0.161 | 0.748 | 0.220 |
| IL-15 (mmol/L) 0kk | 1.82 ± 6.55 | 1.65 ± 7.22 | N/D | | | |
| IL-15 (mmol/L) 3kk | 3.79 ± 10.9 | 0.18 ± 0.94 | N/D | | | |
| *Within-group change (p-value)* | 0.174 | 0.311 | N/D | 0.312 | 0.370 | 0.080 |
| IL-17A (mmol/L) 0kk | 0.14 ± 0.28 | 0.13 ± 0.23 | 0.06 ± 0.14 | | | |
| IL-17A (mmol/L) 3kk | 0.12 ± 0.35 | 0.16 ± 0.28 | 0.050 ± 0.11 | | | |
| *Within-group change (p-value)* | 0.893 | 0.707 | 0.840 | 0.743 | 0.690 | 0.950 |
| TNF-α (mmol/L) 0kk | 8.38 ± 2.79 | 4.94 ± 2.96 | 4.14 ± 2.42 | | | |
| TNF-α (mmol/L) 3kk | 6.90 ± 3.67 | 5.10 ± 5.02 | 5.64 ± 5.01 | | | |
| *Within-group change (p-value)* | 0.197 | 0.892 | 0.248 | 0.366 | 0.437 | 0.106 |
| CRP (mmol/L) 0kk | 6.74 ± 7.24 | 4.29 ± 5.22 | 5.73 ± 9.98 | | | |
| CRP (mmol/L) 3kk | 3.40 ± 1.87 | 4.65 ± 6.49 | 5.44 ± 7.90 | | | |
| *Within-group change (p-value)* | 0.225 | 0.437 | 0.782 | **0.039*** | 0.548 | 0.189 |

Data are presented as mean ± standard deviation (SD). N/D: No Data. * $p < 0.05$: Statistical significance levels.

## *3.5 Associations Between Values*

Correlations for anthropometric markers, cardiorespiratory fitness, and power are presented in Table 14. All markers correlated significantly with $VO_{2max}$ (L/min) ($p<0.001$). Visceral Fat correlated significantly with all anthropometric markers except for VT2. Weight and BMI both correlated significantly with VO2max (ml/FFM/min), VT1, VT1 (FFM), VT2 (FFM), and Power at VT1 and VT2. Fat-Free mass was found to correlate significantly with VO2max

(ml/FFM/min), and VT2 (FFM). Body Fat percentage was found to correlate significantly with VT1, Power, and Power at VT2 (Table 14).

Table 14. Correlations between changes in anthropometric markers, cardiorespiratory fitness, and power in all participants.

| | Weight (kg) | Fat Free Mass (kg) | Fat % | Visceral Fat ($cm^2$) | BMI ($kg/m^2$) |
|---|---|---|---|---|---|
| $VO_{2max}$ (L/min) | **-0.229*** ** | **-0.066*** ** | **-0.145*** ** | **-0.330*** ** | **-0.250*** ** |
| $VO_{2max}$ (ml/kg/min) | -0.231 | -0.068 | -0.142 | **-0.319*** | -0.247 |
| $VO_{2max}$ (ml/FFM/min) | **-0.341*** | **-0.0387**** | 0.031 | **-0.365**** | **-0.361**** |
| VT1 | **-0.277*** | 0.073 | **-0.307*** | **-0.452*** ** | **-0.271*** |
| VT1 (FFM) | **-0.336*** | -0.152 | -0.174 | **-0.481*** ** | **-0.366*** |
| VT2 | 0.369 | 0.243 | 0.043 | 0.191 | 0.414 |
| VT2 (FFM) | **-0.327*** | **-0.381**** | 0.031 | **-0.389**** | **-0.340*** |
| Power | -0.202 | 0.007 | **-0.388**** | **-0.286*** | -0.210 |
| Power at VT1 | **-0.374**** | 0.100 | **-0.453**** | **-0.499**** | **-0.362**** |
| Power at VT2 | **-0.292*** | 0.010 | **-0.268*** | **-0.371**** | **-0.292*** |

Data are presented as Pearson Correlations. * $p < 0.05$, ** $p < 0.01$, *** $p<0.001$: Statistical significance levels.

Significant correlations were found also in glucose profile markers. Weight, Visceral Fat, and BMI correlated significantly with Insulin and HOMA-ir. No correlations were found between anthropometric values and Glucose. (Table 15) Of the cardiorespiratory and fitness markers, no significant correlations were found (Table 16).

Table 15. Correlations between changes in anthropometric markers and glucose profiles in all participants.

| | Glucose | Insulin | HOMA-ir |
|---|---|---|---|
| Weight (kg) | 0.321 | **0.444*** | **0.458*** ** |
| Fat Free Mass (kg) | 0.497 | 0.240 | 0.216 |
| Fat % | 0.808 | 0.089 | 0.113 |
| Visceral Fat ($cm^2$) | 0.475 | **0.370*** | **0.374*** |
| BMI ($kg/m^2$) | 0.303 | **0.469*** | **0.481**** |

Data are presented as Pearson Correlations. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$: Statistical significance levels.

Table 16. Correlations between changes in cardiorespiratory and exercise performance parameters and glucose profiles in all participants.

| | Glucose | Insulin | HOMA-ir |
|---|---|---|---|
| $VO_{2max}$ (L/min) | -0.078 | -0.056 | 0.003 |
| $VO_{2max}$ (ml/kg/min) | -0.130 | -0.028 | 0.037 |
| $VO_{2max}$ (ml/FFM/min) | -0.141 | -0.123 | -0.053 |
| VT1 | -0.127 | -0.147 | -0.097 |
| VT1 (FFM) | -0.181 | -0.186 | -0.119 |
| VT2 | -0.155 | 0.319 | 0.311 |
| VT2 (FFM) | -0.128 | -0.100 | -0.027 |
| Power | 0.065 | -0.62 | -0.030 |
| Power at VT1 | -0.081 | 0.010 | 0.020 |
| Power at VT2 | -0.037 | -0.022 | 0.019 |

Data are presented as Pearson Correlations.

Of the lipid profiles, cholesterol correlated significantly with Weight ($p<0.001$), Visceral Fat ($p<0.001$), and BMI ($p<0.001$). There were no correlations between HDL and any of the anthropometric markers. LDL correlated significantly with Weight ($p<0.001$), Visceral Fat ($p<0.001$), and BMI ($p<0.05$). Triglycerides also correlated significantly with Weight ($p<0.05$), Visceral Fat ($p<0.05$), and BMI ($p<0.05$), but also with Fat Free Mass ($p<0.05$) (Table 17).

Table 17. Correlations between changes in anthropometric markers and lipid profiles in all participants.

| | Cholesterol | HDL | LDL | Triglycerides |
|---|---|---|---|---|
| Weight | **0.464*****| 0.074 | **0.419**** | **0.412*** |
| Fat Free Mass | 0.256 | 0.187 | 0.221 | **0.274*** |
| Fat % | 0.151 | -0.153 | 0.146 | 0.146 |
| Visceral Fat | **0.495***** | 0.109 | **0.456***** | **0.326*** |
| BMI | **0.442***** | 0.067 | **0.407**** | **0.377**** |

Data are presented as Pearson Correlations. * $p < 0.05$, ** $p < 0.01$, *** $p<0.001$: Statistical significance levels.

Correlations were also found between lipid profiles and cardiorespiratory and exercise performance markers. Cholesterol correlated significantly with VT1 ($p<0.05$), VT1 (FFM) ($p<0.01$), VT2 (FFM) ($p<0.01$), and power at VT1 ($p<0.05$) and VT2 ($p<0.01$). HDL correlated significantly only with VT2 (FFM) ($p<0.05$). LDL correlated with VT1 ($p<0.05$), VT1 (FFM) ($p<0.05$), VT2 (FFM) ($p<0.01$), and all power parameters ($p<0.05$). No correlations were found with triglycerides. (Table 18).

Table 18. Correlations between changes in cardiorespiratory and exercise performance parameters and lipid profiles in all participants.

| | Cholesterol | HDL | LDL | Triglycerides |
|---|---|---|---|---|
| $VO_{2max}$ (L/min) | -0.252 | -0.262 | -0.264 | 0.001 |
| $VO_{2max}$ (ml/kg/min) | -0.217 | -0.221 | -0.234 | -0.021 |
| $VO_{2max}$ (ml/FFM/min) | -0.268 | -0.272 | -0. 276 | -0.097 |
| VT1 | **-0.334*** | -0.124 | **-0.338*** | -0.031 |
| VT1 (FFM) | **-0.374**** | -0.117 | **-0.368*** | -0.109 |
| VT2 | -0.046 | 0.661 | 0.361 | -0.419 |
| VT2 (FFM) | **-0.947**** | **-0.342*** | **-0.394**** | -0.127 |
| Power | -0.200 | -0.164 | **-0.185*** | -0.018 |
| Power at VT1 | **-0.319*** | 0.024 | **-0.323*** | -0.130 |
| Power at VT2 | **-0.409**** | -0.241 | **-0.371*** | -0.180 |

Data are presented as Pearson Correlations. * $p < 0.05$, ** $p < 0.01$: Statistical significance levels.

Correlations between inflammatory markers and anthropometry were also found. IL-8, IL-10, and TNF-α correlated significantly with all variables apart from Fat Free Mass, IL-6 correlated only with Visceral Fat ($p<0.05$). There were no correlations also found between any anthropometric markers and IL-1b, IL-17A, or CRP (Table 19).

Table 19. Correlations between changes in anthropometric markers and inflammation markers in all participants.

| | IL-1b | IL-6 | IL-8 | IL-10 | IL-15 | IL-17A | TNF-α | CRP |
|---|---|---|---|---|---|---|---|---|
| Weight | -0.601 | -0.239 | **-0.355*** | **-0.915*** | N/D | -0.242 | **-0.519**** | 0155 |
| Fat Free Mass | -0.411 | 0.018 | 0.147 | -0.125 | N/D | -0.693 | -0.103 | 0.178 |
| Fat % | -0.531 | -0.231 | **-0.414**** | -0.593 | N/D | 0.023 | **-0.395**** | -0.070 |
| Visceral Fat | -0.687 | **-0.307*** | **-0.370*** | **-0.898*** | N/D | 0.184 | **-0.506**** | 0.181 |
| BMI | -0.500 | -0.216 | **-0.377*** | **-0.890*** | N/D | -0.209 | **-0.524**** | 0.168 |

Data are presented as Pearson Correlations. * $p < 0.05$, ** $p < 0.01$: Statistical significance levels. N/D: No Data.

Some inflammatory markers were also found to correlate with cardiorespiratory and exercise performance markers. IL-8 correlated with $VO_{2max}$ (L/min) ($p<0.05$), $VO_{2max}$ (ml/kg/min), Power ($p<0.05$), and Power at VT1 ($p<0.001$) and VT2 ($p<0.05$). IL-10 also correlated with Power at VT2 ($p<0.01$). TNF-α correlated with VT1 and VT1 (FFM) ($p<0.05$) (Table 20).

Table 20. Correlations between changes in cardiorespiratory and exercise performance parameters and inflammation markers in all participants.

| | IL-1b | IL-6 | IL-8 | IL-10 | IL-15 | IL-17A | TNF-α | CRP |
|---|---|---|---|---|---|---|---|---|
| $VO_{2max}$ (L/min) | -0.256 | 0.013 | **0.308*** | 0.202 | N/D | -0.404 | 0.172 | 0.012 |
| $VO_{2max}$ (ml/kg/min) | -0.293 | -0.024 | **0.309*** | 0.247 | N/D | -0.307 | 0.155 | 0.014 |
| $VO_{2max}$ (ml/FFM/min) | -0.204 | 0.115 | 0.058 | 0.243 | N/D | -0.141 | 0.016 | -0.48 |
| VT1 | -0.060 | 0.212 | 0.278 | 0.528 | N/D | -0.478 | **0.315*** | 0.016 |
| VT1 (FFM) | -0.138 | 0.172 | 0.231 | 0.500 | N/D | -0.361 | **0.308*** | -0.031 |
| VT2 | N/D | 0.020 | -0.582 | N/D | N/D | N/D | -0.378 | 0.199 |
| VT2 (FFM) | -0.111 | -0.084 | 0.141 | 0.517 | N/D | -0.153 | 0.173 | 0.038 |
| Power | 0.255 | 0.011 | **0.418**** | 0.515 | N/D | 0.271 | 0.140 | -0.223 |
| Power at VT1 | 0.116 | 0.208 | **0.349*** | 0.590 | N/D | -0.125 | 0.207 | -0.011 |
| Power at VT2 | 0.464 | -0.018 | **0.340*** | **0.964**** | N/D | 0.160 | 0.169 | -0.020 |

Data are presented as Pearson Correlations. * $p < 0.05$, ** $p < 0.01$: Statistical significance levels. N/D: No Data.

# 4 DISCUSSION

The aim of this study was to analyze whether a three-month exercise prescription could create a difference in inflammation markers and/or glucose and lipid profiles and whether this change requires a change in body composition, fitness, or both. This study also explored the effects of the level of individualization in the intervention and its effects on the aforementioned parameters.

## *4.1 Anthropometry and Exercise Performance*

The baseline characteristics of the participants indicated that their body composition had negative effects on their health. The average of all the participants' BMI is 33.77, which indicates obesity (WHO Regional Office for Europe, 2022). The average Body Fat % was 39.3% which is over the reference values (Gómez-Ambrosi et al., 2011). Also, the average Visceral Fat area was over the 100 $cm^2$ reference value (Kim, Choi & Yum, 2006).

Changes in anthropometry were found to be statistically significant only in Group 3. Weight, BMI, Body Fat %, and Visceral Fat all decreased significantly in Group 3, but there was no significant change in Fat Free Mass (FFM). Groups 1 and 2 had no statistically significant changes in any of the anthropometry parameters. The findings suggest that the training program should be tailored to individual needs and finely tuned to induce changes in body composition and anthropometry within a relatively brief intervention period, such as three months.

The results of this study are in line with previous findings. Chávez-Guevara et al. (2020) concluded that exercise training conducted at the intensity maximizing fat oxidation led to a decrease in weight and body fat, while fat-free mass (FFM) remained unaltered. In a separate study, Swift et al. (2014) observed that overweight and obese adults adhering to an exercise program aligned with public health recommendations, similar to the regimen in Group 2, could anticipate a weight loss ranging from zero to two kilograms. O'Donoghue et al. (2020) had similar results in their meta-analysis, where exercise interventions induced a small (0.05-1.01 kg) reduction in weight, but body fat percentage seemed to be more responsive. In this present study, the average weight loss experienced by all participants was 0.97 kgs even though only Group 3 reported significant changes, and there was no significant change in FFM in any of the groups.

All parameters improved significantly only in Group 3. This means that exercise performance and cardiorespiratory parameters also showed a statistically significant improvement in Group 3 when scaled to Weight and Fat-Free Mass, concluding that the most highly individualized exercise intervention had improved the parameters regardless of body size. The percentage of change in VT1 was however higher than in VT2, which could be explained by the fact that VT1 can be improved with lower intensity exercise (Zouhal et al., 2018). Obese, sedentary subjects often exercise at a lower intensity in the beginning since their bodies are not used to the load. VT2 marks the limit between moderate- and high-intensity exercises, which is more difficult to reach (Anselmi et al., 2021).

Exercise performance (peak power, W) however improved statistically significantly in all groups at ventilatory thresholds 1 and 2 after the 12-week intervention, with the greatest changes occurring in Group 3. Improvements in Power at VT1 may be linked to the type of exercise subjects are doing, which was not surveyed in this present study (Zouhal et al., 2018). Also, participants in Group 1 were given comparatively minimal guidance and a less structured framework regarding exercise. This circumstance might have influenced their selection of less demanding activities, consequently leading to an inability to attain the required thresholds for inducing significant changes in these parameters.

Significant differences were observed in $VO_{2max}$ (L/min), $VO_{2max}$ (ml/kg/min), and $VO_{2max}$ (ml/FFM/min) when comparing Group 1 and Group 3, with greater improvements in Group 3. This supports the hypothesis that the variations in training protocols exerted a significant influence on respiratory fitness. There was a significant correlation in changes between weight, body fat %, and BMI versus VO2 at VT1. The relationship between improvements in cardiorespiratory parameters such as $VO_{2max}$ (L/min) and exercise performance measured with power output with body composition has been well studied, and studies have shown that there is no correlation but rather a similarity in responses to exercise load. O'Donoghue et al. (2020) conducted a meta-analysis where they found that a mixed exercise intervention consisting of aerobic and resistance training induced the best results in body composition and cardiorespiratory fitness highlighting further the importance of a diverse exercise program. These changes however were not dependent on each other. Chávez-Guevara et al., (2020) had similar results, where the slight increase in cardiorespiratory parameters could be explained by a change in oxygen intake rather than body composition.

The results of this study are in line with the results of previous ones and support the hypothesis that more personalized interventions lead to bigger changes in anthropometry and cardiorespiratory markers than general guidelines, even though changes in cardiorespiratory fitness seem to be mostly independent of changes in anthropometry.

## *4.2 Glucose and Lipid Profiles*

The three-month exercise intervention did not yield statistically significant changes in glucose and lipid profiles across all groups. However, when comparing the groups, noteworthy differences emerged between Groups 1 and 3 in cholesterol and HDL, as well as between Groups 2 and 3 in insulin. Despite the average values of HDL, cholesterol, and insulin not reaching statistical significance, these observed differences warrant further consideration. The presence of significant distinctions between specific groups suggests that meaningful variations may be associated with the diverse training regimes employed.

Comparing the results with previous findings, a study by Asuako et al. (2017) found that 8 weeks of aerobic exercise training induced a positive change in cholesterol (-0.45 mmol/l), LDL (-0.33 mmol/l), and triglycerides (-0.48 mmol/l) which are much bigger changes than the ones seen in this study. Moreover, a study by Goldhaber-Fiebert et al. (2003) highlighted some similar positive changes resulting from a three-week walking program paired with nutritional advice, although these changes were also relatively small. Apart from individual studies, a meta-analysis by Kelley et al. (2012) found similar effects on cholesterol, LDL, and triglycerides when aerobic exercise was paired with some sort of nutritional recommendations. They found that without a set diet, an aerobic exercise prescription induced significant changes in only triglycerides. All these before-mentioned studies reported no significant changes in HDL, much like the present study. These varying findings may be the results of differences in nutrition as well as differences in intensity, duration, and frequency of exercise training and sample sizes.

Of the glucose profile, insulin and HOMA-ir were found to correlate only significantly with anthropometric markers Weight, and Visceral Fat. The link between obesity and insulin resistance as demonstrated by the glucose profiles has been largely established, and our results are in line with previous studies. (Boden, 2001; Reaven, 1995; Roberts et al., 2013.) These studies have also shown that any associations between glucose profiles and parameters related to cardiorespiratory and exercise performance, such as $VO_{2max}$ and power, arise from

comparable adaptations to similar stressors—adaptations not observed in the context of this study.

## *4.3 Inflammation Markers*

The current research suggests that an individual's cytokine profile undergoes alterations with consistent exercise over time, although the extent of these changes remains a subject of considerable debate. Exercise interventions, particularly in IL-6, TNF-α, and CRP, have shown significant changes in various studies of CRP (Docherty et al., 2022; Fischer, 2006; Gonzalo-Encabo et al., 2021; Park et al., 2005; Pedersen, 2011). For instance, Alves Monteiro et al. (2015) demonstrated a reduction in IL-6 and TNF-α levels over 20 weeks in obese children under the age of 18 exercising three times a week for 50 minutes. This aligns with findings in mice, where exercise inhibited TNF-α expression in adipose tissue (Kawanishi et al., 2010).

Despite the absence of statistical significance, a noticeable reduction in interleukins, CRP, and TNF-α within this study underscores the acknowledged role of exercise in mitigating low-grade inflammation. A suggested explanation for the observed cytokine alterations is that consistent exercise may result in a decrease in body fat. Adipocytes, being a significant origin of pro-inflammatory cytokines such as TNF-α and IL-6, are implicated in this process (Docherty et al., 2022; Laakso et al., 1990). In this study the participants' baseline visceral fat, overall body fat percentage, and BMI were notably higher than average, potentially overshadowing the positive effects of exercise on inflammation markers.

Notably, this reduction in cytokines has also been observed even in the absence of weight loss or changes in body composition, indicating the potential involvement of alternative mechanisms. These may include direct anti-inflammatory effects on immune cells (Nicklas et al., 2008). The findings of this study are more in line with this hypothesis. The results suggest that a change in inflammation markers is independent of a change in anthropometry, but it also could be that any observed significant changes in anthropometry may not have been substantial enough to cause notable shifts in marker concentrations. The lack of findings could also be attributed to the relatively short intervention period of 12 weeks or the possibility that the intensity of exercise in each intervention group was insufficient to induce lasting changes. Additionally, since samples were not collected immediately post-intervention, the acute effects of exercise like the ones often seen in IL-6 might not have been observable anymore.

The findings, however, revealed associations between IL-8 and TNF-α with all anthropometric markers except for fat-free mass, and between IL-10 and all anthropometric markers except for fat percentage and fat-free mass. This observed relationship among these inflammation markers could be explained by the established connections between them and adipose tissue. Previous studies have demonstrated that TNF-α correlates with IL-10 levels and induces IL-8 secretion from adipose tissue (Howard et al., 1993; Standiford et al., 1990). Adipocytes produce several factors that are linked to low-grade inflammation, such as proinflammatory cytokines IL-8, IL-10, and TNF-α, and the rise in these cytokines had previously also been linked to the area of visceral fat (Hotamisligil, 2006; Hotamisligil et al., 1993; Park et al., 2005).

Additionally, TNF-α and VT1 exhibited correlations, both when scaled and not scaled to fat-free mass, aligning with previous research indicating that concentrations of TNF-α and IL-β tend to rise only with prolonged and strenuous exercise (Starkie et al., 2001). As mentioned earlier, obese, and sedentary individuals may encounter challenges in reaching the necessary exercise intensity for significant cardiorespiratory marker changes, especially when initiating exercise, and alterations in VT1 often manifest at lower intensities than VT2. The correlations observed between IL-8 and power may not be related since during exercise, IL-8 is locally produced within the muscle (Pedersen, 2011). A limited systemic IL-8 response is detected solely following intense exercise involving an eccentric component, so likely these two parameters are just independently responding to the physiological demands imposed by the exercise (Ostrowski et al., 2001).

It is not possible to determine based on these findings whether changes in adipose tissue, overall body composition, and fitness alone are the key to reducing inflammation markers or if there is a separate link between the parameters and low-grade inflammation. Given that inflammation has been shown to cause and worsen many diseases, such as atherosclerosis, diabetes, and cardiovascular disease, more research should be done to explore the possibility of exercise intervention as a treatment option in healthcare.

## *4.4 General Guidelines vs. Individualized Exercise Prescription*

As responses to exercise are shaped by personal, genetic, functional, and psychosocial factors, and the external environment, achieving desired results requires dosage recommendations that take these factors into account. Prescriptions should strive to be as individualized as possible to accommodate the diverse influences on exercise outcomes. (Gronwald et al., 2020).

The challenge of adherence remains whether the prescription is individualized or not. In a recent study by Kaseva et al. (2022), it was determined that participant adherence to the ongoing MoMaMo! study was not significantly associated with an individual's personality characteristics or psychological well-being.

The creation of individual training interventions however requires many resources, specialized laboratory equipment, and expertise, rendering it difficult for widespread application within the general population and healthcare system. Acknowledging this challenge, Lehtonen et al. (2022) emphasized the inclusion of self-assessment tools, such as the rate of perceived exertion (RPE), in population-wide exercise prescription guidelines, enabling a comprehensive evaluation of exercise responses concerning physiological thresholds. Lehtonen et al. (2022) advocated also for the adoption of a novel framework to inform the public of the physical activity (PA) guidelines, emphasizing the dual importance of accessibility and efficacy. The purpose of this proposed framework is to facilitate a personalized exercise prescription strategy tailored to the specific needs and capacities of the individual.

## *4.5 Strengths and Limitations*

Participating in the intervention study of the MoMaMo! study required a lot of time and effort from the subject, in addition to passing rather strict admission criteria (age, weight, non-smoking, medication, etc,.). For many people interested in the study, participation may have been impossible in the end due to time management issues. The sample of 89 people who went through all the initial measurements is therefore, a very selected group: they are Finnish women and men aged 19–40 who are overweight and exercise little, but who have had the opportunity to organize their schedules in their life situation so that they can participate in the multi-visit study. The research results can therefore be generalized to apply only to such a group of Finns, and to middle-aged adults at the most.

Measuring maximal oxygen uptake by a direct method requires time, money, trained personnel, and a test subject who agrees to pedal to exhaustion. In this study, 2–3 hours and the work input of four employees (a nurse, a doctor, and two exercise physiologists) were required for one test session pedaling on a bicycle ergometer. Conducting a similar test on hundreds or thousands to collect larger research data is challenging in terms of money and time. The sample size of subjects in this study can therefore be considered quite a good achievement and seems to be in line with other publications in the field of exercise physiology (Peltonen et al., 2013; Rissanen

et al., 2015). Still, given the drop-out rate, certain analyses conducted within the study might have insufficient statistical strength. As a result, the outcomes of this study should be seen as suggestive.

A longer trial may be needed to detect clear differences between groups. However, the three-month duration was chosen because it can be easily recreated in a healthcare environment, and it offers the most effective outcomes in terms of participants staying motivated to follow the plan. Registration and monitoring of actual activity levels during the intervention was also a limitation of the study, as it is not possible to know how closely the participants in each group followed the given guidelines and exercise plan.

To validate these findings, further studies with larger participant groups and longer observation periods are necessary. The information obtained from this study can hopefully be used in the future in the planning and implementation of new overweight and immobility intervention studies.

# 5 CONCLUSION

This study underscores the effectiveness of highly personalized training prescriptions in enhancing cardiorespiratory fitness, exercise performance, and body composition among overweight and obese individuals, surpassing the outcomes achieved with generic guidelines. However, a three-month intervention, regardless of the level of individualization in the training program, may not be sufficient for inducing lasting changes in an individual's baseline inflammation markers, glucose, and lipid profiles.

Obesity and inflammatory markers are intricately linked, with obesity inducing a chronic state of low-grade inflammation characterized by the upregulation of various inflammatory mediators. Understanding the mechanisms through which obesity influences the immune system and inflammation is vital in devising effective strategies to combat obesity-related health risks and associated comorbidities. Regular exercise and lifestyle interventions aimed at mitigating inflammation hold promise as potential approaches to improve the health outcomes of individuals with obesity. However, further research is necessary to fully understand the complex interplay between obesity and inflammatory markers, paving the way for tackling the obesity epidemic on a global scale.

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