Sara Hildesdatter Knudsen

Effect of high-intensity interval training on cardiorespiratory fitness and body composition for women with lipedema

Master's thesis in Clinical Health Science

Supervisor: Anja Bye

Co-supervisor: Arnt Erik Tjønna and Siren Nymo

May 2023



Sara Hildesdatter Knudsen

Effect of high-intensity interval training on cardiorespiratory fitness and body composition for women with lipedema

Master's thesis in Clinical Health Science

Supervisor: Anja Bye

Co-supervisor: Arnt Erik Tjønna and Siren Nymo

May 2023

Norwegian University of Science and Technology Faculty of Medicine and Health Sciences Department of Circulation and Medical Imaging



Acknowledgment

This master's thesis is a part of my master's in clinical health science, at the Norwegian University of Science and Technology (NTNU) in Trondheim. I would like to thank my supervisor Anja Bye for always being available to questions and for the guidance with the writing. I would also like to thank my co-supervisor Arnt Erik Tjønna for being patient with all the questions and for always being available when we needed help in the lab.

I also need to thank my fellow students for interesting years with frustration and joy during the study period.

Thank you to all the participants in the training group that met in a good mood and were motivated and showed up to the supervised exercises and thank you to the participants in the control group.

Abstract

Background: Lipedema is a chronic disorder first described by Allen and Hines in 1940 and is characterized by symmetric enlargement of painful subcutaneous fat in the limbs, primarily affecting females. The lipedema fat may be resistant to reduction through diet and exercise and often has a genetic component. Lipedema has four stages and five types based on the distribution of fat. Patients with lipedema experience discomfort, tenderness, and easy bruising, which can progress to high pain and limited mobility. Lipedema is often underdiagnosed and frequently misdiagnosed as obesity or lymphedema, leading to delayed diagnosis and treatment. High-intensity interval training (HIIT) has gained popularity due to its time efficiency and involved alternating between periods of high intensity and recovery. HIIT has been found to have positive effects on various physiological parameters such as aerobic capacity, triglyceride concentration, and fat-free mass. Studies have shown that HIIT effectively improves fasting blood glucose concentrations, reduces blood pressure, and promotes weight loss in individuals with overweight or obesity.

Aim: The aim was to evaluate the effect of 8-week HIIT on cardiorespiratory fitness and body composition for women with lipedema.

Methods: This is a randomized control trial with 22 participants that were randomized to an exercise group and a control group for comparison. The exercise group conducted an 8-week-long exercise period and the control group lived as normal.

Results: There was no significant difference between the HIIT group and the control group on the VO_{2peak} test, but there was a significant increase (p=0.043) in the HIIT group with 10,2%. There was no significant difference between the HIIT group and the control group for the body composition measurements, however, there was a significant decrease (p=0.018) for the HIIT group in fat distribution in the trunk. There was a significant increase (p=0.008) for the control group in fat distribution in the trunk.

Conclusion: There is a need for more research on this topic to conclude. There is a need for more research with a greater sample size for exercise and its effect on cardiorespiratory fitness and body composition for women with lipedema.

Sammendrag

Bakgrunn: Lipødem er en kronisk sykdom som ble først beskrevet av Allen og Hines i 1940 og karakteriseres med symmetrisk og overflødig fettvev på begge sider i bein og armer som primært rammer kvinner. Lipødem fettet kan være motstandsdyktig for trening og dietter, det har også ofte en genetisk komponent. Lipødem har fire stadier og fem typer basert på fordelingen av fettet. De som har lipødem opplever ubehag, ømhet, og kan lett få blåmerker som kan føre til mye smerte og begrenset mobilitet. Lipødem er ofte underdiagnostisert og feil diagnostisert som fedme eller lymfødem, som fører til forsinket diagnose og behandling. Høy intensitet intervall trening (HIIT) har blitt populært på grunn av at det er tidseffektivt og involverer vekslende perioder med høy intensitet og aktive pauser. HIIT har positive effekter på flere fysiologiske parametere som aerob kapasitet, triglyserid konsentrasjon og fett-fri masse. Studier viser at HIIT er effektiv for å forbedre fastende blodsukker konsentrasjon, redusere blodtrykk og fremme vekttap for individer med overvekt og fedme.

Formål: Målet med studien var å evaluere effekten av 8-uker med HIIT på kroppssammensetning og oksygen opptak for kvinner med lipødem.

Metode: Randomisert kontrollert studie med 22 deltakere som ble randomisert til en treningsgruppe og en kontrollgruppe. Treningsgruppen hadde en 8-ukers lang treningsperiode og kontroll gruppen levde som normalt.

Resultat: Det var ingen signifikant forskjell mellom HIIT gruppa og kontroll gruppa for resultatet på VO_{2peak} testen, men HIIT gruppa hadde en signifikant økning (p=0.043) i oksygen opptak. Det var ingen signifikant forskjell mellom HIIT gruppa og kontroll gruppa på målingene som ble gjort på kroppssammensetning. HIIT gruppa hadde likevel en signifikant nedgang (p=0.018) på målingen for fett i overkroppen, mens kontroll gruppa hadde en signifikant økning (p=0.008) på målingen for fett i overkroppen.

Konklusjon: Det trengs mer forskning på dette temaet for å gjøre en konklusjon. Det trengs mer forskning med større utvalgsstørrelse på effekten av trening på oksygen opptak og kroppssammensetning.

Contents

Ac	knov	wledgment	i
ΑŁ	stra	ct	ii
Sa	mme	endrag	iii
Co	nten	ıts	iv
1	Int	roduction	1
	1.1 1.2	Lipedema High-intensity interval training	
2	Ain	n	3
3	Me	thods	4
	3.1 3.2 3.3 3.4 3.5 3.6 3.7 3.7 3.8 3.9 3.10 3.11	Study design Study participants Intervention – Training protocol Peak oxygen uptake (VO _{2peak}) Anthropometric and body composition measurements Blood pressure Questionaries form I.1 RAND-36. I.2 LYMQOL I.3 Brief pain inventory Standard blood analyses Physical activity habits. Ethics Statistical analysis	4 5 6 7 8 8 8 8
4	Res	sults	
	4.1 4.2 <i>4.2</i> 4.2 4.3	· · · · · · · · · · · · · · · · · · ·	11 11 12
5	Dis	cussion	15
	5.1 <i>5.1</i> <i>5.1</i> 5.2	, ,	16 16
6	Cor	nclusion	20
Re	fere	nces	21
۸ -	none	divac	22

1 Introduction

1.1 Lipedema

It was Allen and Hines that first described lipedema in 1940 as: "abnormally poor resistance to the passage of fluid into the tissue from the blood thus permitting edema to occur" (1). Lipedema is characterized by symmetric enlargement of nodular, painful subcutaneous adipose tissue in the limbs, sparing the hands, feet, and trunk. The unique about lipedema fat is that it is resistant to reduction by diet and exercise (1). Lipedema is a chronic disorder, and it generally manifests during puberty, although it can appear at other times of hormonal change such as childbirth or menopause. This evidence plus the predominant occurrence of lipedema in females suggests the importance of sex hormones in the development of this disorder (1). Suggesting a genetic disorder because lipedema often affects several female members of the same family. Positive family history is common and ranges between 16% and 64%, the number is likely higher due to under-diagnosis (2). Lipedema is different from overweight/obesity because the location of the fat is primarily abdominal or spread widely over the body in obesity compared to lipedema where the fat is symmetrically distributed in the lower extremities. The texture of the skin is also different for overweight/obese and lipedema, thin and soft in lipedema and thicker in obesity (3).

There are four stages and five types of lipedema. Figure 1 shows the four stages of lipedema. With stage one the skin can be smooth, but the underlying fat is increased and contains pearl-sized nodules, with stage two the skin can be indented over pearl-sized fat nodules and larger fat masses (1). With stage three the skin can contain divots and folds over pearl-sized fat and larger fat masses with characteristic deforming fat lobules (1). Stage four is characterized by the development of lymphedema with lipedema better known as lipo-lymphedema and can occur with any stage (1). Figure 2 shows the five types of lipedema. Type one occurs around the hips and buttocks, type two goes from the waist to the knees like riding breeches, and type three goes from the waist to the ankles. Approximately 80% of women with lipedema have type four that involves their arms, therefore this type of lipedema occurs jointly with lipedema affecting the legs and is often combined with type two and three (1). There is not often seen lipedema fat that dominates on the lower legs (1).

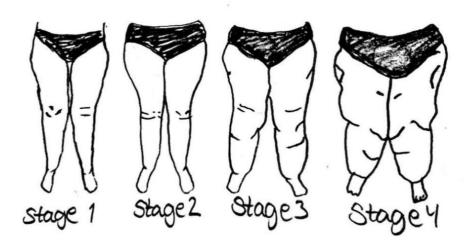


Figure 1. Lipedema stages.

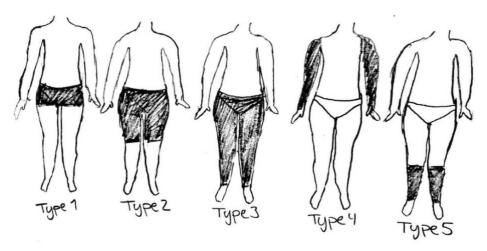


Figure 2. Lipedema types.

Patients with lipedema often experience discomfort, easy bruising, and tenderness of the disproportionately enlarged legs, which may progress to high pain and limited mobility (4). The exact reason why lipedema patients get easy bruising is not yet been established, although it's widely reported by patients with lipedema (5). Pain and tenderness of lipedema tissue are thought to be caused by inflammation in subcutaneous tissue. Lipedema patients also struggle with a lack of understanding, low self-esteem, feeling of hopelessness, and a decreased level of quality of life (6).

Lipedema affects around 11-19% of the female population. These estimates are thought to understate the true prevalence of the disease given its frequency of misdiagnosis and late diagnosis (7). Lipedema is often misdiagnosed as obesity or lymphedema, which it shares several features with. Lipedema involves abnormal deposition of subcutaneous adipose tissue, leading to a bilateral, disproportional volume increase of lower extremities and, in some cases, of arms (8). The diagnosis is often misdiagnosed or underdiagnosed by health care providers because it's no clear diagnostic methods or protocols for lipedema that are available, so to set the diagnosis are physical examination used (6). In many cases, the correct diagnosis is made after many years when the patient has significant limitations, instead of at the beginning of the disease. Because of the lack of proper education and early conservative treatment, it takes time to get the diagnosis, and this can lead to disabilities. Patients affected by this condition experience various ailments that have an immense impact on their daily functioning (6).

Treatment of lipedema is complicated, some studies have investigated the possibility to use physiotherapy and rehabilitation, which are recommended to improve the long-term prognosis of lipedema. The treatment is divided into conservative treatment (non-invasive) and invasive treatment (9). Correct diagnosis and treatment approaches help to prevent possible complications. Physiotherapy and rehabilitation treatment aims to control edema, reduce pain and hypersensitivity, increase the level of physical activity, and improve quality of life. Physicians, physiotherapists, and patients need more information and training about the diagnosis and treatment of lipedema. Complex Decongestive Physiotherapy (CDP) is seen as the gold standard in the conservative treatment of lipedema. CDP has four components of treatment for reducing and controlling edema. The four components are manual lymphatic drainage (MLD), compression garments, physical exercise, skincare, and self-management (9). As mentioned earlier it's a diagnosis where the fat in the legs is not reduced by diet and

exercise, but there are benefits of doing physical activity and many clinics recommend patients with lipedema to be physically active independently from the severity of the disease (10). For women with lipedema, it's important to be in regular physical activity because it can lead to improved blood circulation, and this will lead to less inflammation in the adipose tissue (11).

1.2 High-intensity interval training

Regular physical activity is recommended as an effective lifestyle strategy for weight management and health promotion. Lack of time is a frequently reported barrier contributing to poor attendance and adherence to exercises (12).

In this study high-intensity interval training (HIIT) is being used as an exercise modality, this method has become a popular exercise method due to its time efficiency. HIIT consists of alternating periods of high intensity and active recovery. HIIT as a training method is shown to be effective in improving fasting blood glucose concentrations and reducing blood pressure for individuals with overweight or obesity (13). HIIT also shows an improvement in aerobic capacity and triglyceride concentration and fat-free mass, with an increased lower limb muscle power as a benefit for both young and older individuals (13).

Maillard et.al. (14) showed that HIIT significantly reduces whole-body fat mass. They also showed a significant reduction in total, abdominal, and visceral fat mass. High-intensity training seems more likely to reduce whole-body adiposity and exercises with lower intensity were shown to be more successful in reducing abdominal and visceral fat mass. Reducing central adiposity for individuals with overweight/obesity could contribute to decreasing the risk of cardiovascular disease. HIIT could lead to greater adipose tissue loss than low/moderate continuous training. Its typically very challenging to reduce the size of their legs through diet and exercise for women with lipedema, which is often not the case in women with obesity (15). A study done by Kessler et.al. (16) concluded that HIIT is an effective exercise method to improve some cardiometabolic risk factors such as body mass index, percentage body fat, and insulin sensitivity, as well as peak aerobic capacity.

2 Aim

This study aimed to evaluate the effect of high-intensity interval training (HIIT) on body composition and cardiorespiratory in women with lipedema. We hypothesized that the exercise would change their body composition, especially in the lower body.

3 Methods

3.1 Study design

This was a randomized control trial, with an intervention group and a control group for comparison. The intervention lasted for 8 weeks with the HIIT program for the intervention group and the control group was going to live as normal.

3.2 Study participants

Twenty-two women diagnosed with lipedema aged 18-65 with a BMI 25-35 were randomized to (1:1) a training group and a control group to an 8-week intervention. Figure 3 shows a flow chart of the participants. The exclusion criteria that were set from the start included ongoing eating disorders and/or orthopedic limitations for exercise training on a treadmill. Compliance with the training program of 80% was set as a criterion for completing the study for the intervention group.

Participants were recruited via social media, physiotherapists, posters at GPs, and a user representative from the Norwegian Lymphedema and Lipedema Association (NLLF). The potential participants got at least one week to consider their participation and to sign the consent form. The pretest started with a short conversation and a few questions were asked and documented in eFORSK, a tool for collecting data for clinical trials and an online randomization tool (17). The questions asked were; where the participants first heard about the study, when they got diagnosed with lipedema, and where they got the diagnosis. They also got questions about comorbidities, if they use any kind of medicines, and if they have used some of the medicine in the last 24 hours. There were also collected data on which clinical aids they were using for the lipedema and how often, or if they used equipment, e.g., compression garments, and pulsator. The participants also got some questions about their physical activity habits.

Out of the 22 participants (figure 4) who conducted the pretest, two participants withdrew from the study after the pretest the control group, and 9 participants in the control group completed the posttest. In the HIIT group, 4 participants withdrew after conducting the pretest, and 7 participants completed the HIIT program. In total, there was 6 participant that withdraw from the study after the pretest.

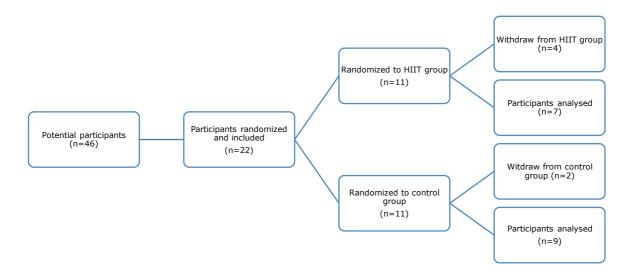


Figure 3. Flow chart over participants. n=numbers of participants.

3.3 Intervention – Training protocol

For the intervention, the women were randomized (1:1) to eight weeks of supervised high-intensity interval training (HIIT) or a control group. HIIT was performed in 4x4 min intervals by walking or running at 85-95% of maximal heart rate (HR_{max}) with 3-minute active recovery (60-70% of HR_{max}) in between intervals. This exercise was performed twice a week on treadmills at the NextMove core facility at NTNU and one exercise they conducted at home. All participants were provided with an activity watch (Fitbit Luxe, California, USA) to keep after the study was completed. The participants in the exercise group were provided with the activity watch at the first exercise and the participants in the control group were provided with the activity watch after they finished the posttest. The HIIT group got recommended to do pool training for the home exercise, and compression garments for the exercises based on the potential benefits of compression garments. Randomization to an intervention group or control group was performed by using eFORSK (17). Body composition, blood pressure, VO_{2max} (maximal oxygen uptake), questionnaire data, and blood samples were measured/collected at the pretest and the posttest. The control group lived like normal and did not change their dietary pattern or exercise habits during their participation in the study.

In Appendix II there is an example of the form that was used to monitor the progression of the exercises for the participants in the HIIT group. In the form the treadmill incline, velocity, heart rate, and rating on the Borg scale after each 4-minute interval and after the 3-minute active breaks were documented. Subjective perception of exertion was assessed immediately after termination by using the Borg 6-20 scale. The Borg scale has a rating of 6-20, where a rating of 6 perceives "no exertion at all" and 20 perceives a "maximal exertion" of effort. By using the Borg scale it's possible to self-monitor how hard the body is working, and it can help to adjust the intensity of the activity by speeding up or slowing down the intensity (18).

To calculate the right heart rate zone for each interval (85-96% of HR_{max}) and for the active recovery (60-70% of HR_{max}) for the exercises there was used the maximal heart rate from the VO_{2peak} test.

3.4 Peak oxygen uptake (VO_{2peak})

 VO_{2peak} was measured on a treadmill by walking or running (Woodway PPS 55 Med, Munich, Germany) at a predefined velocity and incline, using ergo spirometry (Metalyzer II, Cortex Biophysik GmBH, Leipzig, Germany). Before the test was started the participants were informed about the test. The test started with a warm-up period for 10 minutes (\sim 60 % of HR_{max}), familiarization with the treadmill, and previously they got described the procedure of the test. The oxygen test was done either with a walking protocol or a running protocol, depending on the participant. During the test, the velocity was increased by 1 km/h or the incline with 2%, every 1 minute. A levelling off oxygen uptake (VO₂) despite increased workload, and respiratory exchange ratio (RER) \geq 1.05 were used as criteria for reaching VO_{2max}. HR was measured continuously during the test with a heart rate belt and a heart rate watch (Polar, Polar Electro, Kempele, Finland) to define HR_{max}.

Measurement of blood lactate concentration (mmol/L) with Biosen C-line (EKF diagnostics, Leipzig, Germany) was conducted three times during the VO_{2peak} test for each participant. The measurements were conducted before the warm-up, after the warm-up, and after VO_{2peak} test was finished.



Figure 4. VO_{2peak} test with a participant.

3.5 Anthropometric and body composition measurements

Body weight, body mass index (BMI), and waist-to-hip ratio were measured. To measure body composition, there was used an instrument called InBody 770 (Biospace CO, Ltd, Seul, Korea). InBody 770 provides weight, muscle mass, fat percentage, metabolism, and mineral status non-invasively by sending weak electrical signals through the body. The whole test lasts just a few minutes. Before the analysis, the participants have been fastening for at least two hours and the participants have avoided strenuous exercise. The height was measured without shoes or headwear, this was done with equal weight on both legs. The distance between the legs was one foot and the heels were on the ground with a full stretch of the legs. The measurement of height was done with one decimal. The body weight was measured without heavy clothes and shoes, while the participants were standing still. There was drawn 0,5 kg for the remaining clothes and the weight was measured with one decimal.

Circumference of the participant's waist, hip, right calf, and right thigh was measured using a measuring band and a measuring board (figure 5). The participants were standing with the right foot on the measuring board with equal weight on both legs. The measuring board was used to get the same height for the measurement of the calf and tight at pre-and post-test. To make sure the measurement got valid the measurements were done two times for the circumference measuring.

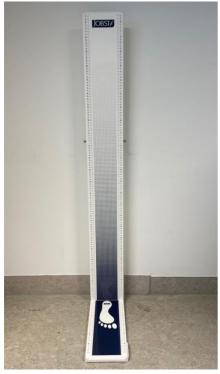


Figure 5. The measuring board was used for the circumference measurement of the calf and thigh.

3.6 Blood pressure

Blood pressure was measured while the participant was sitting down and have been resting for at least five minutes in a quiet room. The blood pressure was measured with an automatic sphygmomanometer (CAS 740 Monitor, MAXNIBP, Branford, USA). Blood pressures were measured at the same time of the day for each participant at pretest and posttest. The first reading was discarded and the mean of the next two consecutive readings with a coefficient of variation below 15% was used in the study, and additional

readings were done if required. The sleeve was placed at heart level on the dominant hand and customized with the size of the participant's arm.

3.7 Questionaries form

3.7.1 RAND-36

RAND 36-item Short Form Health Survey (RAND-36) (19) was used to track potential changes for quality of life and is perhaps the most widely used health-related quality of life survey instrument in the world today. RAND-36 assesses eight health concepts physical functioning, role limitations caused by physical health problems, role limitations caused by emotional problems, social functioning, emotional well-being, energy/fatigue, pain, and general health perceptions (20). Physical and mental health summary scores are also derived from eight RAND-35 scaled.

3.7.2 LYMQOL

LYMQOL (Lymphoedema Quality of Life), legs (21). LYMQOL is a questionnaire that is designed and validated for patients with chronic edema/lymphoedema of one or both legs to measure the quality of life. The questions cover four domains, symptoms, body image/appearance, function, and mood. For each answer, there is a scoring, "not at all=1", "a little=2", "quite a bit=3" and "a lot=4". The total score for each domain was calculated by adding all scores together and dividing by the total number of questions answered (21).

3.7.3 Brief pain inventory

The Brief Pain Inventory (BPI) (22), is a self-administered questionnaire that is being used as a generic pain questionnaire for chronic pain conditions. Using the short form of nine items. The first, optional, items are a screening question about the respondent's pain on the day. The questionnaire is then composed of pain drawing diagrams, four items about pain intensity (worst pain, least pain, average pain, pain right now), two items on pain relief treatment or medication, and one item om pain interference, with seven sub-items (general activity, mood, walking ability, normal walk, relations with other people, sleep, and enjoyment of life) (23).

3.8 Standard blood analyses

Blood collection and blood analyses were performed using procedures for the general biomarkers in clinical use and were performed for all participants at the pre-and posttest. There was collected one 6 ml and one 3,5 ml Li-heparin tube, one 6 ml EDTA tube, and two 4 ml EDTA tubes. One 3,5 ml Li-heparin tube and two 4 ml EDTA tubes were sent to clinical-chemical analyses at St. Olav Hospital. Parameters that were analyzed include triglycerides, HDL-cholesterol, LDL-cholesterol, Total cholesterol, hs-CRP, HbA1c, glucose, hemoglobin, and leucocytes. One 6 ml EDTA tube and one 6 ml Li-heparin tube were collected for later explorative biomarker assays. These blood samples were centrifuged and aliquoted before freezing and stored in the LipidEx-biobank. A blood test from the standard laboratory that was without normal range may indicate a need for following up by a doctor, was reported back to the participant as soon as possible, and were asked to contact their general practitioner. The participants were fasting for at least eight hours before blood sampling. The time of the last meal for the participants was recorded on the patient form.

3.9 Physical activity habits

At the pretest and posttest, there was collected information about the participant's physical activity level. The participants got questions about their physical activity habits and the first question was if they did exercise regularly, if the participant answered "yes" to that question they got three more questions. The first of the three questions were, about how frequently they did exercise, the duration of each exercise, and the intensity of each exercise. For each of the three questions, the participants got a score, and the score forms a summary index of their physical activity (table 1). If the participants answered "no" on the question if they did exercise regularly, and did not answer the questions about the frequency, duration, and intensity got coded as 0 (24). The different types of exercise the participants in this study did was swimming, walking, bicycling, yoga, strength exercise, and group training with dance.

Table 1. Questions and score index about physical activity at the pretest and posttest.

Exercise	Score
How frequently do you exercise?	
 Once a week 	(1)
 2-3 times per week 	(2,5)
 4-7 times per week 	(5)
How long does every exercise last?	
 0-30 minutes 	(0,38) (0,75)
 30-60 minutes 	
>60 minutes	(1,0)
How is the intensity on the exercise?	
 Low intensity 	(1)
 Moderate intensity 	(2)
 High intensity 	(3)

3.10 Ethics

All participants recruited to the study participated voluntarily. The participants got written information about the study and had to sign an informed consent before their involvement in the study, which also included that their biological material could be used in the study. If a research participant should be injured based on participation, NTNU will have the insurance responsibility. The participants were free to withdraw from the study at any time, for no reason, and were free to choose whether the collected data could be used in further research or not. All data were treated confidentially to protect the participant's privacy.

3.11 Statistical analysis

Statistical analyses were performed by using the software program SPSS, version 29.0 (SPSS Inc.).

To investigate if there was a significant difference in the change between the groups the Mann-Whitney U test was performed, by using delta values. Delta values for the posttest and pretest were calculated for the variables, by subtracting the posttest measurements from the pretest measurements.

To investigate if there was a significant difference within the group the Wilcoxon Signed Rank test was used.

All data are presented as the median and interquartile range (IQR). Significance levels for all tests were set to p<0.05. Figures were made by using GraphPad (GraphPad Software, inc. Prism 9, La Jolla, CA, USA).

4 Results

4.1 Baseline characteristics

The baseline characteristics of the participants (n=16) in the study are presented in Table 2, there was no significant difference between the groups two groups.

Table 2. Baseline characteristics of the study participants.

	Training group	Control group	p-value
	(n=7)	(n=9)	
Age (year)	38,3 (17,0)	44,7 (15,0)	0,174
VO _{2peak}	33,7 (10,9)	32,8 (13,9)	0,536
Height (cm)	168,0 (9,0)	167,5 (7,3)	0,351
Weight (kg)	86,4 (20,3)	73,4 (18,8)	0,681
BMI (kg/m²)	29,2 (5,4)	31,0 (8,6)	0,837
PBF (%)	41,0 (8,7)	44,0 (15,5)	0,299
WC (cm)	87,0 (21,0)	86,0 (18,5)	1,000
HC (cm)	104,0 (6,0)	110,0 (20,0)	0,370
Thigh, right (cm)	56,0 (11,0)	55,0 (6,8)	0,681
Calf, right (cm)	43,5 (5,0)	40,0 (4,8)	0,408
Physical activity score			
Intensity	2,00 (2,00)	0,00 (2,00)	0,299
Duration	0,75 (0,75)	0,00 (0,75)	0,408
Frequency	2,50 (2,50)	0,00 (2,50)	0,299

Data is presented as median (IQR). VO_{2peak}: peak oxygen uptake BMI: Body mass index; PBF: percentage body fat; WC: waist circumference; HC: hip circumference

4.2 Effect of the intervention

Seven participants from the HIIT group completed the eight-week of exercises with 80% compliance during the training period. Some of the participants in the HIIT group started the HIIT period by walking on the treadmill and ended by running some parts at the end of the period, but most of the participants started with running. All the participants had an increase in the incline and velocity of their running/walking during the training period. The participants who started with walking had a higher incline than the participants that were running. When they started running the incline was decreased. Out of the notes from the interval sessions, there was an increase in the subjective feeling of exhaustion out of the BORG scale numbers for every participant for each measurement.

4.2.1 HIIT and cardiorespiratory measurements

There was no significant difference between the HIIT group and the control group for cardiorespiratory fitness on the VO_{2peak} test measurements. However, there was a significant increase in VO_{2peak} after exercise training for the HIIT group. Figure 6 shows the relative oxygen uptake for the VO_{2peak} test. HIIT group showed a significant increase (p=0.043) with 10,2% from the pretest to the posttest. The control group showed an increase of 5,7% from the pretest to the posttest, although no significant differences were found within the control group.

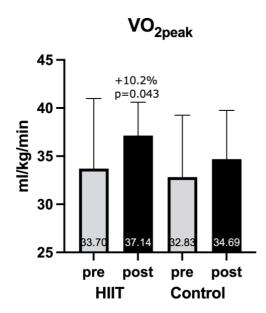


Figure 6. Relative VO_{2peak} pre (gray) and post (black) in HIIT and control group. VO_{2peak} : Peak oxygen uptake

Figure 7 shows the absolute VO_{2peak} measurement. HIIT group showed a significant increase (p=0.046) with an increase of 8,3% from the pretest to the posttest. The control group increased absolute VO_{2peak} by 4,5% from the pretest to the posttest, although there was no significant difference within the control group.

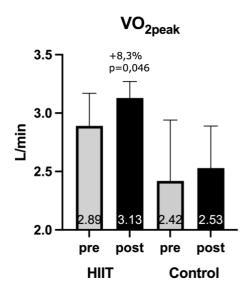


Figure 7. Absolute VO_{2peak} pre (grey) and post (black) in HIIT and control group. VO_{2peak} : peak oxygen uptake

4.2.2 HIIT, anthropometric, and body composition measurements There was no significant difference between the two groups in any of the measurements related to body composition. Although there was a statistical difference within the HIIT group and within the control group for the measurements with fat distribution for the trunk from the pretest to the posttest. Within the HIIT group, there was a significant

decrease (p=0.018) of 5,4% from the pretest to the posttest. The control group had a significant increase (p=0.008) with 5,5% in fat distribution for the trunk within the group from the pretest to the posttest.

Table 3 shows the measurements done for anthropometric and body composition. The percentage of body fat was decreased by 8% for the HIIT group after the 8 weeks of exercise. The control group decreased the percentage of body fat by 1,4% from the pretest to the posttest. HIIT group showed a decrease in body fat distribution for both the right and left leg. Measurements done for the right and left leg show a decrease of 8,7% from the pretest to the posttest. The control group only show an increase for the right leg of 2,3%. Although for these measurements there was not a statistical difference between or within the two groups.

Table 3. Outcome variables for study participants at baseline and after 8 weeks on anthropometric

and body composition measurements.

and body compositi	on measuremen	ι			
	HIIT group		Control group		Group
	(n=7)		(n=9)		difference
					p-value
	Baseline	After 8	Baseline	After 8	
		weeks		weeks	
BMI (kg/m²)	29,2 (5,4)	28,4 (4,0)	31,0 (8,6)	30,3 (8,7)	0,210
Weight (kg)	86,4 (20,3)	84,3 (15,1)	73,4 (18,8)	72,9 (17,9)	0,091
PBF (%)	41,0 (8,7)	37,7 (6,0)	44,0 (15,5)	43,4 (16,4)	0,470
HC (cm)	104,0 (6,0)	103,0 (7,0)	110,0 (20,0)	107,0 (18,5)	0,408
WC (cm)	87,0 (21,0)	83,0 (16,5)	86,0 (18,5)	86,0 (20,3)	0,408
Calf, right (cm)	43,5 (5,0)	44,0 (5,5)	40,0 (4,8)	40,0 (4,0)	0,918
Thigh, right (cm)	56,0 (11,0)	56,0 (10,5)	55,0 (6,8)	54,0 (5,3)	0,606
Body fat					
distribution					
Right leg (kg)	4,6 (1,7)	4,2 (1,4)	4,4 (2,4)	4,5 (2,4)	0,606
Left leg (kg)	4,6 (1,6)	4,2 (1,4)	4,4 (2,4)	4,4 (2,4)	0,606
Trunk (kg)	16,7 (4,9)	15,8 (4,8)*	16,5 (9,5)	17,4 (9,4)*	0,210

Data is presented as median (interquartile range). BMI: Body Mass Index; PBF: percentage body fat; HC: hip circumference; WC: Waist circumference.
*p<0,05

4.3 Physical activity habits

There is a presentation in Appendix III of how the physical activity habits were distributed for the four questions the participants were asked about their physical activity. Out of the 16 participants in this study, 8 participants did exercise regularly, and 8 participants didn't exercise regularly at baseline. The duration for the 8 participants that did exercise was from 0 to 30-60 minutes, and the intensity was from low to moderate. Participants in the HIIT group were more physically active than the control group at the pretest. Five participants in the HIIT group did exercise regularly and two did not, and in the control group there were three who did exercise regularly and six that didn't.

At the posttest, there were 5 participants in the control group that did exercise regularly and four who didn't. There was a spread frequency for the exercise at posttest, and the duration was from 0, 0-30 minutes, and >60 minutes per exercise. Most of the participants did low-intensity exercise, and one did moderate-intensity exercise.

Figure 8 shows the physical activity score for the HIIT group and the control group from the pretest to the posttest. There was a significant difference (p<0.001) between the

groups for physical activity scores at the posttest. There was also a significant difference (p=0.017) within the HIIT group from the pretest to the posttest. The control group got a higher score on the physical activity summary index, and the control group increased their mean score from 0 to 0,75 from the pretest to the posttest, although there was no significant increase.

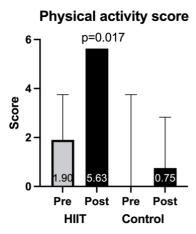


Figure 8. Physical activity summary index score pre (grey) and post (black) in HIIT and Control group.

5 Discussion

This study aimed to investigate the effect of HIIT on oxygen uptake and body composition in women with lipedema. The main findings from this study were that eight weeks of high-intensity interval training showed no significant difference in oxygen uptake and body composition between the two groups. However, there was a significant increase in VO_{2peak} in the HIIT group (p=0.043). In addition, there was also a significant difference within both groups in body fat distribution for the trunk, for the HIIT group there was a significant decrease (p=0.018), and for the control group a significant increase (p=0.008).

5.1 Intervention

The participants in the HIIT group performed two weekly supervised exercise sessions at NTNU and one exercise at home. The exercise at home was supposed to be equal to the exercise they did at the supervised exercises, since women with lipedema could have difficulty with fatigue and heavy feet, they could do a bit different exercise at home, like pool exercise and cycling. In this study, we didn't have access to a swimming facility, but the participants got encouraged to do water exercises for their home exercise. Most of the participants in this study tried to do a similar exercise as the supervised exercise, doing it either on a treadmill or on a hill to walk/run in. Some of the participants had access to a treadmill either at home or in a training facility. Exercise in water was found to be the most beneficial activity for women with lipedema, but there is a lack of knowledge on the possible benefits of aquatic exercise (high cost, difficulty in accessing facilities that offer such training) (25).

It was difficult to follow up on the home exercise, and we had to trust the participants that they did the exercise and at the correct intensity. We urged the participants to write down their pulse and Borg scale at the home exercise and bring that to the supervised exercise so we could document it. A study done by Kessler et.al (16) found that HIIT may not be appropriate or optimal for everyone. HIIT is highly structured and requires at least initial supervision for untrained individuals. To achieve the targeted intensity level, HIIT requires a high degree of motivation, and this exercise method may not be preferred for all people.

The participants in the HIIT group were recommended to use compression garments during the exercise training, to decrease the risk of the feet swelling (10). Compression garments help to promote blood circulation and lymph fluid flow, which can be severely inhibited for patients with lipedema (26). Compression garments may also help to reduce excess fat tissue (9). All the participants in the HIIT group used compression garments that were fitted for their measurements, during the exercise. A study performed by Dudek et.al (25) concluded that using compression garments during exercise was very beneficial and that it may reduce pain and swelling. In a study done by Czerwinska (6), they reported that the circumference of the lower extremities tends to increase without compression. The use of compression garments helped to maintain and reduce the circumference. Although there is a need for larger-scale studies to confirm this statement. Compression therapy does not directly reduce adipose tissue, but it's thought to be useful in alleviating symptoms. A recent study by Paling and Macentyre (27) shows that the longer patients wear compression garments during the day, the reduction of symptoms is higher.

5.1.1 Effect of HIIT and cardiorespiratory fitness

The VO_{2peak} result is affected by the body weight, and a decrease in body weight has an impact on the oxygen uptake test because the oxygen uptake is measured in milliliters of oxygen absorbed by the body per minute divided by body weight. A study by Dudek et.al. found that physical activity is an important part of self-management and an important aspect of health-related outcomes in women with lipedema (25).

A meta-analysis exploring the increase of VO_{2max} , found out that with ~8 weeks of exercise, the expected increase in VO_{2max} was between 300 and 500 ml (28). The improvements depend on which exercise and the magnitude of exercise, but it will also depend on whether the participants are untrained or trained at baseline and the age of the participant. Participants in the HIIT group increased their oxygen uptake with a mean of 344 ml, this is within the expected increase. This was a group of participants that were not familiar with HIIT training before the intervention.

By completing the HIIT program, the participants got a positive experience and can do this kind of exercise in the future. This will improve their general health. Physical activity should target weight control and realistic weight loss if possible. Research has shown that regular exercise can alleviate part of the metabolic complications of obesity in the absence of weight loss (29).

The control group also had an increase in oxygen uptake although it was not significant, and they did not conduct the HIIT program. This could have been affected by, that the control group had an increase in physical activity (appendix III and Figure 8) from the pretest to the posttest. The control group did low-intensity exercise compared to the HIIT group which did high-intensity training.

5.1.2 Effect of HIIT and body composition

There was no significant difference in body composition between the HIIT group and the control group from the pretest to the posttest. The only significant difference was within both groups for body fat distribution for the trunk. Where the control group had a significant increase and the HIIT group had a significant decrease. A reason the participants didn't achieve a change in their body composition may have been that the participants did not get a diet restriction or guidance. It's limited how much the body composition changes in 8 weeks with only exercise and due to the known challenge of losing the lipedema fat and reducing the size of the legs (1). This may also be a reason why the body composition remained similar from baseline to after the exercise intervention. Except for the change in trunk fat distribution, that may be because it's difficult for women with lipedema to lose the lipedema fat in the legs, but they will lose the non-lipedema fat with training (15). The fat in the trunk may have been decreased because there is no lipedema fat in the trunk and therefore the participants in the HIIT group increased fat distribution in the trunk by conducting the training program. The loss of abdominal fat will be beneficial for general health and the growth of normal fat is thought to promote the growth of lipedema fat (30).

The HIIT group did decrease more of their percentage of body fat than the total body weight, this result could be explained by beta-3 adrenergic receptors that are located mainly in the adipose tissue, and beta-adrenergic receptor sensitivity in adipose tissue is increased by exercise, these factors might explain why HIIT is effective in reducing body fat on individuals that are overweight/obese (31). The study done by Batacan et.al (31)

also showed an absence of weight loss despite the observed decrease in body fat, this may be a consequence of gain in muscle mass. Exercise like HIIT is known to recruit more fast type II muscle fibers leading to greater muscle hypertrophy and muscle mass (31). This may have been an explanation for the results of our study and why it was not a significant change in total body weight for the two groups. A meta-study done by Dupuit et al. (32) investigated the effect of HIIT on body composition for women before and after menopause and found that only training interventions longer than 8 weeks had a significant effect on body weight. While interventions shorter than 8 weeks are effective in reducing total fat mass. Only the interventions ≥8 weeks significantly reduced abdominal fat mass. Another meta-analysis by Türk and collaborators (29) showed a significant reduction in percentage body fat after HIIT compared to moderate-intensity continuous training (MICT) this finding also showed no changes regarding weight, BMI, or waist circumference reduction. For women with lipedema, there is a common problem with loss of muscle mass and mobility (26). Lipedema fat is different from non-lipedema fat. It has been demonstrated that lipedema adipose tissue has larger adipocytes, increased macrophage density, and increased dermal blood and lymphatic vessels compared to the normal fat (33). A theory of why lipedema fat is so hard to lose is that the size of fat cells and the geloid layer of hyaluronic acids and water move the fat cells farther away from blood vessels and this leads to the slow release of fat (30).

This intervention showed no significant change in body composition after HIIT and this may have been because, unlike obesity, the fat tissue for lipedema patients is resistant to exercise. Even if the fat tissue for lipedema is resistant to exercise, exercise is known to have an important effect on adipose tissue (9). A study done by Esmer et. al. (9) concluded that regular exercise and an active lifestyle may help prevent the development of complications related to lipedema. The fat tissue for patients with lipedema is highly resistant to exercise may this show an explanation for why the participants did not decrease more of their body weight and fat distribution in their legs, which are different from individuals with overweight/obesity.

Fat distribution was changed for the legs of the HIIT group and increased by 8,2%, but the circumference remained the same. The control group had no change in either fat distribution or circumference of the legs. Reduction of non-lipedema fat can result in a dramatic size disparity between the trunk and enlarged fat in the limbs (1). The participants may have gained more muscle mass and therefore increased the fat distribution. The difference between the HIIT group and control group in fat distribution in their legs may have been due to the use of compression garments, during exercises.

5.2 Study limitation

In this study, there was a small sample size, where 22 participants were randomized and 16 of these participants got analyzed, due to the participants that withdraw from the project. In the data set, there was one outlier in the HIIT group. This outlier was one of the participants that got a change of their life situation, so the participant increased weight during the intervention. This could influence the result of the oxygen uptake and body composition testing.

There was large variability among the participants for the oxygen uptake measurements, some of the participants got a higher oxygen uptake and some had very low oxygen

uptake. These spread values could have had an impact on the results of the oxygen uptake test, if there was a more equal group the results would have been different

The intervention period was from October to January, and since the intervention period lasted over the Christmas holiday the participants got an extra week of training because there was no organized training during this one week. In a study, examining weight gain during the holiday (mid-November to early or mid-January), the participants had a mean weight gain of 0.37 ± 1.52 kg during this period (34). This could have influenced our results for the body composition measurements. Also, the VO_{2peak} measurements could have been affected since the result of this test will be affected by an increase in body weight.

The fall is typically a period when there is a lot of sickness and many participants got sick during this period. Four out of the 7 participants in the HIIT group got sick during the 8 weeks of exercise, but all the participants that got sick, were in the middle of the training period, so they got some weeks of exercise before the posttest. But this could have an impact on the results of the VO_{2peak} test. Because of the period of sickness, the participants were offered one extra week of training.

When measuring the circumference of the thigh, calf, hip, and waist, there was a chance of variability since the measurement was done differently from the pretest and the posttest. The measurement was performed by a different person for each measurement done on the pretest and the posttest. Because of the difference in measuring method from person to person, the result for measurement with a measuring band may not be valid. We used a measuring board and wrote down the height of the board when measuring the tight and calf, but it was not easy to see if it was measured at the same height at the posttest as the pretest. Due to personal variation, the results might have been more valid if the same person measured the same participant at both the pretest and posttest.

Caloric restrictions are more efficient for weight loss than exercise, but exercise is more efficient for visceral fat storage (35). A hypocaloric diet resulted in significantly larger weight loss in studies comparing caloric restriction and exercise training. Exercise training tends to show a larger decrease in visceral adipose tissue compared to caloric restriction (35). This study had no diet restriction, hence, there could have been a different result if we combined a diet restriction and exercise together. On the other side, when this study doesn't have a diet restriction, we can just investigate the effect of HIIT.

For this study, 6 participants withdraw from the intervention after they conducted the pretest, as the participants were free to withdraw without a reason. However, some stated a reason why they withdraw e.g., lack of time due to work and other commitments, and because they did not have the energy to show up to the supervised exercises. A participant withdrew because of leg pain, and another was offered to participate in a lipedema surgery study. Patients with lipedema often have fatigue, one study reported that ~75% women with lipedema complained about fatigue (1).

The participants in the control group have been more physically active during this study period than before, although there was no significant increase. The control group may have been more physically active because they were participating in an exercise study. This can explain why the control group also increased their oxygen uptake and decreased

their body weight. The participants in the control group did low-intensity exercises and the physical activity that is recommended for lipedema patients are non-weight bearing exercises. There is no research on lipedema and HIIT and little research on exercise in general. So, there are few studies to compare the result in this study. Many websites are advising on physical activity and how to deal with lipedema. Physical activities that are recommended for lipedema patients are swimming and exercises in water, cycling, yoga, and stretching, strength training is also recommended (36, 37).

The participants in this study were an untrained group and not so familiar with running on a treadmill. The oxygen uptake test could have been affected by that the participants were not familiar with the treadmill and this type of test on the pretest. In the post-test, the participants were more familiar with this kind of test, and the HIIT group was also more familiar with the treadmill at the posttest. This could lead the participants to be able to push themselves more. The participants in the HIIT may be more familiar with their bodies and how hard they could push themselves through the test.

6 Conclusion

In this study, there was no statistically significant difference between the HIIT group and the control group for the effect of HIIT on body composition for women with lipedema. However, the HIIT group showed a significant increase (p=0.043) with 10,2% in oxygen uptake from the pretest to the posttest. There was also a significant change in the fat distribution in the trunk for both groups, the HIIT group had a significant decrease (p=0.018) with 5,4%, while the control group had a significant increase (p=0.008) with 5,5%.

This is a study with a small sample size, and there is a need for more research on this topic to draw conclusions if HIIT has an effect on the oxygen uptake and body composition of women with lipedema. There is a need for more research on the effect of exercise on women with lipedema in the future, with a larger sample size of participants to determine if there is an effect of HIIT for women with lipedema.

References

- 1. Torre YS, Wadeea R, Rosas V, Herbst KL. Lipedema: friend and foe. Horm Mol Biol Clin Investig. 2018;33(1).
- 2. Wiedner M, Aghajanzadeh D, Richter DF. Differential diagnoses and treatment of lipedema.
- 3. Al-Ghadban S, L. Herbst K, A Bunnell B. Lipedema: A Painful Adipose Tissue Disorder. In: Szablewski L, editor. Adipose Tissue: An Update. 4: BoD-Books on Demand; 2019.
- 4. Langendoen SI, Habbema L, Nijsten TE, Neumann HA. Lipoedema: from clinical presentation to therapy. A review of the literature. Br J Dermatol. 2009;161(5):980-6.
- 5. Sucker C, Schmidt-Lucke J-A, Litmathe J. Hämatomneigung bei Lipödem: Kutane Genese oder Gerinnungsdefekt?
- 6. Czerwińska M, Teodorczyk J, Spychała D, Hansdorfer-Korzon R. The Usefulness of the Application of Compression Therapy among Lipedema Patients-Pilot Study. Int J Environ Res Public Health. 2023;20(2).
- 7. Katzer K, Hill JL, McIver KB, Foster MT. Lipedema and the Potential Role of Estrogen in Excessive Adipose Tissue Accumulation. Int J Mol Sci. 2021;22(21).
- 8. Buso G, Depairon M, Tomson D, Raffoul W, Vettor R, Mazzolai L. Lipedema: A Call to Action! Obesity (Silver Spring). 2019;27(10):1567-76.
- 9. Esmer M, Schingale FJ, Unal D, Yazıcı MV, Güzel NA. Physiotherapy and rehabilitation applications in lipedema management: A literature review. Lymphology. 2020;53(2):88-95.
- 10. Forner-Cordero I, Forner-Cordero A, Szolnoky G. Update in the management of lipedema. Int Angiol. 2021;40(4):345-57.
- 11. lipødemforbund NI-o. Diagnostisering: Norsk lymfødem-og lipødemforbund; [Available from: https://www.nllf.no/lipodem/#diagnostisering.
- 12. Li F, Kong Z, Zhu X, Chow BC, Zhang D, Liang W, et al. High-intensity interval training elicits more enjoyment and positive affective valence than moderate-intensity training over a 12-week intervention in overweight young women. J Exerc Sci Fit. 2022;20(3):249-55.
- 13. Nobari H, Gandomani EE, Reisi J, Vahabidelshad R, Suzuki K, Volpe SL, et al. Effects of 8 Weeks of High-Intensity Interval Training and Spirulina Supplementation on Immunoglobin Levels, Cardio-Respiratory Fitness, and Body Composition of Overweight and Obese Women. Biology (Basel). 2022;11(2).
- 14. Maillard F, Pereira B, Boisseau N. Effect of High-Intensity Interval Training on Total, Abdominal and Visceral Fat Mass: A Meta-Analysis.
- 15. Warren Peled A, Kappos EA. Lipedema: diagnostic and management challenges. Int J Womens Health. 2016;8:389-95.
- 16. Kessler HS, Sisson SB, Short KR. The potential for high-intensity interval training to reduce cardiometabolic disease risk. Sports Med. 2012;42(6):489-509.
- 17. Midt-Norge Kf. eFORSK Klinforsk: Klinforsk; 2021 [Available from: https://www.klinforsk.no/info/Informasjon.
- 18. Services USDoHH. Perceived Exertion Centers for Disease Control and Prevention2022 [updated june 3, 2022. Available from: https://www.cdc.gov/physicalactivity/basics/measuring/exertion.htm.
- 19. Folkehelseinstituttet. Norsk versjon av RAND 36-Item Short Form Health Survey 2015. Available from:

https://www.fhi.no/kk/brukererfaringer/sporreskjemabanken/norsk-versjon-av-rand-36-item-short-form-health-survey/.

- 20. Bozzette SA, Hays RD, Berry S, Kanouse D.
- 21. Vaughan KC, Sue; Loce, Jane; Veigas, Debbie; Riches, Katie; and Hilliam, Rachel. A quality of life measure for limb lymphoedema (LYMQOL). Journal of Lymphoedema. 2010;5(1):26-37.
- 22. Stavanger H. Kartleggingsskjema BPI 2010 [Available from: https://helse-stavanger.no/seksjon/NKB/Documents/Kartleggingsskjema/kartleggingsskjema%20BPI.p df.
- 23. Lin NPaC. The Brief Pain Inventory (BPI). Journal of Physiotherapy. 2016;62(52).

- 24. Kurtze N, Rangul V, Hustvedt BE, Flanders WD. Reliability and validity of self-reported physical activity in the Nord-Trøndelag Health Study: HUNT 1. Scand J Public Health. 2008;36(1):52-61.
- 25. Dudek JE, Białaszek W, Gabriel M. Quality of life, its factors, and sociodemographic characteristics of Polish women with lipedema. BMC Womens Health. 2021;21(1):27.
- 26. Exercise therapy Lipedema Medical Solutions 2023 [Available from: https://www.lipedema.net/exercise.html.
- 27. Paling I, Macintyre L. Survey of lipoedema symptoms and experience with compression garments. Br J Community Nurs. 2020;25(Sup4):S17-s22.
- 28. Bacon AP, Carter RE, Ogle EA, Joyner MJ. VO2max trainability and high intensity interval training in humans: a meta-analysis. PLoS One. 2013;8(9):e73182.
- 29. Petridou A, Siopi A, Mougios V. Exercise in the management of obesity. Metabolism. 2019;92:163-9.
- 30. Herbst K. Lipedema and Obesity. 2014.
- 31. Batacan RB, Jr., Duncan MJ, Dalbo VJ, Tucker PS, Fenning AS. Effects of high-intensity interval training on cardiometabolic health: a systematic review and meta-analysis of intervention studies. Br J Sports Med. 2017;51(6):494-503.
- 32. Dupuit M, Maillard F, Pereira B, Marquezi ML, Lancha AH, Jr., Boisseau N. Effect of high intensity interval training on body composition in women before and after menopause: a meta-analysis. Exp Physiol. 2020;105(9):1470-90.
- 33. Ishaq M, Bandara N, Morgan S, Nowell C, Mehdi A, Lyu R, et al. Key signaling networks are dysregulated in patients with the adipose tissue disorder, lipedema. International Journal of Obesity. 2022;46.
- 34. Yanovski JA, Yanovski SZ, Sovik KN, Nguyen TT, O'Neil PM, Sebring NG. A Prospective Study of Holiday Weight Gain. N Engl J Med. 2000;342(12):861-7.
- 35. Verheggen RJHM, Maessen MFH, Green DJ, Hermus ARMM, Hopman MTE, Thijssen DHT. A systematic review and meta-analysis on the effects of exercise training versus hypocaloric diet: distinct effects on body weight and visceral adipose tissue. Obes Rev. 2016;17(8):664-90.
- 36. Lipoedema T. talklipoedema.org. [cited 2023]. Available from: https://www.talklipoedema.org/the-blog/lipoedema-and-exercise/.
- 37. Wright T. Exercise Therapy Lipedema.net [Available from: https://www.lipedema.net/exercise.html.

Appendixes

Appendix I: Information Form/Consent Form



Versjon 4 (14.06.22)

Vil du delta i forskningsprosjektet LipidEx

FORMÅLET MED PROSJEKTET OG HVORFOR DU BLIR SPURT

Dette er et spørsmål til deg om å delta i et forskningsprosjekt for å undersøke effekt av 8 uker med intervalltrening på lipødem. Vi ønsker å finne ut om denne treningstypen kan føre til mindre smerter, bedre livskvalitet, samt en endret blodprofil og kroppssammensetning. Vi spør om du vil delta siden du tidligere har fått diagnosen lipødem, og ikke driver med regelmessig intervalltrening.

HVA INNEBÆRER PROSJEKTET FOR DEG?

Prosjektet involverer to testdager før og etter en 8-uker lange intervensjonsperioden hvor vi på begge testdagene vil måle kroppssammensetning, blodtrykk, kondisjon og blodprøver. Alle deltakere må komme fastende til disse testdagene pga blodprøvene som skal tas, men vil få mulighet til å spise før videre målinger blir gjennomført. Deltakeren vil bli tilfeldig trukket ut til å delta enten i en treningsgruppe eller i en kontrollgruppe. Det er altså like stor sannsynlighet for at man havner i kontrollgruppen som i treningsgruppen. Alle deltakerne skal fylle ut en aktivitetsdagbok i hele intervensjonsperioden. De som havner i treningsgruppen, trener to ganger i uken ved NTNU sine treningsfasiliteter NextMove på Øya i Trondheim i til sammen 8 uker. Det vil da være intervalltrening med høy intensitet som gjennomføres fortrinnsvis på tredemølle (gange eller løping), men sykkel vil også være et alternativ. Treningen tilpasses til hvert enkelt. I tillegg gjennomfører alle i treningsgruppen en treningsøkt selv hver uke. Deltakerne i treningsgruppen vil få en aktivitetsklokke som skal brukes i løpet av treningsperioden og kan beholdes etter studien er slutt. Deltakerne som havner i kontrollgruppen skal fortsette sitt vanlige liv som før de 8 ukene, men delta på de to testdagene. Disse deltakeren vil få tilbud om treningsopplæring ved NextMove i etterkant av siste test, samt også få sin egen aktivitetsklokke som de kan beholde etter studiens slutt. Alle deltakerne vil bli spurt om å fylle ut spørreskjema på de to testdagene, samt underveis i studien. Etter at resultatene er behandlet vil alle deltakerne bli invitert til en presentasjon av resultater ved NTNU sine lokaler på Øya. Deltakelse i denne studien skal ikke innebære avvik fra ordinær behandling, men man kan ikke delta på andre kliniske intervensjonsstudier i løpet av de 8 ukene. I prosjektet vil vi innhente og registrere opplysninger om deg på de målingene som blir gjennomført på testdagene, samt de svarene som gis på spørreskjema i løpet av studien, og aktivitetsdagboken.

MULIGE FORDELER OG ULEMPER

Det er ikke forventet særlig risiko relatert til denne studien annet en typiske ubehag som stølhet etter trening. Dersom vi ser at treningen gir uventet ubehag, vil vi forsøke å endre belastningen ved å justere treningen og apparatene som brukes til treningen. Blodprøvene kan i enkelte tilfeller føre til en forbigående bloduttredelse.

FRIVILLIG DELTAKELSE OG MULIGHET FOR Å TREKKE DITT 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. Det vil ikke ha noen negative konsekvenser for deg eller din behandling hvis du ikke vil delta eller senere velger å trekke deg. Dersom du trekker tilbake samtykket, vil det ikke forskes videre på dine opplysninger og ditt biologiske materiale. Du kan kreve innsyn i opplysningene som er lagret om deg, og disse vil da utleveres innen 30 dager. Du kan også kreve at dine opplysninger i prosjektet slettes og at det biologiske materialet destrueres. Adgangen til å kreve destruksjon, sletting eller utlevering gjelder ikke dersom materialet eller opplysningene er anonymisert eller publisert. Denne adgangen kan også begrenses dersom opplysningene er inngått i utførte analyser, eller dersom

materialet er bearbeidet og inngår i et annet biologisk produkt. Dersom du senere ønsker å trekke deg eller har spørsmål til prosjektet, kan du kontakte prosjektleder (se kontaktinformasjon på siste side).

HVA SKJER MED OPPLYSNINGENE OM DEG?

Opplysningene som registreres om deg skal kun brukes slik som beskrevet under formålet med prosjektet, og planlegges brukt til 2025. Eventuelle utvidelser i bruk og oppbevaringstid kan kun skje etter godkjenning fra REK og andre relevante myndigheter. 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. Du kan klage på behandlingen av dine opplysninger til Datatilsynet og institusjonen sitt personvernombud. Alle opplysningene vil bli behandlet uten navn og fødselsnummer eller andre direkte gjenkjennende opplysninger (=kodede opplysninger). En kode knytter deg til dine opplysninger gjennom en navneliste. Det er kun prosjektleder som har tilgang til denne listen. Etter at forskningsprosjektet er ferdig, vil opplysningene om deg bli oppbevart i fem år av kontrollhensyn.

DELING AV OPPLYSNINGER OG OVERFØRING TIL UTLANDET

Som en del av gjennomføringen av prosjektet kan det bli aktuelt å overføre innsamlede opplysninger om deg til andre land. Dette vil i så fall kun anonymiserte blodprøver som blir analysert av et laboratorium i utlandet. NTNU er ansvarlig for at overføringen av opplysninger skjer i samsvar med norsk rett og EU sin personvernlovgivning (GDPR). Koden som knytter deg til dine personidentifiserbare opplysninger vil ikke bli utlevert.

HVA SKJER MED PRØVER SOM BLIR TATT AV DEG?

Blodprøvene som tas av deg skal oppbevares i en forskningsbiobank tilknyttet prosjektet. Biobanken heter LipidEx, er lokalisert på Akutten og Hjerte-lungesentret ved NTNU. Ansvarshavende for biobanken er prosjektleder Anja Bye. Biobanken opphører ved prosjektslutt. Dersom det blir aktuelt å bruke et laboratorium i utlandet for analyse av blodprøvene, vil kun EØS-land være aktuelt. Blodprøver vil bli sendt komplett anonymisert, og laboratoriet vil destruere eller returnere blodprøvene til NTNU etter avsluttet analyse.

FORSIKRING

Du er dekket av forsikring gjennom universitetet når du deltar i dette prosjektet.

OPPFØLGINGSPROSJEKT

Dersom det blir aktuelt med et oppfølgingsprosjekt til LipidEx, så kan det hende vi tar kontakt med deg igjen.

GODKJENNINGER

Regional komité for medisinsk og helsefaglig forskningsetikk har gjort en forskningsetisk vurdering og godkjent prosjektet (461077). NTNU er ansvarlig institusjon, og prosjektleder Anja Bye er ansvarlig for personvernet i prosjektet. Vi behandler opplysningene basert på ditt samtykke i henhold til GDPR.

KONTAKTOPPLYSNINGER

Dersom du har spørsmål til prosjektet eller ønsker å trekke deg fra deltakelse, kan du kontakte Anja Bye, 932 32 057, Anja.Bye@ntnu.no. Dersom du har spørsmål om personvernet i prosjektet, kan du kontakte personvernombudet ved institusjonen: thomas.helgesen@ntnu.no.

Ved andre spørsmål i forbindelse med prosjektet, ta kontakt med masterstudentene som står for daglig drift. Hedda Aasland Eidet heddae@stud.ntnu.no (mobil: 45440067), Sara Knudsen Sarahkn@stud.ntnu.no (mobil: 99422831) eller Johanne Sæther johasaet@stud.ntnu.no (mobil: 936 00 741).

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

Appendix II: Example for registration at exercise sessions

Stigning ved RER 0,95: CPET Max puls: Max stigning: Hastighet ved RER 0,95: Max hastighet: 85-95 %:

V'O2/kg (ml/kg/min): 28

				Intervall 1				Pa	use			Intervall 2				Pau	se			Intervall 3				Pa	use			Intervall 4			Komme
Uke	Trening nr	Date	Stigning	Hastighet	Puls	Borg	Stigning	Hastighet	Puls	Borg	Stigning	Hastighet	Puls	Borg	Stigning	Hastighet	Puls	Borg	Stigning	Hastighet	Puls	Borg	Stigning	Hastighet	Puls	Borg	Stigning	Hastighet	Puls	Borg	1
1	1	06.01.2020	1,5	7,5	170	16	1,5	5	139	13	2	7	173	17	2	4,7	137	12	2	7,4	176	17	1,5	5,1	144	13	1,7	7,5	178	18	1
•	2	08.01.2020																													1
	3	10.01.2020																													
2	4	13.01.2020																													1
2	5	15.01.2020																													1
	6	17.01.2020																												 I	
3	7	20.01.2020																											\neg		1
3	8	22.01.2020																												 I	
	9	24.01.2020																												I	
4	10	27.01.2020																											-		1
4																														I	
	11	29.01.2020 31.01.2020																													1
5	13	03.02.2020																											-		1
,																														I	1
	14	05.02.2020																												 I	
	15	07.02.2020																												ı	•
6	16	10.02.2020																													
	17	12.02.2020																													
	18	14.02.2020																											\rightarrow		1
7	19	17.02.2020																													1
	20	19.02.2020																													1
	21	21.02.2020																													
8	22	24.02.2020																											\longrightarrow		-
	23	26.02.2020																											\longrightarrow		-
	24	28.02.2020																													
9	25	02.03.2020																												i	-
	26	04.03.2020																												<u> </u>	
	27	06.03.2020																											\longrightarrow		
10	28	09.03.2020																											\longrightarrow		
	29	11.03.2020																													
	30	13.03.2020																													
11	31	16.03.2020																													
	32	18.03.2020						-														-									-
	33	20.03.2020						-											-			-		-							1
12	34	23.03.2020																													-
	35	25.03.2020																													4
	36	27.03.2020]

Appendix III: Training habits

	HIIT group (n=7)		Control group (n=9)	
	Baseline	After 8 weeks	Baseline	After 8 weeks
Regularly				
Yes	5	7	3	5
No	2		6	4
Frequency				
0	2		6	4
1	1			1
2	2		1	1
3	1	7	1	1
4				
5			1	1
6	1			
7				1
Duration (min)	_		_	
0	2		6	4
0-30	1	_	_	1
<i>30-60</i>	4	7	2	3
>60			1	1
Intensity	_			
0	2		6	4
Low	1		_	4
Moderate	4		3	1
High		7		

