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Cardio training of older adults with central obesity

Background

More than 2.8 million people die each year due to obesity or being overweight and excess bodyweight constitute the fifth largest risk factor for death globally(1). Given its increasing prevalence, effects on socioeconomic costs and the ever growing list of illnesses related to obesity there is need for more effective, preventative strategies(2). Primary intervention and changes in life-style can help to combat obesity but further research is still warranted into causality in order to overcome this diverse problem.

Abdominal obesity is a well-established risk factor for cardiovascular disease (3-6) and all-cause mortality (7). Abdominal obesity is caused by high amounts of visceral adipose tissue (VAT) (5), which is fat located inside the abdominal cavity (6). Other risk factors include metabolic syndrome (8), smoking (9, 10) elevated blood lipids (11) and physical inactivity (12).

Further, the interest of the interactions between host and gut microbiota interactions have recently gained a lot of attention as an altered/dysfunctional microbiota have been linked to obesity, ill-health and a growing number of diseases. Recent evidence even suggests that the gut microbiome may play a role in energy balance and could be a mediating factor between obesogenic feeding and the impaired nutrient sensing seen in obesity. (13, 14) Furthermore, the characterization of "normal" microbiota is not firmly established in where the between studies variation is large, suggesting the need for more studies of the bacterial community characterization especially as data on taxonomic and functional changes in the gut microbiota of obese patients are scarce.

Physical activity is a potentially modifiable determinant of both type 2 diabetes (T2D) and obesity. In a systematic review, moderate-intensity physical activity were associated with a 30% lower risk of T2D, although the optimal amount of weekly PA was not determined (15). Patients with obesity or diagnosed with T2D routinely receive recommendations to increase daily PA (e.g. the WHO recommendation of 150 min PA per week). However, present recommendations have been reported to be insufficient to promote a healthy lifestyle (16). It is thus urgent to find better strategies into increasing the level of physical activity in the community.

In summary, interventions targeting older individuals with central obesity and evaluated with high precision measurements has the potential to increase the health and thereby the quality of life of a steadily increasing number of elderly suffering from obesity.

Methodology

Expected outcomes

Primary measured outcomes

- Visceral adipose tissue as measured by DXA

Secondary measured outcomes

- Blood lipids
- Blood pressure
- Fasting glucose
- Adiposity (Weight, BMI, waist circumference)
- Physical fitness and functioning (e.g. cardiovascular fitness and muscle strength)
- Resting metabolic rate
- Health-related quality of life (QoL - this includes aspects of psychological well-being and satisfaction)

- Self-reported physical activity (IPAQ)
- Perceived health
- Microbiota composition analysis from stool samples
- Dietary habits

Plan of investigation

The present research proposal has its origin in an ongoing population-based intervention study, the Healthy Ageing Initiative (HAI) that aims to investigate risk factors for NCDs. The individuals identified as having central obesity within the HAI study will be invited to the present 10-week randomized intervention study.

IDENTIFYING INDIVIDUALS ELIGIBLE FOR THE PRESENT INTERVENTION STUDY - short description of HAI

All individuals residing in the Umeå municipality is invited to HAI when they turn 70 years old. So far, over 3500 individuals have participated in the study with a participation rate over 70%. The participants visit the clinic at 2 occasions a week apart (please see Johansson et al.(17), for further details surrounding the test procedure). At the first visit, traditional and potential novel risk factors for non-communicable diseases are collected, blood samples sent for analyses, and they go home with accelerometers to collect data on physical activity and sedentary behavior. At the one-week follow up visit the participants receive, based on the test results, a tailored intervention aiming at decreasing the risk of diabetes and cardiovascular diseases through counseling regarding main risk factors such as physical inactivity, unhealthy diet, tobacco use and harmful use of alcohol. The basis in the therapy is a cognitive behavioral therapeutics approach using motivational interviewing(18) and prescription-based exercise(19).

We will invite those that have central obesity defined as more than 1 kg for women or 2 kg for men of VAT-mass (approximately 50% of the total cohort) at the visit to HAI. The cut-offs used for VAT mass translates the cut-off values that have been proposed for waist circumference (88 cm for women and 94 for men). Based on visitors from the last 6 month (400 men and women), around 200 will meet the inclusion criteria.

Exclusion criteria

We will exclude participants on basis on conditions that are contraindicated of training or ability to perform the training program. The exclusion criteria are:

- Physical disability which affects ability to perform the exercises of the training program
- Heart failure or severe degenerative condition, e.g. malignant cancer, multiple sclerosis etc.
- myocardial infarction or stroke the last year
- Heart condition that can worsen with aerobic training, e.g. angina pectoris

Any uncertainties regarding participation that may arise during the baseline test anamnesis will be discussed with the physician in charge of the study.

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DESCRIPTION OF THE PROPOSED 10-week RANDOMIZED INTERVENTION STUDY

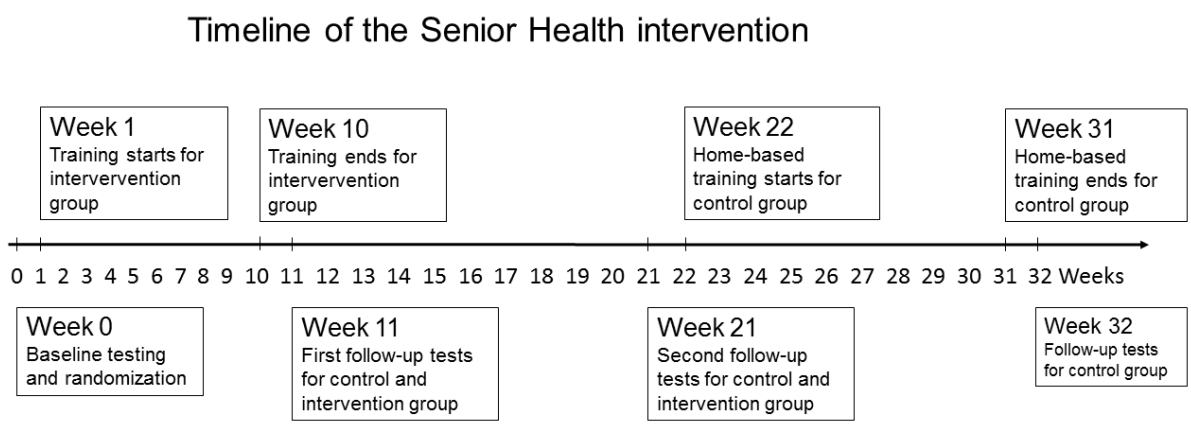

Figure 1. Timeline of the two-step intervention which starts with a traditional randomized controlled trial followed by digitalized form of the intervention that is offered the control group.

The training program

Participants will train in groups of 10 persons, three times a week for 10 weeks and each session will last for 45-60 min. The training program is developed and led by senior students from the bachelors program of exercise physiology of Umeå University. Each session starts with 5-10 min warmup. The training program will focus on station-based, aerobic exercise with the inclusion of resistance exercises using predominantly only bodyweight as resistance. The intensity of the exercise will be aimed at 60-80% maximal exhaustion and each exercise bout will last for 60 sec with 20 sec rest between bouts.

The program is progressive and individualized, starting the first week at a moderate pace so that the participants can learn the exercises properly. Also, each exercise has different difficulty levels, which makes them easy to individualize and progress in. During the exercises, the participants are instructed to reach 13-17 of the Relative Perceived Exertion Borg scale (RPE Borg)(20), which is a self-assessment scale from 6 to 20 and where 6 is no exertion and 20 is maximal exertion. 13 represent somewhat hard and 17 represents very hard.

If the participants experiences discomfort or light-headiness, they are instructed to pause the activity and consult the instructors before they continue the exercise. Additionally, training bands will be provided to both the instructor led and home-based training group in order to reduce the risks of falls in relation the exercises.

Anthropometrics

Height and weight are measured and BMI is calculated. Blood pressure is measured with a mercury sphygmomanometer after 5 min rest with the subject in a supine position. Blood samples are collected for analysis of blood glucose, insulin, HbA1c, CRP and blood lipids.

Body composition

In addition to BMI, body composition is measured with a Lunar iDXA and the CoreScan application (GE Healthcare, Wauwatosa, WI, USA). Using this new software objective measures of visceral fat

mass can be measured in the abdominal region by a computerized algorithm based on the attenuation of the X-ray radiation. By this method we can distinguish visceral fat from the subcutaneous fat that is regarded as more favorable. The results are derived in grams and cubic centimeters. In addition, total fat mass is derived from total body scans, and the amount of gynoid fat is estimated automatically using the region of interest program. Also lean body mass of the total body is measured.

Isometric muscle strength

Isometric muscle strength of the non-dominant hand is measured using a validated isometric hand dynamometer (Jamar, Lafayette Instrument, USA). The better of two trials will be used in further analysis.

Physical capacity

Level of aerobic fitness is determined using an electrically braked ergometer cycle using Åstrands submaximal test.

Stool sample processing and extraction

Stool samples are collected at baseline, 1 week and after 16 weeks intervention for group i and ii. Samples from the 50 non obese subjects (group iii) are only collected at baseline and after 1 week. Stool samples is collected and immediately stored at − 18 °C. Bacterial DNA is extracted from fecal samples using the QIAamp DNA Stool mini kit (Qiagen, Germany) according to the manufacturer's protocol.

Microbiome sequencing

The purified bacterial DNA will then be analyzed using next generation sequencing (NGS). 16S rRNA gene sequencing is a well-established method for studying phylogeny and taxonomy of samples from complex microbiomes. Unlike capillary sequencing or PCR-based approaches, next-generation sequencing (NGS) is a culture-free method that enables analysis of the entire microbial community within a sample. Samples will be sequenced on the Illumina MiSeq System (San Diego CA, USA).

Questionnaire

The participants complete a comprehensive questionnaire that covers socioeconomic and psychosocial conditions, self-rated health, personal health history and family history of CVD and diabetes, quality of life, physical activity, tobacco consumption, eating habits and a food frequency questionnaire.

Hospital Anxiety Depression Scale (HADS) is used to measure depression and anxiety(21). In addition SF-36 is used to generate scores for physical and mental health and will be used with SF-6D(22). The SF-6D is a widely used classification for describing health derived from a selection of SF-36 items and is composed of six multi-level dimensions: physical functioning, role limitations, social functioning, pain, mental health and vitality.

Statistical analysis

Primary analyses will be conducted on an intention-to-treat basis, all participants will be included regardless of whether they completed the follow-up assessment visit. To handle missing data, we will use methodology based on last observation carried forward for participants who did not attend the post-assessment visit. The mean change between pre-intervention and post-intervention measures will be analyzed using the *t*-test when change data are normally distributed otherwise the nonparametric Wilcoxon matched-pairs signed-rank test will be used. Mixed-model analysis will be used to evaluate the change of weight during the intervention to control for relevant covariates. Analyses will be carried out using the SPSS statistical package.

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Inclusion from HAI over 6 month (approximately 400 individuals in total) with about 50 % of the cohort meeting the inclusion criterion generates close to 200 subjects. With a modest assumption of participation rate of 50%, this leave 100 individuals to be randomized into a control group or an intervention group (n=50 per group). For the selected cohort with central obesity in HAI, the mean and SD for VAT-mass is 2905 ± 817 g for men and 1620 ± 538 g for women. Preliminary power calculations based on a 20% decrease in VAT mass, α=0,05 and β=0.8 concludes that each group needs to consist of at least 33 subjects for men and at least 45 women. As we will analyze the %-change in VAT over time, we do not need to separate the analysis on sex and thus, there should be enough power to detect the above mentioned changes in VAT mass.

Ethical considerations

Only the research leader will have access to social security numbers from where the identity can be traced from individual data. No individual data will be presented. Permission for this studiy will be obtained from the Umeå University Research Ethics Committee and will conform to the World Medical Association Declaration of Helsinki.

Clinical relevance

There are great health gains to be made when overweight persons starts training, including; reduced risk of hypertension and high blood lipids, reduced risk of diabetes and cardiovascular disease. If you already suffer from high blood pressure or diabetes then increased physical activity is a common treatment as it has been shown to improve the condition. Furthermore, after the initial contol period, the control group is also offered to receive training and thus the health effects that may arise as a consequence thereof.

Last, there is an urgent need to find an effective, inexpensive and evidence based method to treat patients with central obesity. Hopefully, our study can demonstrate the effectiveness of a digitalized training program that hopefully can be distributed to patients in need of reducing their central obesity towards a healthier life.

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