Inland Norway University of Applied Sciences

Faculty of Social Sciences

Department of Sports Science

Magnus Kleiven

Master thesis

N-3 polyunsaturated fatty acids and progressive resistance training does not increase muscle mass and muscle strength in obese individuals compared to placebo

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Abstract

Introduction: Obesity induces many physiological changes that harm muscular function. Usual treatment for obesity is exercise and diet. N-3 PUFA have shown to have a certain benefit as to increasing muscle mass and strength. The goal of this study was to examine the effect of 23 weeks of n-3 PUFA supplementation combined with 13 weeks of progressive resistance training on muscle mass and strength in obese individuals.

Method: Thirty-five middle-aged obese participants (age 48.3 ± 6.4, BMI 34.3 ± 3.9) participated in the study. They were allocated into one of two groups; PUFA (n= 17; 1000mg n-3 PUFA) or CON (n=18; 1000mg of high oleic sunflower oil). Both groups combined their 23 weeks of supplementation with 13 weeks of 2 weekly supervised resistance training sessions. DXA, ultrasound and HUMAC were measured at three time-points: baseline (T1), pre-training (T2) and post-test (T4).

Results: Between the groups, there was no significant difference in isometric strength, lean body mass and muscle thickness after 7 weeks of supplementation (resp; $p = 0.99$, $p = 0.87$, $p = 0.81$). After 13 weeks of combined resistance training, CON increased significantly in isometric strength (17.01 ± 11.67%, $p = 0.006$) and PUFA did not (12.14 ± 14.52%, $p = 0.18$). In muscle thickness, PUFA showed a significant change (12.03 ± 10.23%, $p = 0.001$) and CON showed no significant change (6.68 ± 8.78%, $p = 0.2$). None of the groups increased in lean body mass ($p = 0.90$), and there was no significant difference in any test parameters between the groups (isometric strength: $p > 0.99$, lean body mass: $p = 0.90$, muscle thickness: $p = 0.41$).

Conclusion: 7 weeks of n-3 PUFA supplementation does not increase muscle mass or muscle strength. After 13 weeks of combined resistance training, there was no significant difference observed between PUFA and CON. The effect of n-3 PUFA is still unclear and should be investigated further.

1. Literature review

Obesity is increasing on a world basis and comes with many consequences for both the individual and the society (Afshin et al., 2017; Caballero, 2019). The cause of obesity varies, including sedate lifestyle, genetics, and increased food intake (especially fast-food, processed food, food with high-fat content etc) either individually or combined (Gardner et al., 2018; Goodarzi, 2018; Hall et al., 2019; Tuomilehto et al., 2001). The World Health Organization (WHO) has defined obesity as: "Abnormal or excessive fat accumulation that may impair health." The Body Mass Index (BMI) is a simple index for weight to height ratio that is commonly used to classify obesity in adults. Obesity is a BMI greater than or equal to 30 (WHO, 2020). Obesity induces physiological changes that harm physical function, is associated with increased fat mass, fat infiltration of muscle, a shift towards a more inflammatory milieu, reduced muscle contraction and reduced muscle mobilization (Bell et al., 2016; Tallis et al., 2018; Wannamethee & Atkins, 2015).

One understudied consequence is the reduced skeletal muscle function in obese individuals (Hulston et al., 2018; Maffiuletti et al., 2007; Tomlinson et al., 2014). We know little of the underlying mechanisms linking impaired muscle function to obesity and how the results of resistance exercise are affected in obese individuals. The most promising measures to counteract the loss of muscle mass and function are lifestyle interventions involving resistance exercise and nutrition (Donnelly et al., 2009; Witard et al., 2016). N-3 PUFA have been shown to induce many health benefits (Shahidi & Ambigaipalan, 2018). These include its effect on reducing inflammatory response caused by either obesity or ageing (Dupont et al., 2019; Tortosa-Caparros et al., 2017). N-3 PUFA supplementation has been shown to have a positive effect on muscle health, which may cause muscle hypertrophy and muscle strength (Huang et al., 2020). Nutritional interventions increasing the intake of n-3 PUFA led to a reduction of age-induced atrophy and enhancement in the effects of resistance exercise in elderly women (Anandacoomarasamy et al., 2008; McGlory et al., 2019; Smith et al., 2015). The potential mechanisms through which n-3 PUFA affect muscle are still not clear, but several interesting hypotheses have been raised (Tachtsis et al., 2018).

Based on the literature it seems resistance training in combination with n-3 PUFA supplementation is a promising countermeasure against obesity-related loss of relative strength, muscle mass and function (DeFina et al., 2011; Felix-Soriano et al., 2021; Smith et al., 2015).

In this context, both the individual and combined effects of interventions are of great interest. In the following, I will describe the physiological factors that affect muscle hypertrophy- and strength and see whether n-3 PUFA supplementation or resistance training combined can aid muscle hypertrophy and strength and summarise findings from previous studies.

1.1 Obesity and muscle function

Obesity causes high blood pressure, coronary heart disease, high LDL cholesterol, high levels of triglycerides, and chronic pain (Pi-Sunyer, 2002). These health complications can lead to metabolic syndrome, insulin resistance, cardiovascular diseases, inflammation, and type 2 diabetes (Wannamethee & Atkins, 2015; Westphal, 2008). One thing that is clear is that high levels of free fatty acids (FFA) in the blood stream can create a more inflammatory milieu in skeletal muscle (Pillon et al., 2012; Varma et al., 2009).

Excessive adipose tissue has shown to induce myositis and myosteatosis which are inflammation and fat infiltration in skeletal muscle (Addison et al., 2014; Hilton et al., 2008). Fat infiltration and inflammation will cause the muscle to be less contractile and lose function by inhibiting insulin sensitivity, insulin-stimulated glucose uptake and induce insulin resistance (Hilton et al., 2008; Wang et al., 2006; Wu & Ballantyne, 2017). The excess of nutrients in the adipose tissue stimulates them to release pro-inflammatory cytokines such as tumor necrosis factor α (TNF- α) and interleukin 6 (IL-6), and reduces the production of adiponectin, lead them to a more inflammatory state (Ellulu et al., 2017). Adiponectin has many physiological functions, as for the skeletal muscle by promoting fatty acid oxidation, insulin sensitivity amplifying glucose uptake by way of activating AMPK in the muscle cells. It also has antioxidant effects that reduces inflammation through activation of AMPK (Khoramipour et al., 2021). When it comes to the inflammatory properties, TNF- α is a polypeptide cytokine that is associated with muscle wasting by promoting muscle catabolism and it is mediated by nuclear factor-kB (NF-kB). NF-kB increases the activity of the ubiquitin-proteasome pathway (UPP)

that accelerates the regulated degradation of muscle proteins and promotes muscle weakness (Reid & Li, 2001; Thoma & Lightfoot, 2018). IL-6 is a cytokine that is produced by inflammatory conditions and infections via stimulations of TNF-α or through stimulation of Toll-like receptors after binding of pathogenic patterns of microbes (Uciechowski & Dempke, 2020). When elevated, IL-6 reduces the production of fibronectin, transferrin, and albumin (Tanaka et al., 2014). These proteins serve in different ways that can aid the skeletal muscles, such as cell growth, fat metabolism, and transportation of hormones, vitamins, and nutrients (Czub et al., 2019; Gomme et al., 2005; Hocking et al., 2008). Methods to treat obesity is vital to prevent further consequences from happening. The different methods are everything from surgery, medicine and lifestyle changes (Powell et al., 2007), where the latter includes the most used way which is diet and resistance training (Ho et al., 2012; Moreno et al., 2014).

1.2 Resistance training

Resistance training (RT) is a well-documented form of exercise that has been shown to increase muscle mass, muscle strength, lean body mass, reduce fat mass, and improve physical function (Jabekk et al., 2010; Westcott, 2012; Willis et al., 2012). There are numerous physiological factors that determine skeletal muscle strength and size, such as muscle fibre thickness and length, fibre type composition, and degree of neural activation of the muscle (Fitts et al., 1991). These factors can be changed by the adaptions when doing resistance training (Hughes et al., 2018). Resistance training is also associated with a reduced risk of low-grade inflammation related diseases (Calle & Fernandez, 2010). Dias and colleagues did a study on obese adolescents and saw that strength training can improve endothelial function and increase adiponectin (Dias et al., 2015). Since it is known that obesity causes IL-6 and TNF-α to elevate, causing a more pro-inflammatory response in the muscle, resistance training should be able to prevent them from elevating (Phillips et al., 2012).

A meta-analysis done by Sardeli and colleagues (2018) showed that RT has a tendency of reducing IL-6, and they suggest that the increase of muscle mass and high volume of RT have a potential saying in how much the inflammatory markers would decrease (Sardeli et al., 2018). A study by Greiwe (2001) on frail elderly saw that with resistance training for three months, TNF-α in the muscle decreased by 34% and muscle protein synthesis increased by 83% (Greiwe et al., 2001). When it comes to IL-6, a study done by Forti and colleagues (2014)

on elderly individuals showed that 12 weeks of progressive resistance training lowered IL-6 (Forti et al., 2014).

Even though strength training may cause short term inflammatory response, it promotes a more anti-inflammatory profile in the body such as increasing interleukin-10 that has a role of preventing inflammatory pathologies (Helmark et al., 2010; Iyer & Cheng, 2012). Insulin resistance is often caused by inflammation (Wu & Ballantyne, 2020), and it has been showed that some individuals with insulin resistance does not respond that well to resistance training (Alvarez et al., 2017; Orsatti et al., 2022). Indeed, insulin resistance makes the muscle cell less responsive to signalling by activating UPP that induces muscle protein degeneration (Wang et al., 2006). To promote better function and strength in the skeletal muscle, by increasing either muscle mass or strength, muscle protein synthesis needs to be elevated (Witard et al., 2022). By doing so, resistance training aids with increasing the muscle protein synthesis up to 48 hours (fasted state) after exercise (Moore, 2019) but is better combined with protein intake (Deldicque et al., 2005). Energy expenditure is crucial for reducing fat mass accumulated over time. By exercising, in this case resistance training to increase muscle mass, the resting metabolic rate will increase as well (Aristizabal et al., 2015; Zurlo et al., 1990). The reduction of fat mass is not only done by exercising, but also trough diet. When looking at n-3 PUFA, it seems to have some interesting effects on either increasing lean body mass, muscle mass, muscle strength, or reducing inflammation (Calder, 2006; Heileson & Funderburk, 2020; Lopez-Seoane et al., 2021; Wang & Huang, 2015).

1.3 N-3 PUFA supplementation

Research has shown that n-3 PUFA have many health benefits. It reduces triglyceride levels, inflammation and helps endothelial function (Casanova et al., 2017; Huang et al., 2019; Kiecolt-Glaser et al., 2011). High levels of triglycerides can have an influence on inflammation and vice versa (Feingold & Grunfeld, 2000; Welty, 2013). One thing that is featured when discussing the effects of n-3 PUFA, is the influence it has on reducing triglycerides and inflammation in skeletal muscle (Calder, 2013; Kiecolt-Glaser et al., 2011; Yanai et al., 2018). N-3 PUFA has an effect on triglycerides by changing different transcription factors such as; retinoid X receptor alpha (RxAα), sterol regulatory element binding proteins (SREBP) and

peroxisome proliferator-activated receptors (PPARs), each playing prominent roles in controlling lipid metabolism (Shearer et al., 2012). Inflammation has a key role in catabolic effect of the skeletal muscle (Costamagna et al., 2015; Haddad et al., 2005; Reid & Li, 2001). N-3 PUFA looks to reduce inflammation by inhibit activation of transcription factor NF-κB, as well as inhibiting TNF-α and IL-6 by activating PPARɣ (Calder, 2013; Liu et al., 2017).

This means, by reducing the inflammation, we can make the muscles more receptive to signals during exercise and increase muscle hypertrophy and strength (Kamolrat et al., 2013; Liu et al., 2019). A study done on older healthy subjects show that n-3 PUFA increases thigh muscle volume, muscle strength and lower intramuscular fat content (Yoshino et al., 2016). Another study done on older women have shown that n-3 PUFA rich diet combined with resistance training can increase muscle hypertrophy (Strandberg et al., 2019). However, in Dalle and colleagues' study on healthy older adults showed that n-3 PUFA increased isometric strength but did not increase muscle mass, induce anabolic responses, or reduce inflammation (Dalle et al., 2021). Other studies also did not find any significant reduction in inflammatory markers (Deger et al., 2016; Kyriakidou et al., 2021).

Another consequence of obesity is muscle atrophy which is causing loss of muscle strength and size (Gao et al., 2018; Roy et al., 2016). Since it is shown that n-3 PUFA can create a higher rate of muscle protein synthesis by promoting AKT/mTOR signalling pathway and induces muscle hypertrophy. In this way it attenuates muscle atrophy (Bodine et al., 2001; Gingras et al., 2007). A study by Miotto and McGlorry (2019), looked at immobilization of legs and supplementation of n-3 PUFA, showing that n-3 PUFA can attenuate muscle atrophy in young women after weeks of immobilization (McGlory et al., 2019; Miotto et al., 2019)

For the muscle to grow, it needs a high muscle protein turnover, and it is proposed that n-3 PUFA influences muscle protein synthesis (Bird et al., 2021; Brook et al., 2021; Smith et al., 2011). Muscle protein synthesis is necessary for muscle growth (Atherton & Smith, 2012). It looks like n-3 PUFA has an impact on the regulation of muscle protein synthesis by influencing different signalling pathways that promotes muscle growth such as mTOR, AKT, and Insulin growth factor 1 (IGF-1) (Jaiswal et al., 2022; Schiaffino & Mammucari, 2011). A study done by Smith and colleagues (2011) claims that omega-3 can increase rate of muscle protein synthesis and increase muscle strength and hypertrophy in older adults (Smith et al., 2011). The above-

mentioned studies were conducted on young, middle-aged, and old adults (usually healthy) and few on obese.

There are a little number of studies that look at n-3 PUFA individually or combined with resistance training on muscle hypertrophy and strength. It is still unclear whether not n-3 polysaturated fatty acids alone or combined with resistance training increase muscle hypertrophy and strength in obese individuals. This has led me to the primary objective of this thesis.

1.4 Objective and problem statement

Objective: The purpose of this study is to investigate if n3-PUFA supplementation for 7 weeks with no additional resistance training increases muscle mass and strength in obese individuals compared to placebo, and if n-3 PUFA supplementation combined with 13 weeks of resistance training increases muscle mass and strength compared to placebo combined with resistance training.

Problem statement: Does individual or combined effect of ingesting n-3 PUFA and resistance training increase muscle mass and strength in men and women between the age of thirty and sixty?

2. Introduction

Obesity induces many physiological changes that harm muscular function (Pi-Sunyer, 2002). Several studies even suggest that these changes decrease muscle mass and strength (Morgan et al., 2020; Valenzuela et al., 2020; Wannamethee & Atkins, 2015; Zhu et al., 2019). The proposed downside is the inflammatory response caused by too much accumulated fat (Pillon et al., 2012; Varma et al., 2009). Indeed, changes from obesity could have a negative impact on maximal strength and hypertrophy, which is necessary for daily living and physical functions (Tomlinson et al., 2016). The one factor for loss of muscle function is inflammation, caused by great amount of food consumption and sedentary lifestyle, creating an accumulation of fat that exceeds what the human body needs and causes obesity (Costamagna et al., 2015; Ellulu et al., 2017; Lipina & Hundal, 2017; Wright & Aronne, 2012). Two known pro-inflammatory cytokines that induces muscle loss is IL-6 and TNF-α (Popko et al., 2010; Tanaka et al., 2014). When these inflammatory markers are secreted, they cause a negative effect on muscle strength and hypertrophy, by causing muscle waist, reduced muscle protein synthesis, and reduced lipid metabolism (Biolo et al., 2003; Haddad et al., 2005; Reid & Li, 2001; Tanaka et al., 2014).

Resistance training is a well-known form of exercise that induces many physiological changes that benefits muscle function (Westcott, 2012; Willis et al., 2012). Two known benefits of resistance training are muscle hypertrophy and muscle strength (Mangine et al., 2015). To increase muscle size and strength, is not only done by exercising but also through diet, by using n-3 PUFA supplementation (Smith et al., 2015). Some studies shows that ingesting n-3 PUFA influences the skeletal muscle by promoting signalling pathways such as AKT/mTOR that effect muscle hypertrophy and strength (Bodine et al., 2001; Dupont et al., 2019; Strandberg et al., 2019). However, another study show that it only increases muscle strength, but not its size (Dalle et al., 2021).

Some studies have investigated the effect of n-3 PUFA on either muscle protein synthesis or inflammation (Kiecolt-Glaser et al., 2011; Kiecolt-Glaser et al., 2012; Smith et al., 2011). Kiecolt-Glaser (2011, 2012) looked at the effects of n-3 PUFA on inflammation in healthy medical students, healthy middle-age and older adults and observed a reduction in inflammatory markers by supplementation of n-3 PUFA. IN Smith (2011) who looked at muscle protein synthesis, observed an increase when using n-3 PUFA. However, there are studies that

contradicts the reduction of inflammation (Deger et al., 2016; Kyriakidou et al., 2021). Deger- and Kyriakidou and colleagues (2016, 2021) did not find any significant change in inflammatory markers in their studies.

To our knowledge, only two studies have looked at long-time effect of n-3 PUFA on muscle mass and strength (Smith et al., 2015; Strandberg et al., 2019). Smith and colleagues (2015) conducted a study lasting 6 months, on healthy older adults (age 60-85yrs). They had two groups, one ingesting n-3 PUFA and the other corn oil (no exercise), and they were tested in body mass, muscle volume, 1RM strength. They observed an increase in muscle mass and muscle strength after ~3 months and after 6 months. Strandberg and colleagues (2019) used recreationally active women in the age of 65-70yrs and were divided in three groups; 1) control, 2) resistance training, and 3) resistance training combined with n-3 PUFA. They trained twice a week for twenty-four weeks and were instructed to eat salmon, mackerel, and herring (fish and seafood > 500g/ week). They found significant increase in muscle hypertrophy as well as upregulation of mTOR and down-regulation of inflammation. This indicates that n-3 PUFA can influence muscle function and muscle mass.

For that reason, we aim to get further insight in whether obese individuals can increase their muscle mass and strength through supplementation of n-3 PUFA alone or combined with progressive resistance training. We examined whether seven weeks of n-3 PUFA supplementation would increase muscle mass and strength, also with thirteen weeks of combined progressive resistance training compared to placebo in obese individuals. Because training alone can induce great benefit to muscle mass and strength, but since n-3 PUFA have shown some benefits in overall health and aiding in muscle hypertrophy and strength. This could help the ordinary individual on the street to become healthier and stronger. On that note, the hypotheses were:

1) 7 weeks of n-3 PUFA supplementation will not increase muscle mass and strength in obese individuals compared to placebo.
2) 13 weeks of combined progressive resistance training and n-3 supplementation will increase muscle mass and strength in obese individuals compared to placebo.

3. Methods and materials

The present paper is part of a large study including a total of 151 participants with a BMI under (<30) or over 30 (>30), of which 95 completed the study. The main goal of the whole study is to search for the effects of resistance training and ingestion of n-3 polysaturated fatty acids to improve health and muscle function in individuals with obesity and healthy controls.

3.1 Participants

Fifty-seven healthy obese middle-aged male and female participants (F = 30 / M = 27, aged 45.95 ± 8.02, BMI 34.46 ± 4.56), with no underlying diseases (metabolic syndrome, smoking, damage in skeletal muscle system etc) were recruited to participate in this study. They were allocated in a stratified randomized manner, ensuring BMI-and sex-matched groups. 22 participants did not complete due to unknown reasons. They were divided into one of two supplementation groups, n-3 PUFA (PUFA: n = 17, M/F: n = 8/9) or placebo (CON: n = 18, M/F: n = 11/7). The data form DXA, Ultrasound and HUMAC are used from thirty-five participants. All participants data are presented in HUMAC, whiles data from thirty-two is used from DXA and ultrasound. In DXA, three participants do not have post-test results in DXA, and only two in ultrasound due to either COVID-19 or other reasons unknown. All participants who completed all three test points manage to use the dosage prescribed to them throughout the entire study. Subject characteristics and physiological parameters are presented in Table 1.

Table 1: *Characteristics and physiological parameters at baseline.*

	PUFA (n = 17)	CON (n = 18)
Age (years)	46,6 ± 7,5	49,9 ± 5,3
BMI (KG/M^2)	34,5 ± 4,3	34,1 ± 3,5
Sex (M / F)	8 / 9	11 / 7
Lean body mass (kg)	58,2 ± 11,3*	60,5 ± 10*
Muscle thickness in vastus lateralis (cm)	2,8 ± 0,7*	2,6 ± 0,6*
Isometric knee extension at 60^o (Nm)	212 ± 81	210 ± 53

*Values are mean ± SD, * = using data from n = 16.*

All participants received written information about the study and had the opportunity to ask questions before signing the consent form. Participants were informed that they could withdraw from the study at any time without giving a reason. They all gave their written consent to participate (Appendix A). The study was approved by the Regional Committees for Medical and Health Research Ethics (REK), region South-East (# 2019/818) and registered in clinical trials (NCT04279951). The study was conducted in accordance with the Declaration of Helsinki. The study was funded by Inland Norway University of Applied Sciences (INN) and Helse Sør-øst Regional health authority. The data collection was carried out at INN dept. Lillehammer.

3.2 Experimental design

An overview of the intervention is presented in figure 1. The entire study was done in a randomized controlled 2x2 factorial design study and consisted of 151 individuals (which of 95 completed), 38 people with a BMI under 30 (<30) and 57 with a BMI over 30 (>30). The intervention consisted of a seven week of supplementation of n-3 PUFA or placebo, followed by three weeks of simultaneous supplementation and familiarisation to resistance exercises, and thirteen weeks of simultaneous supplementation and resistance training.

All performance tests and body composition tests measurements were conducted at Inland Norway University of Applied Sciences. The test data were collected on different days. Day one started with DXA, followed by ultrasound, muscle biopsy, blood sampling, glucose test and blood pressure. Day two consisted of 1RM leg press, knee extension, maximal reps at 70% of 1RM knee extension, HUMAC, and step-test. These tests were collected at four different points, baseline (T1), before familiarisation to resistance exercises with supplementation (T2), before ten weeks of resistance training with supplementation (T3) and post-test (T4). In this paper, I will be using results from DXA (lean body mass; kg), ultrasound of M. vastus lateralis (muscle thickness; cm) and HUMAC (isometric knee extension, knee joint at 60°) from time-points T1 (baseline), T2 (pre-training) and T4 (post-test).

Figure 1: *Overview and time course of the present project including supplementation period, familiarization period, resistance training period and test-points (T1-4).*

3.3 Supplementation

Participants received a total amount of 1000 mg n-3 PUFA per day (EPA: 500mg and DHA: 270mg and 300-400 ppm astaxanthin) or 1000 mg of high oleic sunflower (placebo with 300-400 ppm astaxanthin) oil in identical capsules, ingested twice a day for 23 weeks (Rimfrost AS). They took four capsules in the morning and four in the evening. If they forgot to take it in the morning, they took them all in the evening. Previous studies have shown a plateau in red blood cell phospholipid EPA and DHA content, and muscle phospholipid EPA and DHA content at 2 and 8 weeks, respectively (McGlory et al., 2019). Thus, with a pre-resistance training supplementation period of 7 weeks, we expected participants in the n-3 PUFA group to be near a plateau for muscle phospholipid EPA and DHA content prior to initiation of the training intervention. Supplementation of EPA and DHA to a combined daily level of 1000 mg is well within recommended daily intake of n-3 polysaturated fatty acids (1 E%) and is not associated with adverse effects (EFSA, 2012). Supplements were marked with the id-number of the participant. A third party with no knowledge of the study handled the participant allocation list. During the intervention, participants were advised to restrict their ingestion of fish to once per week to minimize the amount of n-3 PUFA in their system.

3.4 Training Intervention

The training intervention started after seven weeks of n-3 PUFA supplementation and consisted of two days per week of supervised sessions for thirteen weeks. The familiarisation period was conducted with two sessions a week, with the purpose of introducing the exercises such as leg-press, knee extension, knee flexion, bench press and one-arm row. Warm-ups were conducted on an ergometer bicycle for 5-10 minutes at a self-paced intensity and the exercises were set at 2x10RM. This was to prevent any risk of injuries and make a smooth transition to the training intervention. At test-point two and three (T2 and T3), the strength test was used as “training sessions” for the purpose of testing and training.

During the entirety of the resistance training intervention, all participants completed the same contralateral training protocol for the legs. This means that one leg performed one resistance training protocol of 3x10RM, whereas the other leg performed 3x30RM. For the legs, the training protocol consisted of the exercises previous mentioned, the same goes for exercises

on the upper body. For the upper body, resistance training was performed as bilateral exercises and done with 3x10RM. Rest-time was set at 2 minutes, and customisation on the exercises was initialised if the subjects had any difficulties in either hips (leg-press: wider stance and outward rotation in the knees), knees (knee extension: reduce range-of-motion) or lower back (leg-press: back-pad lowered). Training days were set with minimum one day of rest and the time of day was set between 07AM to 18PM. The results from ultrasound and HUMAC will be taken from protocol 3x10RM of the legs.

3.5 Testing procedures

The testing procedures was completed as followed: On day one, at baseline, we registered their height and weight to make sure we got the correct BMI and lean mass at DXA-scan. Before scanning, subjects were asked if they fasted, and instructed to remove all metal and be clothed down. Clothing during scan for men; underwear or shorts and for women; sports bra and shorts. If the subject were too tall or wide, scanning started on one side first, then the other. If they were not in a fasted state, a new day would be appointed for DXA. Ultrasound were tested right after DXA, and at baseline, an anatomic map was made of the legs so the pictures would be more reliable at each test-points (description coming). On day two, at baseline, the subject was registered in HUMAC with the right settings for further tests (description coming) so that every time they performed day 2 the correct settings was in place. Before performing day two, it was necessary with least 48 hours between the days because of stiffness caused by biopsy.

3.5.1 Body composition

Body composition, measured in lean body mass (LBM, kg), was measured with DXA (Podigy Advanced PA +302047, Lunar, San Francisco, CA, USA) according to the manufacture's procedures. M. vastus lateralis thickness (VLT) was measured by using a B-mode ultrasound with a 50-mm linear matrix transducer (L12-5, Philips, Bothell, WA, USA), ultrasound system (HD11XE (Philips, Bothell, WA, USA) with the program Echo Wave II (2.7.1, Lithuania). A water-soluble transmission gel was applied to the transducer and was placed at a 90-degree angle at the measuring point which was 50% of the distance between the joint gap in the knee joint and trochanter major. Subjects were asked to tighten their thigh and the measurement was

taken on the most prominent parts of M. vastus lateralis (VL). Three pictures were taken of each leg at every test point. These pictures were analysed with a plugin from Imagej (Seynnes & Cronin, 2020). On the first test, measurement point, and other characteristics (birthmarks, scars, and moles) was marked on a plastic folder that lay on the subject's VL. This folder was used to find the same measuring point in the subsequent tests, to ensure that the measurements were as reliable as possible. Ultrasound has been shown to be a reliable and valid measurement method for muscle architecture (Kwah et al., 2013). Subjects were asked to avoid exercising for the last 48h before testing, and too fast for the last 12h.

3.5.2 Strength test

The intervention effect on muscle strength were measured by changes in isometric knee extension strength. The tests were conducted unilateral with standardised settings for each subject. Subjects performed a standardised warm-up on a bicycle for 5 minutes self-paced speed. Prior to the isometric test, a series of 1RM-tests performed (leg press and knee extension) that contained of 4 sets of gradually increasing weight and gradual decrease in number of repetitions (10rep/50%, 6rep/70%, 3rep/80%, and 1rep/ 100% of expected 1RM). If the 1RM lift was approved, the wight increased by a minimum of 2.5kg in leg press, and 1.25kg in knee extension. Participants received 2-minute break between attempts and the test was not completed until the participants received one lift failed at 2.5kg in leg press, 1.25 kg knee extension over the last successful lift. All test was performed using the same equipment and a minimum of 48h after the previous habituation or resistance training session.

The isokinetic and isometric unilateral knee extension were evaluated using HUMAC Norm dynamometer (CSMi, Stoughton, Massachusetts, USA) according to the manufacturer's procedures.

The participants were seated on a chair with a four-point seat belt, the axis of rotation and the knee joint were placed in line with the rotation axis of the dynamometer. The thigh was fastened with moderate force and the leg was strapped two fingers above the ankle joint. All setting were noted at pre-test and used at all test-points. Maximal isokinetic torque was measured at 60° sec-1 and 240° sec-1. Three submaximal attempts were used as warm-ups at each angular velocity, then they got three attempts immediately after each other. The participants got thirty seconds rest-time between submaximal attempts and test, while they got sixty second rest-time between test and warm-up attempts too new angular velocity. After

isokinetic test, the isometric strength test was next and were measured as maximal voluntary contraction (MVC) at 60° angle at the knee joint. Each subject got one warm-up attempts, and two attempts to create maximal power for five seconds with thirty second rest-time between attempts. The highest measured value was used for further analyses.

3.6 Statistics

Alle descriptive data are presented as mean and standard deviation (mean ± SD) unless otherwise is stated. For repeated measurements, a two-way repeated measurements ANOVA were fitted with time and group as the explanatory variable. Plotting and calculation of effect size (ES) was done using Microsoft Office Excel 2016 (Microsoft, Redmond, USA). To see changes between the different groups, a two-way ANOVA was used. ANOVAs and figures were made, using program GraphPad Prism 9 (GraphPad Software, inc. California). The level of significance was set an Alpha ($p<0.05$). Effect size (ES) was interpreted by Cohen's d. ES was calculated by taking the mean change in one group minus the mean change in the other group, divided by pooled standard deviation approach between interventions. Effect size will be classified as: 0,0-0,3 = no effect, 0,3-0,5 = small effect, 0,5-0,75 = moderate effect and >0,75 = high effect (Malt, 2020).

4. Results

4.1 Baseline

At baseline, there were no significant difference in isometric strength, lean body mass and muscle thickness between PUFA and CON (respectively; p = 0.999, p = 0.879, p = 0.745).

4.2 Isometric knee extension

After 7 weeks of supplementation, there were no significant difference between PUFA and CON in isometric strength (p = 0.998) and showed no effect between the groups (ES = 0.07). After 13 weeks of combined resistance, there were no significant difference between the groups (p >999) and showed no effect (0.02). There was no difference in percent change between the groups in T1-T2 and T2-T4 (resp. p= 0.81, p = 0.44). In CON there were a significant percent change from T1-T2 to T2-T4 (17.01 ± 11.67%, p = 0.006, Figure 2), and in PUFA there was no significant change from T1-T2 to T2-T4 (12.14 ± 14.52%, p = 0.185).

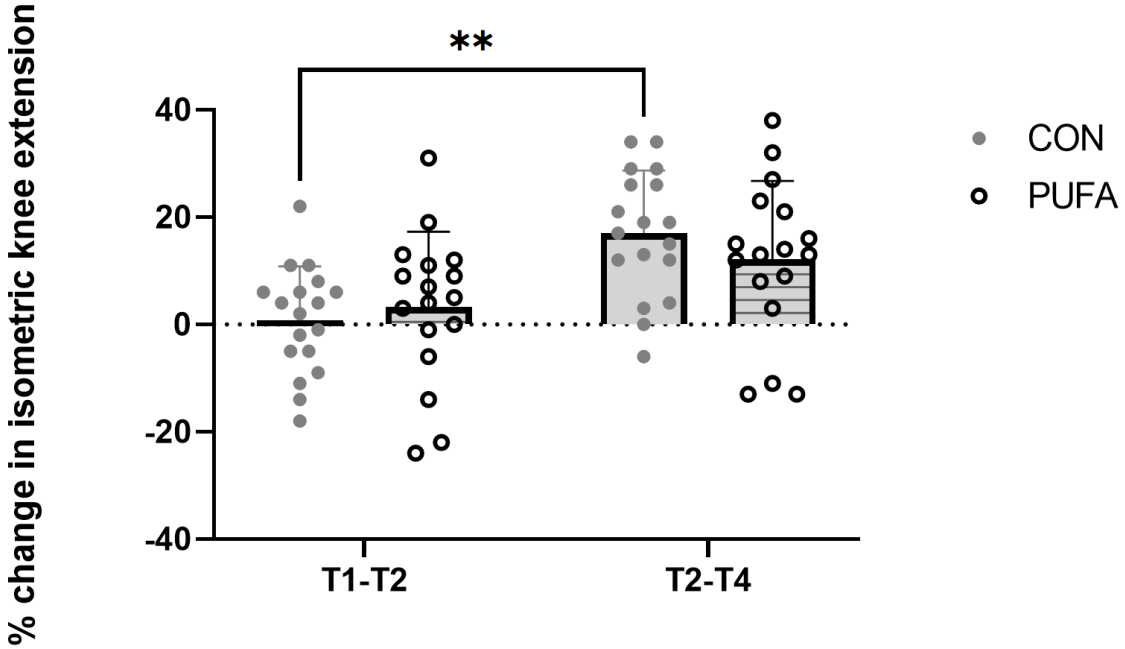

Figure 2: *Individual and summarised percent changes in PUFA and CON in isometric knee*

*extension at 60° (MVC) from baseline to pre-training (T1-T2) and from pre-training to post-test (T2-T4) in the intervention period for PUFA and CON. ** = 0.006.*

4.3 Lean body mass

There was no statistically significant difference in lean body mass between PUFA and CON after 7 weeks of supplementation (p = 0.88). It was a small effect between the groups after 7 weeks of supplementation (ES = 0.31). After 13 weeks of combined resistance training there was no significant difference and no effect between the groups (p = 0.90, ES = 0.27) There was no difference in percent change between the groups in T1-T2 and T2-T4 (resp. p= 0.95, p = 0.77). There were no significant percent change from T1-T2 to T2-T4 in both groups (PUFA: 1.63 ± 2.87%, p = 0.78, CON: 0.91 ± 1.77%, p = 0.99, Figure 2).

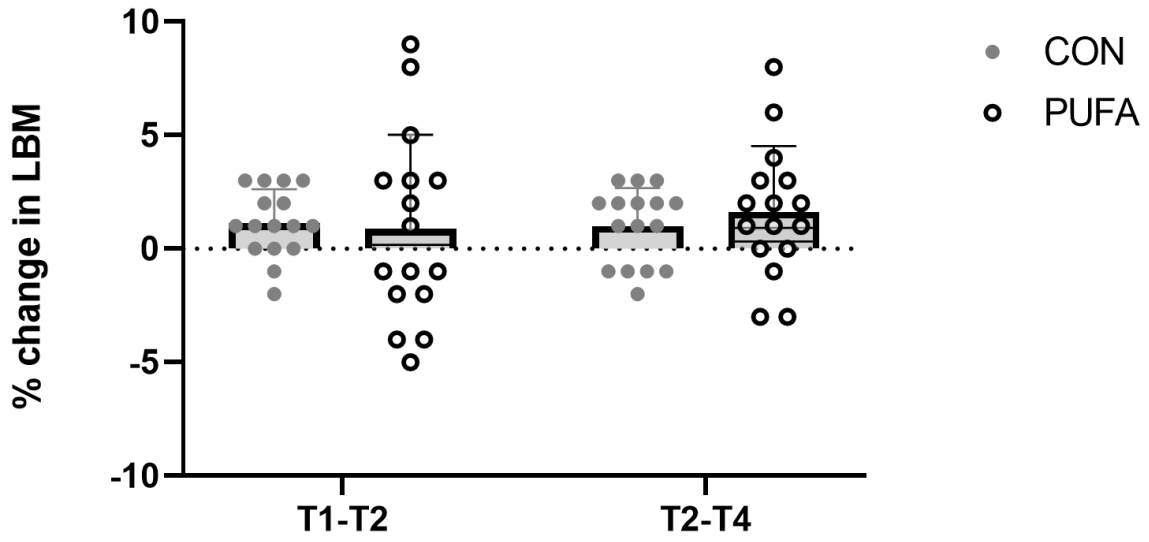

Figure 3: *Individual and summarised percent changes in PUFA and CON in LBM from baseline to pre-training (T1-T2) and from pre-training to post-test (T2-T4) in the intervention period for PUFA and CON.*

4.4 Muscle thickness vastus lateralis

In muscle thickness, after 7 weeks of supplementation there was no significant difference between PUFA and CON (p = 0.80) but there was a small effect between the groups (ES = 0.45). There was no significant difference between the groups after 13 weeks of combined resistance training (p = 0.11) but there was a moderate effect between the groups (ES = 0.71). There was no difference in percent change between the groups in T1-T2 and T2-T4 (resp. p= 0.80, p = 0.11). In PUFA, there was a significant increase in muscle thickness in percent change from T1-T2 to T2-T4 (12.03 ± 10.23%, p = 0.001, Figure 4) and no significant change in CON (6.68 ± 8.78%, p = 0.225).

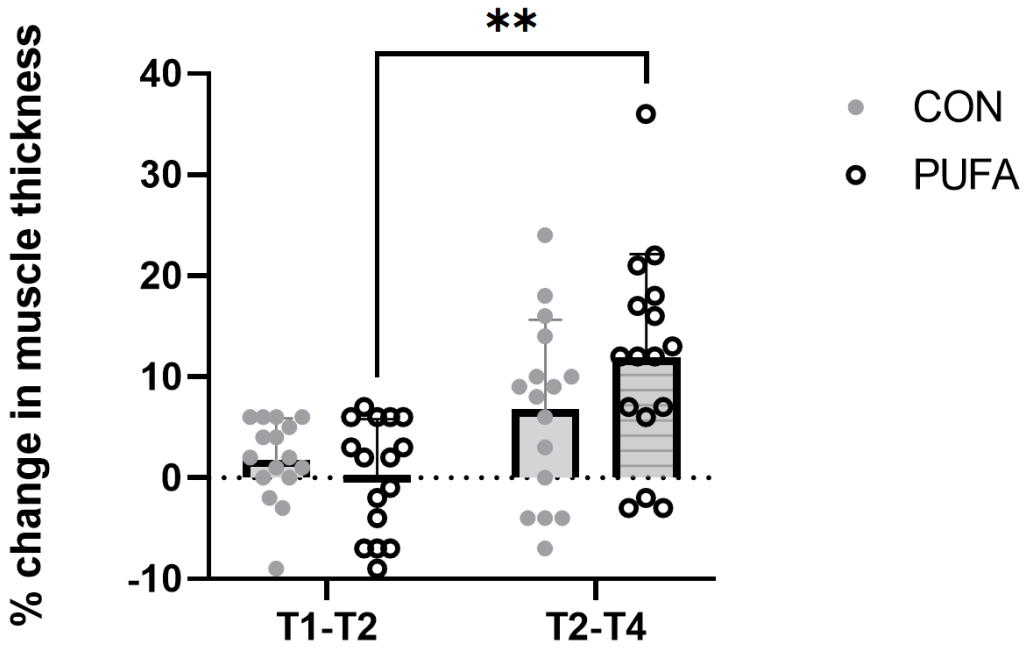

Figure 4: *Individual and summarised percent changes in PUFA and CON in muscle thickness in VL from baseline to pre-training (T1-T2) and from pre-training to post-test (T2-T4) in the intervention period for PUFA and CON. ** = 0.001.*

5. Discussion

The main finding of this study is that after 7 weeks of supplementation, there was no significant increase in isometric strength, muscle thickness or lean body mass between the groups. Nor was any significant difference observed after 13 weeks of combined resistance training in any testing parameters between the groups. However, PUFA had a significant percent change in muscle thickness, and CON had a significant percent change in muscle strength.

5.1 Isometric strength

In this study, we found that there was no significant difference in isometric strength between groups. However, there was a high effect in CON and a small effect in PUFA. A study done by Dalle (2021) found an increase in PUFA and not placebo. Their study used healthy older subjects, whereas we used healthy middle-aged obese. They were supplementing with n-3 PUFA 3g/day with a ratio of 410mg DHA and 540mg EPA (or placebo) for 14 weeks with combined with 12 weeks, 3 sessions per week (3x10-15) of supervised resistance training (Dalle et al., 2021), where we had 23 weeks of n-3 PUFA supplementation with 1g/day with a ratio of 270mg DHA and EPA 500 (or placebo) combined with 13 weeks, 2 sessions a week (3x10) of supervised resistance training. What can be observed is that Dalle (2021) used a high dosage, different training protocol, and older participants. The use of high n-3 PUFA dosage may have something to do with the fact that as you get older, more inflammatory markers increases (Singh & Newman, 2011) and to attenuate loss of muscle mass, it is necessary to do resistance training to gain muscle mass and strength (Mayer et al., 2011). What can be seen in Brook and colleague's study (2021) is that after 6 weeks of resistance training (3 x a week) with n-3 PUFA supplementation (3.7g/day), gave no significant changes in maximum voluntary contraction in both if their groups (Brook et al., 2021). These are similar results in our study, however a difference in their study is the participants. They were healthy older women, and in ours it was healthy middle-aged obese. In our study, there was probably no need for high dosage of n-3 PUFA to reduce inflammation because of lower levels of inflammatory markers (Wyczalkowska-Tomasik et al., 2016). While inflammation can be factor for strength gains, variability in strength after unilateral resistance training is a factor (Hubal et al., 2005). Hubal

and colleagues (2005) found wide ranges in response to resistance training in men and women, all from -32 to +149% in isometric strength (MVC) and some participants showing little to no gains.

Rossato and colleagues (2020) discussed the effects of n-3 PUFA on muscle strength in young- and older adults and did not find enough studies on muscle mass and n-3 PUFA to draw a conclusion that is works (Rossato et al., 2020). The effect of n-3 PUFA on muscle strength should therefore be further investigated, not just on young- and older adults, but also obese.

5.2 Lean body mass

In our study, there was no significant increase in LBM between groups. To our knowledge, there are almost no studies conducted looking at n-3 PUFA and LBM in obese individuals. A meta-analysis done by Delpin and colleagues (2021) who looked at different studies on the general population found no effect of n-3 PUFA on lean body mass. They concluded that studies that further investigate the effect of n-3 PUFA on LBM, should use a higher dosage of n-3 PUFA (>3g day) and be done for a longer period of time (>12 weeks) (Delpino & Figueiredo, 2021). Our study intervention lasted for 23 weeks, but our dosage of n-3 PUFA was set at 1000mg (1g), so by this meaning, if the dosage was higher, it could passably give a better effect on LBM. This is not the case for Smith and colleagues (2015) and Brook and colleagues (2021). In their study, they found no changes in body composition body weight, total-body fat, or intramuscular fat content after either 6 weeks or 6 months of n-3 PUFA therapy with a dosage between 3.7g and 4 g a day (Brook et al., 2021; Smith et al., 2015). There seems to be a correlation between fat mass and inflammation, and this attenuates the possibility of increasing LBM (Bekkelund & Jorde, 2017). However, a study done by Keicolt-Glaser and colleagues (2012) looked at inflammation in healthy middle-age obese for 4 months and saw that with either low dosage of n-3 PUFAs (1.25g /d) or high dosage (2.5g /d), it reduces IL-6 and TNF-α in obese adults. This could make the skeletal muscle more responsive to resistance training and increase LBM.

There are some studies that contradict these findings when using n-3 PUFA supplements on inflammation, such as Deger and colleagues (2016) and Kyriakidou and colleagues (2021). They saw no significant changes between groups when it came to reduction of inflammatory

markers (Deger et al., 2016; Kyriakidou et al., 2021). The methods used in these studies are different. Deger used maintenance hemodialysis patients, with 12 weeks of either n-3 PUFA or placebo (Deger, 2016), and Kyriakidou used healthy males with 4 weeks of n-3 PUFA or placebo. The studies are of short period a small sample size which might have a saying on their findings.

Even if n-3 PUFA does not give any effect on lean body mass, resistance training should have given an effect. There is evidence that resistance training increases lean body mass in overweight, trained, postmenstrual and elderly women, to name a few (Jabekk et al., 2010; Thomas et al., 2021; Vargas et al., 2019). We should have expected some increase in lean body mass in obese individuals. However, there is a study by Álvarez and colleagues (2017) that investigated the effect of response in resistance training in obese women with insulin resistance. They found that not all obese respond after 12 weeks of resistance training. In 49% of these individuals, they found an increase in fat mass, inflammatory markers, and reduced fat-free mass while resistance training (Alvarez et al., 2017). A study done by Wang and colleagues (2006) shows that insulin resistance induces muscle wasting in mice by activation of UPP (Wang et al., 2006). Mice and humans have similar genomes, this could mean similar effect in humans (Emes et al., 2003). If insulin resistance is the case for the participants in this study is not certain but could be a possibility.

In Beals and colleagues (2018) study they looked at MPS in obese individual during resistance training and their findings was that obesity attenuates MPS after resistance training, even after consuming protein (Beals et al., 2018). This can have something to do with the mechanisms of pro-inflammatory markers has on MPS, however this is not clear.

5.3 Muscle thickness

Our study found no significant difference between the groups after 7 weeks of supplementation or combined with 13 weeks of resistance training. This does not match the results from previous studies that see an increase in muscle mass when supplementing n-3 PUFA (Brook et al., 2021; Smith et al., 2015; Strandberg et al., 2019). What can be observed in each mentioned study is that supplementing n-3 PUFA alone or combined, gives an increase in muscle mass.

Our study differs from the others in that we used obese individuals and had a longer intervention period. For muscles to grow, muscle protein synthesis needs to be elevated and this is not something the is measured in this study but is still a contributing for factor for muscle mass. There is a study done by Smith and colleagues (2011) investigating the effects of n-3 PUFA (4g/day) for 8 weeks in healthy older adults, and they saw that muscle protein rate increased in the participants who had n-3 supplementation compared to placebo (Smith et al., 2011). Our study used 1g/day, and since it is a lower dosage than Smith (2011), it might have an influence on how high levels of muscle protein synthesis.

In Brook and colleague's study (2021), they used older women and their study lasted 6 weeks, but they did not see significant change in MPS (Brook et al., 2021). Since we can see that 8 weeks of n-3 PUFA improve MPS more than 6 weeks, it should in theory be an improvement when supplementing for 23 weeks. The mechanism of how n-3 PUFA affect muscle growth is still not clear, but according to a review of Tachtsis and colleagues (2018), n-3 PUFA affect MPS by the activation of mitogen-activated protein kinase (MAPKs), which phosphorylate member of mTOR signalling pathway (Tachtsis et al., 2018). Since this is looked at in this study, we cannot say for sure of this is the case for us or not. Further investigation must be made.

5.4 Practical Implications

BMI is a very good index when used in a population level in general, but it does not necessarily mean that you are obese, in the sense of having high fat mass compared to muscle mass. Before starting the intervention, certain criteria were to be met and one was that the subjects did not train strength training more than once a week and endurance training less than 3h a week (Appendix A). It was specified six months before intervention started. However, it could be that some of the participants trained for years in their youth and then stopped. There is evidence of muscle memory, meaning they would be more responsive to exercise (Snijders et al., 2020). Some of the individuals had physical jobs, for instance farming. Even though they did not exercise with intention, they still lift and do heavy work.

Ultrasound is a reliable test. However, mistake that could be made is human error. The angle, and how hard the probe is pressed against the skin might influence the results.

During the entire intervention, COVID-19 was spreading and infected most of the participants in the last intervention round. The disease causes muscle fatigue because of its effect on the lungs with shortness of breath (Ali & Kunugi, 2021; Lopez-Leon et al., 2021). This might then be a contributing factor for how the participants responded to resistance exercise while ingesting n-3 PUFA.

A systematic review and meta-analysis done by Snachez-Remirez and colleagues on COVID-19 and its effects on the human body, showed that the most common effect is fatigue and reduced physical capacity (Sanchez-Ramirez et al., 2021). A review by Ali & Kunugi (2021) explains the possible mechanisms of why COVID-19 can be damaging for the skeletal muscle. Even though its dynamics is unclear, it might create are more inflammatory milieu for individuals that are more likely to get COVID-19 (Ali & Kunugi, 2021). This might be a contributing factor to as of why the participants did not gain more muscle mass or strength.

5.5 Conclusion

In conclusion, the present study demonstrates that 7 weeks of n-3 PUFA supplementation does not increase isometric strength, lean body mass or muscle thickness in vastus lateralis in obese individuals compared to placebo. After 13 weeks of combined resistance training, there was no significant difference between PUFA and CON in any test parameters. There was no significant increase in lean body mass in either group. However, there was a significant change is isometric strength in CON and not PUFA, and a significant change in muscle thickness in PUFA and not in CON. What the effects of n-3 PUFA does for muscle mass or strength are still not clear and should be studied further by also looking at muscle protein synthesis and inflammatory markers.

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Appendix A Written informed consent

Appendix A (Vedlegg 1): Written informed consent (Samtykkeskjema)

Høgskolen i Innlandet

FORESPØRSEL OM DELTAKELSE I FORSKNINGSPROSJEKTET

ALFA OG OMEGA I LIVSSTILSTERAPI

- STYRKETRENING OG OMEGA-3 SUPPLEMENTERING FOR FORBEDRET HELSE OG MUSKELFUNSJON MED I INDIVIDER MED OVERVEKT OG FRISKE KONTROLLER

Dette er et spørsmål til deg om å delta i et forskningsprosjekt for å undersøke hvordan økt fettmasse og omega-3 supplementering påvirker muskelmassen ved styrketrening. Du får dette informasjonsskrivet fordi du har vist interesse for studien.

For å delta i studien må du være mellom 30 og 60 år og være utrent (trene styrke mindre enn en gang i uken og utholdenhet mindre enn 3 timer i uken). Personer med ustabil kardiovaskulær sykdom, sykdom eller skade som hindrer tung styrketrening, sykdom i muskel- skjelettsystemet, alvorlige mentale lidelser, allergi mot lokalbedøvelse, røykere eller personer som har brukt medisiner eller preparater med steroider de siste to månedene vil bli ekskludert fra studien.

Fedme rammer hver femte voksne person i Norge og er forbundet med en rekke helseutfordringer. Blant disse utfordringene er tap av muskelmasse, -kvalitet og funksjon, noe som bidrar til å redusere livskvaliteten. Fedme gir også en rekke andre fysiologiske endringer som kan bidra til å redusere responser på livsstilterapi med trening. Personer med fedme oppnår ikke de ønskede forbedringene i muskelfunksjoner og helsetilstand som typisk medfølger slik terapi. Vi vet lite om hvorfor, men det er trolig flere grep som kan tas for å øke effekten av treningen. Vi kan endre kroppens indre miljø, slik at den blir mottakelig for trening. Dette kan for eksempel gjøres gjennom endringer i kosthold. Vi kan også ta i bruk alternative treningsmetoder som omgår den iboende motstanden mot vekst i muskulaturen. Sannsynligvis vil en kombinasjon av slike terapier (kombinasjonsterapi) føre til bedret trenbarhet. Hovedmålet med denne studien er å skaffe kunnskap om hvordan livsstilterapi kan optimaliseres for å omgå de fysiologiske utfordringene knyttet til fedme. Dette skal vi gjøre gjennom å kombinere inntak av et omega-3 supplement med to ulike styrketreningsprotokoller. De to protokollene gjennomføres på hvert sitt bein innad i deltakerne. Det ene beinet vil da trene 3 sett med 10 repetisjoner og det andre vil trene 3 sett med 30 repetisjoner. Sammenligningen innad i en deltaker fjerner forskjeller i genetikk, kosthold og livsførsel mellom treningsprotokollene og gjør det lettere å finne eventuelle forskjeller.

HVA INNEBÆRER PROSJEKTET?

Deltakere i prosjektet skal deles i to grupper: en intervensjonsgruppe og en referansegruppe. Intervensjonsgruppen skal innta enten omega-3 eller placebo, gjennomfører alle tester og gjennomføre 13 uker med styrketrening. Referansegruppen skal gjennomføre noen av testene og skal ellers fortsette å leve sitt vanlige liv. For intervensjonsgruppen består prosjektet av tre perioder (se figur 1). Periode 1 går over 7 uker hvor du inntar omega-3 tilskudd eller placebo uten å gjøre andre endringer i livsførselen din.

Supplementeringen med omega-3 eller placebo fortsetter også gjennom de to neste periodene. Periode 2 er tilvenning til styrketrening og varer i 3 uker. Periode 3 er et styrketreningsprogram på 10 uker hvor hele kroppen trenes to ganger per uke. I periode 2 og 3 får du personlig oppfølging av en av våre bachelor- eller masterstudenter på alle økter. Før og etter hver av periodene gjennomføres en rekke tester for å måle effekten av omega-3 supplementeringen og styrketreningen (se tabell 1). I periodene med trening vil det være to oppmøter i uken og øktene vil vare ca 1 time. I ukene med testing vil det være 2-3 oppmøter i uken. Det vil være mulig å trene både på dagtid og ettermiddag.

Deltakere i referansegruppen vil få tilbud om å livsstilveiledning etter endt prosjektdeltakelse og vil få tilbud om en periode med veiledet styrketrening.

Gjennom prosjektperioden kan du ikke bruke kosttilskudd som inneholder omega-3. Antall fiskemiddager skal begrenses til en middag med hvit fisk per uke.

I prosjektet skal vi innhente og registrere opplysninger om deg gjennom følgende tester (se figur 1 for tidspunkter)

Tabell 1: Oversikt over tester og tidspunkt for intervensjonsgruppene og referansegruppenlgruppen

Intervensjonsgruppe	**Referansegruppe**

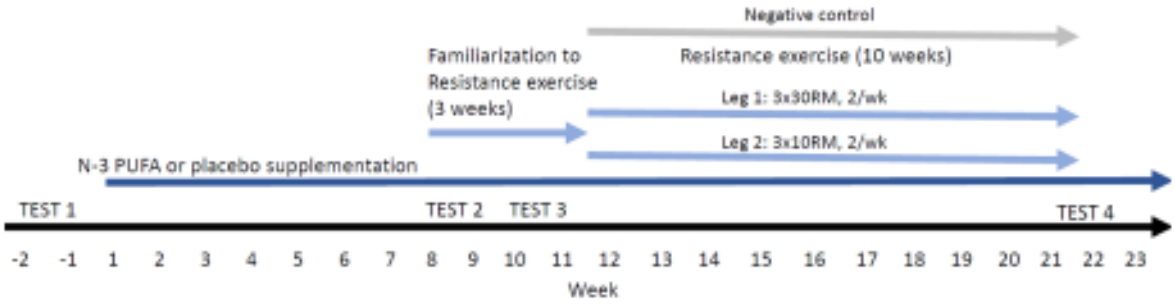
• Styrketester i beinpress og kneekstensjon (2xT1, 2xT2, T3, T4)
• Utholdenhetstester
  ○ 6 minutters step test (TEST 1, 2, 4)
  ○ Sykkeltest på ett bein (TEST 2, 4)
• Måling av kroppssammensetning med DXA-scan (TEST 1, 2, 3, 4)
• Måling av muskeltverrsnittsareal og fettinfiltrasjon med MR (TEST 2, 4)
• Måling av midjeomkrets (TEST1, 2, 4)
• Måling av muskeltykkelse i låret med Ultralyd (TEST 1, 2, 3, 4)
• Oral glukosetoleransetest (TEST 1, 2, 4)
• Blodprøver (TEST 1, 2, 3, 4)
• Biopsier (TEST 1, 2, 3, 4)
• Inntak av deuterium for måling av muskelproteinsyntese i lårmuskulaturen (tre siste ukene av treningsperioden)
• Blodtrykk (TEST 1, 2, 4)
• Spørreskjema om helse, muskel- og skjellet-plager (TEST 1, 2, 4)
• Kostregistreingsskjema (TEST 1, 2, 4)
• Avføringsprøver (TEST 1, 2, 4)
	• Styrketester i kneekstensjonsapparat
	• Måling av kroppssammensetning med DXA-scan (TEST 2, 4)
	• Oral glukosetoleransetest (TEST 2, 4)
	• Blodprøver (TEST 2, 4)
	• Spørreskjema om helse, muskel- og skjellet-plager (TEST 2, 4)

Testene vil fordeles på to testdager som vil ta ca 2-3 timer hver. Testdag 1 må gjøres på dagtid da flere av testene (blodprøve, DXA og biopsi) denne dagen må gjøres fastende. Testdag 2 kan gjøres på dagtid og ettermiddag.

Hensikten med de ulike testene

Flere studier finner at personer med overvekt ser ut til å ha en redusert evne til å bygge muskler og bli sterkere ved styrketrening. Det er også mulig at de to ulike treningsprotokollene (3x10 og 3x30) vil gi ulik effekt. For å undersøke disse spørsmålene måler vi effekten av styrketrening og omega-3 på styrke (beinpress og to typer

kneekstensjon), utholdenhet (6 minutters step-test og ettbeins sykling) og muskelmasse (DXA, ultralyd, MR og muskelvekst ved hjelp av deuterium og muskelvekst på cellenivå i biopsiene) med flere ulike tester. Videre ønsker vi å undersøke effektene av styrketreningen på flere helsevariabler knyttet til overvekt og risikofaktorer for diabetes og hjerte-karsykdom (oral glukosetoleransetest, blodprøver, blodtrykk midjemål og fettmasse). Biopsiene fra låret kan hjelpe oss å forklare mekanismene (for eksempel: hvilke gener som slås av og på og hvordan cellene virker) bak endringene og eventuelle forskjeller vi finner i styrke og muskelvekst. I tillegg til det som skjer inne i muskelfibrene vil muskelveksten være avhengig av det miljøet som er rundt muskelen. To viktige bidragsytere til dette miljøet er betennelse, som ofte er økt ved overvekt, og kommunikasjon fra andre vev via signaler som inngår i det vi kaller metabolomet. Betennelsesstatus og metabolomet blir målt i blodprøvene. To viktige bidragsytere til både betennelse og metabolomet er fettvev og bakteriene i tamen, som begge påvirkes negativt av overvekt. Tidligere studier viser at omega-3 kan ha en positiv effekt på tarmbakteriene og fettvevet og derigjennom bidra til bedre helse og bedre forhold for muskelvekst. For å forstå hvordan tarmbakteriene påvirkes av trening og omega-3 og igjen potensielt påvirker treningseffekt tar vi også avføringsprøver. Kosthold er en faktor som påvirker effekten av trening samt de fleste andre målene i denne studien. Vi gjør derfor 3 runder med kostregistrering gjennom studien. Overvekt fører ofte med seg plager blant annet i form av muskel- og skjelettplager, endret mage- tarmfunksjon og kan også påvirke livskvaliteten. Ved hjelp av flere spørreskjema ønsker vi å undersøke om styrketrening i kombinasjon med omega-3 kan redusere muskel- og skjelettplager, gastrointestinale plager og forbedre livskvaliteten.



Figur 1: Oversikt over studien

MULIGE FORDELER OG ULEMPER

Totalt vil det tas 4 biopsier fra hvert bein i intervensjonsgruppen og 2 i hvert bein for referansegruppen. Noen vil synes denne typen vevsprøver er ubehagelig. Man blir typisk støl i muskulaturen i 1-2 dager etter biopsien. Inngrepet vil etterlate små arr, som hos de fleste forsvinner med tiden. I svært få tilfeller vil biopsitakning kunne føre til at følelsen i huden rundt biopsien forsvinner over en lengre periode. Biopsitaking er også forbundet med en viss infeksjonsfare. Risikoen for disse komplikasjonene er svært liten ved bruk av prosedyrene som benyttes i dette prosjektet. Biopsiene tas fra lårmuskelen på utsiden av låret ca midt mellom kneet og hoften. Vi setter først en dose lokalbedøvelse (samme type som hos tannlegen) før vi steriliserer området. Selve biopsien tas med en nål med en diameter på 2,1 millimeter som føres inn i lårmuskelen. For å få nok vev må vi inn 2-3 ganger i samme hull ved hvert testtidspunkt. Du vil få klare instrukser om hvordan du skal behandle såret i etterkant av prøvetagningen. Blodprøvene i studien anses ikke å ha noen risiko.

For å kunne måle hvor raskt nye proteiner bygges inn i muskulaturen må du i løpet av de tre siste ukene i prosjektet innta en større og to mindre doser med tungtvann. Det er ingen kjente helsekonsekvenser ved inntak av de dosene som anvendes i studien, men lett svimmelhet kan forkomme. For å unngå dette vil dosen fordeles over flere inntak og du vil følges opp av testpersonalet i perioden hvor svimmelhet kan inntreffe.

Styrketreningen vil mest sannsynlig føre med seg helsemessige forbedringer. I tillegg forventer vi en gjennomsnittlig økning i muskelmasse på ca. 2 kg for deltakerne i studien. Deltakelse i studien vil kunne gi mer kunnskap og erfaring med styrketrening og kan bidra til å etablere trening som en rutine i hverdagen. Deltagelse i studien vil gi mulighet til å gjennomføre en rekke tester du ellers ikke ville hatt tilgang til.

Skulle vi oppdage noe som avviker fra det vi forventer og/eller gir oss mistanke om helseproblemer vil det bli tatt initiativ til videre medisinsk oppfølging.

FRIVILLIG DELTAKELSE OG MULIGHET FOR Å TREKKE SITT SAMTYKKE

Det er frivillig å delta i prosjektet. Dersom du ønsker å delta, undertegner du samtykkeerklæringen på siste side. Du kan når som helst og uten å oppgi noen grunn trekke ditt samtykke. Dersom du trekker deg fra prosjektet, kan du kreve å få slettet innsamlede prøver og opplysninger, med mindre opplysningene allerede er inngått i analyser eller brukt i vitenskapelige publikasjoner. Dersom du senere ønsker å trekke deg eller har spørsmål til prosjektet, kan du kontakte Håvard Hamarsland (tlf: 93445916, mail: havard.hamarsland@inn.no) eller Stian Ellefsen (tlf: 97666521, mail: stian.ellefsen@inn.no).

HVA SKJER MED OPPLYSNINGENE OM DEG?

Opplysningene som registreres om deg skal kun brukes slik som beskrevet i hensikten med prosjektet. Du har rett til innsyn i hvilke opplysninger som er registrert om deg og rett til å få korrigert eventuelle feil i de opplysningene som er registrert. Du har også rett til å få innsyn i sikkerhetstiltakene ved behandling av opplysningene.

Alle opplysningene vil bli behandlet uten navn og fødselsnummer eller andre direkte gjenkjennende opplysninger. En kode knytter deg til dine opplysninger gjennom en navneliste. Det er kun prosjektmedarbeiderne i studien som har tilgang til denne listen.

Opplysningene om deg vil etter endt prosjekt flyttes over i en generell biobank (se senere) og anonymisert innen 31.12.2028.

HVA SKJER MED PRØVER SOM BLIR TATT AV DEG?

Alle blod- og vevsprøver, samt øvrig informasjon som innhentes i prosjektet, inklusiv informasjon som blir utledet fra det biologiske materialet, vil bli lagret i kodet tilstand i en forskningsbiobank tilknyttet prosjektet og vil ved prosjektslutt bli overført til den generelle biobanken «The TrainOME – humane cellers tilpasning til trening og miljø» (REK-id: 213483), situert ved Høgskolen i Innlandet/Sykehuset Innlandet. TrainOME-prosjektet er igangsatt for å avdekke sammenhenger mellom individers tilpasningsevne til trening, også kalt trenbarhet, og kroppslige/cellulære særtrekk. Gjennom den generelle biobanken skal prøvene analyseres sammen med prøver fra en rekke andre prosjekter, hvor den overordnete målsettingen er å studere faktorer som er bestemmende for generell trenbarhet. Dette innebærer generell analyse av cellebiologiske og genetiske trekk som for eksempel cellers form/utseende/evne til å dele seg og vokse, arvematerialets sammensetning (inklusiv DNA-sekvens og epigenetisk modifisering), proteinsyntese, proteinforekomst og -funksjon, RNA-uttrykk og -regulering, hormonforekomst, kroppens indre miljø (metabolomet), og mange flere mål. Det biologiske materialet vil bli anonymisert innen 31.12.2038, hvorpå det vil bli destruert innen fem år. Forskningsdata som har blitt utledet av materialet vil deretter bli oppbevart i anonymisert tilstand på sikker server på ubestemt tid, sammen med øvrige data innhentet i prosjektet. Professor Stian Ellefsen er hovedansvarshavende for forskningsbiobanken.

Noen analyser skal gjøres hos samarbeidspartnere ved andre institusjoner. Analyse av muskelproteinsyntese skal gjøres ved universitetet i Birmingham i England. Analyse av muskelcellenes evne til å vokse, spesialisere seg og dele seg skal gjøres ved Universitet i Oslo (cellene holdes i live etter biopsitaking og er gjenstand for eksperimenter på laboratoriet). Prøvene som blir sendt til våre samarbeidspartnerne vil være kodet. Det vil dermed ikke være mulig å finne tilbake til din identitet basert på prøvene alene. Eventuelle restmaterialer fra analysene vil enten bli destruert eller returnert til oss etter at analysene er gjennomført (senest innen 31.12.2026).

GENETISKE UNDERSØKELSER

Det vil bli innhentet informasjon om din genetiske sammensetning. Denne informasjonen skal primært gi innsikt i sammenhengen mellom individuelle responser på styrketrening, målt som muskelvekst, og individuell genetisk variasjon. Altså å forstå hvorfor noen responderer bedre på styrketrening enn andre. Dette perspektivet er forankret i målsettingen med den generelle biobanken "Trainome - humane cellers tilpasning til trening og miljø" (REK-id: 2013/2041), hvortil prøvene skal overføres etter prosjektlutt. Forståelse for hvilken rolle ulike gener spiller for muskelvekst er på et tidlig stadium. Det er derfor ikke mulig å gi genetisk veiledning basert på analysene i studien. Det skal ikke gjøres analyser som kobler enkeltmutasjoner til bestemte helseutfordringer. Genetiske data er unike og er derfor i prinsippet ikke anonyme, selv om koblingsnøkkelen som kobler deg til dine data blir slettet. Alle genetiske data (inkludert transkriptomdata) skal oppbevares på sikker server hos Tjenester for sensitive data (TSD).

FORSIKRING

Som deltaker i studien er du forsikret gjennom Høgskolen Innlandets forsikring hos Gjensidige.

OPPFØLGINGSPROSJEKT

Det kan bli aktuelt med et oppfølgingsprosjekt for å undersøke reproduserbarheten i treningsrespons. I den sammenheng vil deltakere kunne bli kontaktet igjen etter endt studie med informasjon om oppfølgingsstudien.

ØKONOMI

Studien og biobanken er finansiert gjennom forskningsmidler fra Høgskolen i Innlandet og Sykehuset Innlandet. Det finnes ingen økonomiske egeninteresser og alle som deltar som forskere og prosjektmedarbeidere, mottar kun vanlig lønn i løpet av prosjektperioden. Rimfrost AS har bidratt med omega-3 og placebo til studien. Rimfrost AS har skriftlig frasagt seg alt ansvar og rett til å påvirke resultat eller publikasjoner som resulterer fra prosjektet.

GODKJENNING

Regional komité for medisinsk og helsefaglig forskningsetikk har vurdert prosjektet, og har gitt forhåndsgodkjenning (2019/818)

Etter ny personopplysningslov har behandlingsansvarlig Høgskolen innlandet og prosjektleder Håvard Hamarsland et selvstendig ansvar for å sikre at behandlingen av dine opplysninger har et lovlig grunnlag. Dette prosjektet har rettslig grunnlag i EUs personvernforordning artikkel 6 nr. 1a og artikkel 9 nr. 2a og ditt samtykke.

Du har rett til å klage på behandlingen av dine opplysninger til Datatilsynet.

KONTAKTOPPLYSNINGER

Dersom du har spørsmål til prosjektet kan du ta kontakt med Håvard Hamarsland, tlf: 93445916, epost: havard.hamarsland@inn.no.

Personvernombud ved institusjonen er Anne Sofie Loftshus (anne.lofthus@inn.no).

JEG SAMTYKKER TIL Å DELTA I PROSJEKTET OG TIL AT MINE PERSONOPPLYSNINGER OG MITT BIOLOGISKE MATERIALE BRUKES SLIK DET ER BESKREVET

Sted og dato

Deltakers signatur

Deltakers navn med trykte bokstaver