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Physiological changes following 8 weeks of moderate exercise in older men.

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Abbreviations

1-minHRR	One Minute Heart Rate Recovery
BMC	Bone Mineral Content
BMD	Bone Mineral Density
BMI	Body Mass Index
BP	Blood Pressure
CAD	Coronary Artery Disease
CRP	C - Reactive Protein
ELISA	Enzyme-Linked Immunosorbent Assay
HDL	High-density Lipoprotein
HF	Heart Failure
HR	Heart Rate
HR_{max}	Maximal Heart Rate
HRR	Heart Rate Recovery
Hs CRP	High- Sensitivity C - Reactive protein
LDL	Low- Density Lipoprotein
MI	Myocardial Infarction
MS	Metabolic Syndrome
RER	Respiratory Exchange Ratio
RET	Resistant Exercise Training
SD	Standard Deviation
ST2	Suppression of Tumorigenicity 2
VO_{2max}	Maximal Oxygen Uptake

Abstract

BACKGROUND: Like in many other countries in the world, the proportion of older people in Norway will increase considerably in the coming decades. This fact will lead to a greater need for investment in elderly and health care. Aging is associated with an increase in body fat, a decrease in muscle mass and aerobic capacity among others. Physiological changes due to aging may lead to an increased probability of disease incidence and early functional disability. Exercise could improve the quality of life in the elderly population. It is long known that many risk factors that lead to several diseases such as cardiovascular diseases are affected by exercise. The aim of the present study was to find if 8 weeks of moderate exercise in older men had any impact on cardiovascular risk factors.

METHODS: Twenty four participants between ''70 – 75'' old were chosen from the ''Generation 100'' study. They were randomly assigned to either moderate intensity exercise training or control group. The control group was instructed to maintain their diet and exercise habits during the time of the study. Moderate group was subject to supervised 50 minutes treadmill Training sessions at 70 % of maximal heart rate, three times a week. Parameters measured at baseline and after 8 weeks of study period included weight, waist circumference, body composition, resting heart rate, maximal oxygen uptake (VO_{2max}), heart rate recovery (HRR) and blood analysis.

RESULTS: With the exception of LDL, no significant differences were observed between the two groups. Within the moderate group body fat decreased significantly by 9.3% (p=0.063) after the exercise intervention. There was a trend towards a 6.1% increase in VO_{2max} within the moderate exercise group (p= 0.084). Between the groups there was a significant difference in the values of LDL (p= 0.03). Further there was a trend in values of HDL in differences between the groups (p= 0.09). Unexpectedly, within the control group there were significant changes in values of LDL, HDL and waist circumference (p=0.05), (p=0.01) and (p=0.025), respectively.

CONCLUTION: Eight weeks of moderate exercise resulted in more favourable changes in several cardiovascular risk-factors. Most notable improvements are body fat and maximal oxygen uptake (VO_{2max}).

Contents

1. Background

'' A man is as old as his arteries'' ~ Thomas Syndenham, English physician (1624-1689)

Increased energy consumption and contraction of muscles that are required for body movement are called physical activity. The role of exercise is to use repetitive movements which are both structured and planned (Chodzko-Zajko, Proctor et al. 2009). Exercise is a form of physical activity that is performed to maintain and improve physical condition of the body. Physical exercise that lasts a long time and involves large muscles groups that move in rhythmic fashion is called aerobic exercise training. Another type of physical activity is resistant strength training (RET); this refers to an exercise method where weight is used to develop the size and strength of skeletal muscles (Chodzko-Zajko, Proctor et al. 2009).

1.1 Exercise training and health

According to World Health Organisation (WHO), the recommended amount of daily exercise is not achieved neither by adults nor younger people regardless where in the world (Hallal, Andersen et al. 2012). The key reasons researchers' point out lower physical activity in the modern world is the new technologies that have been developed (Hallal, Andersen et al. 2012). Physical activity is important for all body systems, like the cardiovascular system and skeletal muscles. The role of physical activity is to stimulate these systems to develop properly and achieve their optimal function (Booth, Laye et al. 2008). Combination of inactivity and obesity is a severe risk factor and mortality predictor (Lee, Sui et al. 2009). Obesity is referred as risk factor since chronic diseases and premature death can be fatal consequences of obesity (Lee, Sui et al. 2009). The consequences of obesity i.e. cardiovascular diseases (CVD) can be reduced with both moderate and high intensity exercise (Lee, Blair et al. 1999, Farrell, Cortese et al. 2007). The quantity of exercise is crucial since the long term exercise provides more effective prevention of chronic diseases than short term exercise. In this sense may exercise be similar to medicine considering the quantity of medicine dosage provides different effect (O'Gorman, Karlsson et al. 2006). How exercise affects the human body on a molecular level is still a new area of research. It was recently demonstrated how exercise affects signaling pathways in cells (Egan and Zierath 2013). How regulatory molecules in the body are affected by physical activity is another important issue that has come to clarity. In addition to these new research about fitness and health , there are many benefits of exercise on health that has long known about (Egan and Zierath 2013). As mentioned the recommended amount of exercise is not achieved in all populations around the world. In U.S, for instance only 3.8 % of the population achieves the minimum recommended amount of moderate exercise (Troiano, Berrigan et al. 2008).

1.2 Aging and effects on body functions

Aging in humans leads to an increase of body fat and reducing muscle mass, muscle glycogen levels, aerobic capacity , sensitivity to insulin (Brozek, Grande et al. 1963, Reaven and Reaven 1980, Chodzko-Zajko, Proctor et al. 2009). Despite absence of pathology, physiological systems become increasingly weaker due to aging (Masoro 1995). Activities of daily living are gradually affected by age related physiological changes. These physiological changes occur in organ systems and tissues. These factors eventually create a challenge to physical independence in the elderly population (Holloszy. J.O and Kohrt.W.M 1995). With increasing age, the loss of muscle mass leads to lower skeletal muscle performance, and decreased maximal aerobic capacity measured as VO_{2max} (Holloszy. J.O and Kohrt.W.M 1995). Compared to young people older adults need more frequent submaximal exercise to minimize the loss of body function (Chodzko-Zajko, Proctor et al. 2009). The changes that occur in the body composition are crucial. These changes in body composition include decrease of muscle mass, accumulation of fat in the body, among others (Janssen and Ross 2005, Racette, Evans et al. 2006). Further risk associated with this condition is CVD (Singh 2004, Kay and Fiatarone Singh 2006). Neural function will also be affected due to aging; the conduction speed will progress slower and slower in neural pathway. This is because of a decrease in the number of motor neurons that play an important role in neural function (Vandervoort 2002). As a consequence of aging, skeletal mass is also reduced. Skeletal mass is measured as bone mineral density (BMD) and bone mineral content (BMC). Reduced MBD and BMC increase the probability of rupture in the bone (Suominen 2006).

1.3 Benefits of exercise in older individuals

One study, emphasized on aging and how important it is to exercise for older adults. This study shows that regular exercise has a great effect on aging (Chodzko-Zajko, Proctor et al. 2009). Several studies have shown that regular exercise has a positive effect on the risk factors of chronic diseases (Holloszy. J.O and Kohrt.W.M 1995, Holloszy 2000). The results have shown that aerobic exercise has great influence on metabolic and cardiovascular systems in the elderly population. Furthermore the loss of the physical function can be attenuated by regular exercise (Chodzko-Zajko, Proctor et al. 2009). Not only aerobic exercise but skeletal strength training also confers to protection against chronic diseases. Metabolic disorders are one of the reasons that lead to chronic diseases (Egan and Zierath 2013). Obesity and diabetes mellitus type 2 are examples of chronic conditions that can be prevented with regular exercise. One of the treatment methods that are used to treat these conditions is regular exercise (Haskell, Lee et al. 2007, Colberg, Sigal et al. 2010). Other possible consequence of inactivity is obesity (Hill and Peters 1998). Obesity is one of the biggest health problems in the world; in the US above 60% of the population are overweight (Flegal, Carroll et al. 2010). According to this study on obesity, an individual with BMI of 30 or above belong to the category of obesity. While BMI between ''25.0 to 29.9'' indicates overweight (Flegal, Carroll et al. 2010). Mortality that may be caused due to obesity can be prevented and eliminated with exercise (Lee, Blair et al. 1999, Church, LaMonte et al. 2005, McAuley, Sui et al. 2009). Different treatment methods were compared in a study done on diabetes mellitus 2 (Knowler, Barrett-Connor et al. 2002) According to this study pharmacological drugs provided less impact than recommended diet program combined with regular exercise (Knowler, Barrett-Connor et al. 2002).

Recent studies on exercise training on older men between 71 – 77 years have shown that 12 weeks of high intensity (aerobic) exercise improved their aerobic capacity. In the same study an increase in the size of skeletal muscle was also observed (Harber, Konopka et al. 2012). Effect of aerobic and strength training on the elderly population were compared. It was found that strength training had better impact on maintaining the muscle mass and resting metabolic rate, while aerobic exercise provided more effective results on influencing cardiovascular risk factors (Davidson, Hudson et al. 2009). Otherwise, even moderate exercise has a positive impact on the factors of significance for CVD (Mora, Cook et al. 2007). Healthy life style leads to longer life span for people. Not only physical health but also mental health is an essential factor in achieving good lifestyle (Seeman, Berkman et al. 1995).

Indications of healthy lifestyle can be e.g. low levels of low-density lipoprotein (LDL) and triglycerides. On the contrary, high levels of high-density lipoprotein (HDL) are recommended (Holloszy 2000, Young 2006). Other indications of healthy lifestyle could be normal values for blood pressure, body composition and glucose (Holloszy 2000, Young 2006). Regular exercise is recommended for both prevention and treatment of various diseases. The strong recommendation is justified by the large amount of studies that have dealt with exactly this area (Chodzko-Zajko, Proctor et al. 2009). In addition, training is also effective treatment of preventing conditions such as depression and stroke (Brosse, Sheets et al. 2002, Gordon, Gulanick et al. 2004).

There is much evidence to suggest that regular exercise throughout life is a very great investment for health in the future, when individuals get older. Several studies have compared older athletes with sedentary elders. According to these studies, there are major differences between these two older groups. Studies have shown that older athletes have benefited from training with lower body fat and maintenance of higher muscle mass compared to other elders with no athletic background (Going, Williams et al. 1995, Holloszy. J.O and Kohrt.W.M 1995, Sugawara, Miyachi et al. 2002). While still other studies that focused on oxygen consumption and oxygen transport, concluded that elderly people with athletic backgrounds have better capacity for both transport and consumption of oxygen.

This is proof of that athletic elders have higher oxygen capacity (Ogawa, Spina et al. 1992, Proctor, Shen et al. 1998). Metabolic and cardiovascular stress is caused by several factors, such as exercise training and it varies from one individual to another. Studies that took into account the metabolic and cardiovascular stress found sedentary elders experienced higher metabolic stress (Seals, Hagberg et al. 1984, Coggan, Abduljalil et al. 1993) and higher cardiovascular stress compared to athletic elders (Hagberg, Allen et al. 1985). Another study has also concluded that effect of training is preventing a rapid development of inability in oldness (Wang, Ramey et al. 2002).

1.4 Exercise training and the effects on biomarkers of cardiovascular health

CVD includes diseases that occur in heart and blood vessels and is a leading factor of mortality in older people (Dantas, Jiménez-Altayó et al. 2012). Biomarkers or biological markers are biological parameters such as enzymes, hormones, blood pressure etc. which can be measured and quantified from biological samples among others. Biomarkers are used as a tool for identification of the presence of various diseases such as CVD (Vasan 2006). Different biomarkers can be used to indicate different type of diseases. Troponin I and T, D-dimer, ventilation perfusion scan, treadmill stress test, electrocardiography, B-type natriuretic peptide are examples to biomarkers which is associated with CVD (Vasan 2006).

A study has shown that high-intensity exercise affects cardiovascular biomarkers causing a reduction of LDL and an increase of HDL (Kraus, Houmard et al. 2002). Regular physical activity is highly associated with low incidence of CVD (Lee, Sui et al. 2011). Several studies have shown that increase in physical activity results in less chance of getting diseases including CVD (Erikssen, Liestol et al. 1998, Gregg Ew and et al. 2003, Lee, Sui et al. 2011). However the effect of exercise provides short term benefits on the cardiovascular risk factors. Another study also confirms effects of exercise on CVD, but has concluded that these effects will last optimally 5-7 years ahead and further these effects decreases over time (deFilippi, de Lemos et al. 2012). As indication of certain diseases the biomarkers are measured from biological sample (Sun and Jia 2012). Certain biomarkers that are associated with heart disease are used to see how the disease progresses. This process is also called pathogenesis. With help of cardiac biomarker, the proper and early treatment of CVD is crucial to eliminate the risk of death (Sun and Jia 2012). In one study, levels of LDL and C-reactive protein (CRP) were compared among patients with MI (Myocardial infarction) and healthy individuals. On the basis of achieved results it was found that patients with MI had higher concentration of both LDL and CRP compared to healthy participants (Goud, Nayal et al. 2012). Not only exercise, but also quitting smoking is likewise important step to prevent CVD (Blair, Kampert et al. 1996, Manson, Greenland et al. 2002). As the effect of exercise it has been observed mild changes of individual risk factors, such as only 5 % changes in blood lipids (Leon and Sanchez 2001, Kraus, Houmard et al. 2002). While overall effect of exercise on CVD factors is tends to be major. How exercise training affects the biological mechanisms that influence risk of disease is still unclear, but there is no doubt that exercising generally helps reduce the risk of CVD (Mora, Cook et al. 2007). The effect of exercise in altering cardiovascular risk factors differs from one individual to another (Thompson, Buchner et al. 2003). These changes which are achieved with exercise have usually a moderate effect in the majority; moreover these changes also tend to be short termed (Fagard 2001, Leon and Sanchez 2001, Thompson, Crouse et al. 2001, Kraus, Houmard et al. 2002, Whelton, Chin et al. 2002). It has been indicated that regular exercise causes changes in CRP concentration; these changes have also been found to be moderate (Tisi, Hulse et al. 1997, Adamopoulos, Parissis et al. 2001). Another novel biomarker of CVD is LDL (Welch 2013). LDL is linked to several diseases including coronary artery disease (CAD). Patients with CAD usually have high levels of LDL. Thus, values of LDL are used as one of indications of the presence of disease (Welch 2013).

The same way the LDL is used; high values of CRP can also be used to indicate heart diseases including CAD (Danesh, Wheeler et al. 2004). CRP is released in the liver and is an acute inflammatory response; therefore the elevated CRP values are not only indicating circumstances of heart disease but also other conditions (Pepys and Hirschfield 2003, Jaffe, Babuin et al. 2006). In another study, it is also shown that CAD is associated with high levels of CRP (Ridker 2003). This reinforces the idea that CRP values can safely be used as one of the indicators for CAD. Although there has been controversy about CRP, it is indeed a risk marker or a risk factor in the development of the arteriosclerotic vascular disease (ASVD) (Pearson, Mensah et al. 2004, Mackman and Taubman 2008), then it was discovered in a genetic study that CRP did not have a causative role in CVD. Thus, CRP is considered more as a risk marker than risk factor (Wensley, Gao et al. 2011).

It has been shown that regular exercise leads to high HDL values while providing the opposite effect on the LDL and total cholesterol levels. This indicates that exercise positively affect LDL cholesterol levels. High HDL, low LDL and cholesterol values are ideally suited for the good health in the elderly. These were determined on the basis of the results obtained by comparison of athletic and sedentary older individuals (Williams 1998).

Another novel biomarker of CVD is suppression of tumorigenicity 2 protein (ST2) (Ahmad, Felker et al. 2012, Ahmad, Fiuzat et al. 2012). In a recent study, it was investigated whether exercise has positive benefits on ST2 levels (Ahmad, Felker et al. 2012). According to results achieved from this study was that benefits varied from one person to another and depended greatly on whether they had low initial levels. In this study they found that exercise has possibly most positive impact on participants who had low initial levels of ST2 (Ahmad, Felker et al. 2012). Other key findings of this study notes that levels of ST2 protein increases proportionally with the degree of severity of heart failure (HF). This means the higher ST2 level the worse the condition of the patients with HF (Ahmad, Felker et al. 2012).

1.5 Moderate intensity exercise

Physical exercise performed with 50 % to 70 % of maximal heart rate is referred to as moderate intensity training. A study found that 12 weeks of moderate exercise resulted in no significant differences in body composition and weight among both young and older people (Wilmore, Royce et al. 1970, Sidney, Shephard et al. 1977). Little change in body fat and weight among participants in training studies which progresses over short periods is expected (Wilmore, Royce et al. 1970, Sidney, Shephard et al. 1977). As a result of the training, an increase in muscle oxidative capacity and muscle glycogen reserves especially in the elderly was observed (Meredith, Frontera et al. 1989). Furthermore neither moderate nor high intensity exercise provides significant increase in cardiac output in the elderly (Seals, Hagberg et al. 1984). Volume of blood (mL) that is pumped by heart minutes is referred as cardiac output and is calculated by multiplying the heart rate by stroke volume. Meredith et al. show that physiological variables such as diastolic/systolic blood pressure and resting heart rate were not affected after 8 weeks of moderate exercise (Meredith, Frontera et al. 1989).

1.6 Hypothesis

Eight weeks of moderate exercise in older men will improve cardiovascular risk factors and quality of life.

2. Methods

This project was performed in cooperation with the "Generation 100'' study. For more information see REK number: 2012/381

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2.1 Participants

Twenty four participants aged between ''70 – 75'' were chosen from the ''Generation 100'' study. They were randomly assigned to either 8 weeks of moderate intensity exercise training or control group. The control group were instructed to maintain their diet and exercise habits during the time of the study. Eleven participants were randomized to the moderate exercise group while thirteen participants to the control group.

Based on similar studies done in this field and previous experience in our lab, the number of participants was estimated. Participants in our study could not have the following diseases and conditions; uncontrolled hypertension, alcohol or drug abuse, active cancer, cardiac and pulmonary diseases and disabilities incompatible with exercise. Moreover anyone who would participate had to sign the declaration form.

The baseline testing of both control and moderate group were performed in cooperation with the '' Generation 100'' study. The pre-tests were performed before the study period while the post-tests were performed right after the 8 weeks.

2.2 Training intervention

Exercise training was accomplished at the exercise facility at NTNU/St.Olavs hospital. Participants who belonged to the training group performed moderate intensity training as planed three days a week. Training session lasted for 50 minutes at 70 % of maximal heart rate. Moderate exercise training was accomplished on a treadmill. All participants received assistance during training hours. Training intensity was supervised with help of polar heart rate monitors and the BORG scale (see appendix). This was done to ensure that participants exercised at 70 % of maximal heart rate. The BORG scale was used to determine how strenuous the exercise was for the participants.

2.3 Weight, waist and height measurements

Weight and height of participants were measured using the standard procedures of the research post at St.Olavs hospital. Height of the participants was determined without shoes. This was performed with equal weight on both legs. In following the procedures, distance between the legs had to be a foot. The height was measured with one decimal, and it was made sure that heels were in the ground at full stretch their legs. Heights of the participants were used during calculation of BMI and VO_{2max} test. The weight was determined such that participants was standing still and did not wear shoes and heavy clothes. For the remaining clothes it was drawn 0.5 kg of weight. The weight was also measured with one decimal. Measurements of waist circumference were performed with regular exhaust measuring the circumference one cm over the navel. Participants had to stand upright under the measurement of waist. Measurement of waist circumference is determined to the nearest 0.5 cm.

2.4 Body composition

An instrument called *Inbody* 720 (Biospace Co, Gangnam- gu, Seoul, Korea) was used to measurement of body composition in this study. This instrument works by sending weak electrical signals through the body to measure weight, muscle mass, fat percentage, metabolism, and mineral status among others. All participants who took this test were advised to fast at least 2 hours before the test. Moreover, they were also requested to avoid strenuous exercise before this test.

2.5 Blood sampling

All participants were requested to fast over night before blood sampling. Several blood samples were taken from the vein in the arm. It was taken one 3 ml heparin tube from each participant. For analysis, the heparin tube was further sent to clinical-chemical analyses at St.Olavs hospital. Parameters that were ordered included High sensitivity C-reactive protein (HsCRP), total cholesterol, glucose, HDL, LDL and triglycerides. In addition to the heparin tube, 6 ml EDTA and two 6ml serum were collected. Blood from the EDTA and serum was centrifuged before freezing. Except for the heparin tube, all the blood samples were frozen at -80 degrees and stored in the ''Generation 100'' biobank.

Analysis results which indicates for a need for following up by a medical doctor, was reported back to participant. These participants were also recommended to contact health personnel.

2.6 Resting heart rate

According to procedures, the participants should have to relax about 5 minutes prior to measurements resting heart rate. Both these measurements were done automatically. It was conducted two automatically measurements and average of these two measurements were used. Moreover, 2 minutes pauses were taken between these two measurements.

2.7 Maximum oxygen uptake

All measurements related to oxygen uptake were performed during running or walking on a treadmill. By using the instrument *Metamax II* (Cortex, Leipzig, Germany), measurements of HR, VO_{2max}, HRR and respiratory exchange ratio (RER) values were performed. The test of maximal oxygen uptake (VO_{2max}) started with 10 minutes warm –up. Suitable preferences on the treadmill for individual adjusted inclination and speed were chosen by the testing personnel. The next step was to increase the speed or inclination. Usually this was done by increasing the speed by 1 km/h or by increasing by 2 % inclination. This step was performed around every two minutes. This procedure was performed until participants were no longer capable to improve workload due to exhaustion, or until all the criteria for maximal oxygen uptake were fully achieved. As a criterion, it is expected RER values higher than 1.1 in measurements of VO_{2max}. During the test, both heart rate and oxygen uptake were measured continuously. In order to validate the degree of impact, participants were asked immediately after the test. For validation were Borg intensity scale used. The scale ranges from 6 to 20, while 6 is lowest, 20 is highest tiring. $VO_{2\ max}$ is referred as the highest achieved oxygen uptake by a participant under the test. Heart rate were measured and recorded 1 minute after the completed test, this referred as 1-minute recovery or heart rate recovery (HRR).

2.8 Biobank

Biobank of the ''Generation 100'' project (G-100) were used. This biobank can be found at heart and lung centre, St.Olavs hospital. The person responsible for this biobank is Professor Ulrik Wisløff. Biological material collected in this project was and will be used in further research. In order to use their biological material, the participants signed a consent form which includes permission to do research with their biological material. Only researchers responsible for this project will have access to the personal information and collected data. Both the collected data and personal information from participants will be stored in a locked place. Data and samples from each participant were linked to a serial number. Data and samples of participants were treated without name, ID number or other directly recognisable information. Just certain researchers have access to the list that links the serial number to personal information of participants. Personal information and data from each participant will be stored until 2020. Furthermore the biological material will be stored until 2025. Before closure of the biobank, it will be send an application to REK.

2.9 Enzyme- linked immunosorbent assay (ELISA)

This test method uses colour change as indication to identify proteins based on antibody and antigen interaction. ELISA kit used in present study is particularly for measurements of ST2 protein/ IL-1 R4. ST2 levels in plasma were measured both in baseline and post-test by Quantiqine Human ST2/IL-1 R4 Immunoassay kit (R&D Systems, Minneapolis, USA). Samples were measured by following the manufacturer's instructions.

2.10 Statistical analysis

By using *Shapiro-Wilk* test it was determined that all pre and post-tests of maximal HR, VO_{2max}, RER and HRR in both groups were normally distributed. Therefore, parametric test called *independent sample T-test* where chosen to compare differences of parameters between groups. Within the groups differences were performed by a parametric test called *paired sample T-test* for normally distributed values and *Wilcoxon signed-rank test* for non-normally distributed values. The chosen significant levels were $p \leq 0.05$, $^{\#}0.05 < p < 0.1$

Weight and waist circumference*;* According to statistical analysis done with *Shapiro-Wilk test*, in the control group pre and post values of weight were normally distributed. While pre and post values of waist circumference were not normally distributed. In moderate exercise group pre weight and waist were normally distributed. Thus, post values of weight and waist were not normally distributed. Due to the presence of abnormally distribution, the comparison of the groups was performed by a non-parametric statistical test called *Mann-Whitney u* test.

Resting heart rate*;* all pre and post values in resting heart rate of both control and moderate group were normally distributed. Comparison between groups in resting HR was done by a parametric test called independent sample *T-test.*

Body composition; Comparison of groups of body fat was done by *T-test.* All results of body fat in both groups were normally distributed. While pre values of muscle percentage in both groups were normally distributed, the post values were not. All results of BMI in groups were not normally distributed. Comparison of muscle percentage and BMI between control and moderate group were performed by using *Mann-Whitney U* test.

Blood analysis; It was used parametric *T-test* to compare differences of total cholesterol, LDL and ST2 values between groups since all pre and post-test results were normally distributed. In both groups all results of HDL and hs-CRP from baseline to post-test turned out to be non-normally distributed, thus non-parametric test used in comparison. Results of triglycerides show that all results were normally distributed except of post values in moderate exercise group. While in values of glucose only pre values moderate exercise group were normally distributed. Statistically differences of HDL, Hs-CRP, triglycerides and glucose in groups were compared by *Mann-Whitney U* test.

3. Results

3.1 Weight and waist circumference

Height, weight and waist circumference of participants are shown in Table 1. Differences in weight and waist circumference were compared within and between the two groups. Statistical calculation showed that differences between the groups were not significant (P = 0.542) and (p= 0.787), respectively. Eight weeks of exercise did not induce a significant change in weight within the moderate group. There was a non-significant decrease in waist circumference, from 99.2 (± 14, 5) cm pre to 96.6 (±15, 1) cm post, within the moderate group. Differences within the control group also had a significant decrease in waist circumference, from 97.9 (±10, 2) cm pre to 95.1 (±11, 2) cm post.

Table 1: Height, weight and waist of participants in the moderate and the control group before (Pre) and after (Post) the period of 8 weeks

Parameters	Control group (n= 13)		Moderate group (n= 11)		Group differences
	Pre Mean ± SD	**Post Mean ± SD**	**Pre Mean ± SD**	**Post Mean ± SD**	**p-value**
Height, cm	178,3 ± 7,0	178,3 ± 6,8	174,4 ± 3,4	174,4 ± 3,4	~~0,947~~
Weight, kg	82,6 ± 12,9	81,4 ± 12,7	82,7 ± 15,0	81,8 ± 16,0	0,542
Waist, cm	97,9 ± 10,2	95,1 ± 11,2*	99,2 ± 14,5	96,6 ± 15,1	0,787

Values presented as mean ± SD, *p≤0.05, # 0.05<p<0.1, SD (standard deviation).

3.2 Resting heart rate

Resting heart rate of participants is shown in Table 2. There was no significant difference in resting heart rate from baseline to post testing in control and moderate group (p=0.717 and p=0.962 respectively). There was no difference between the two groups either (p=0.747).

Table 2: Resting heart rate of participants in in the moderate and the control group before (Pre) and after (Post) the period of 8 weeks

Parameters	Control group (n= 13)		Moderate group (n= 11)		Group differences
	Pre Mean ± SD	**Post Mean ± SD**	**Pre Mean ± SD**	**Post Mean ± SD**	**P-value**
Resting HR	69 ± 15,0	68 ± 14,0	66 ± 10,7	66 ± 11,7	0,747

Values presented as mean ± SD., *p≤0.05, #0.05<p<0.1, SD (standard deviation); HR (heart rate)

3.3 Body composition

Body fat, muscles percentage and BMI values of participants are shown in table 3. In the moderate group body fat decreased significantly by 9.3% (p=0.063) after the exercise intervention. There were no significant changes in muscle mass or BMI within or between groups.

Table 3: Body fat, muscle mass and BMI of participant in the moderate and the control group (Pre) and after (Post) the period of 8 weeks

Parameters	Control group (n= 13)		Moderate group (n= 11)		Group differences
	Pre Mean ± SD	**Post Mean ± SD**	**Pre Mean ± SD**	**Post Mean ± SD**	**p-value**
Body fat, %	24,2 ± 5,6	23,8 ± 6,0	26,9 ± 8,2	24,4 ± 7,4*	0,163

Muscles, %	34,5 ± 4,9	34,5 ± 4,8	33,5 ± 3,5	33,6 ± 3,5	0,416
BMI, kg/m^2	25,9 ± 3,0	25,7 ± 3,1	27,2 ± 4,8	26,9 ± 5,3	0,365

Values presented as mean ± SD., *p≤0.05, #0.05<p<0.1, SD (standard deviation); HR (heart rate); BMI (body mass index)

3.4 Maximal oxygen uptake and heart rate recovery

HR, VO_{2max}, HRR and RER values of participants are shown in Table 4. There was a trend towards a 6.1% increase in VO_{2max} after 8 weeks of moderate exercise (p= 0.084). However changes in VO_{2max} values compared to control group did not prove to be significant (p= 0.220). No changes were found in HRR and RER.

Table 4: HR, VO_{2max}, HRR and RER of participants in the moderate and the control group (Pre) and after (Post) the period of 8 weeks

Parameters	Control group (n= 13)		Moderate group (n= 11)		P-value
	Pre Mean ± SD	**Post Mean ± SD**	**Pre Mean ± SD**	**Post Mean ± SD**	
Maximum Heart Rate	157,1 ± 20,0	158,9 ± 13,7	167,1 ± 15,3	166,6 ± 14,0	0,493
VO_{2max}, mLx kg^{-1} xmin^{-1}	31,4 ± 5,5	31,9 ± 6,0	32,9 ± 8,0	34,9 ± 9,0#	0,220
Heart Rate Recovery	128 ± 16,1	123 ± 24,5	130 ± 11,6	124 ± 16,8	0,992
Respiratory exchange ratio	1,14 ± 0,1	1,10 ± 0,1	1,14 ± 0,1	1,10 ± 0,1	0,664

Values presented as mean ± SD., *p≤0.05, #0.05<p<0.1, SD (standard deviation); VO_{2max} (maximal oxygen uptake)

3.5 Blood analyses

Values of total cholesterol, LDL, HDL, triglycerides, glucose, hs-CRP and ST2 are listed in Table 5. There was a significant change in differences between two groups in values of LDL (p= 0.03). Within the control group there was a significant increase by 1.8% in values of LDL. Further, differences between two groups in values of HDL showed to have a trend (p=0.09). Within the control group there was a significantly decrease by 7.1% in the values of HDL. There were no changes in total cholesterol, HDL, triglycerides, glucose or ST2 neither within nor between the groups.

Table 5: Blood analysis of participants in the moderate and the control group (Pre) and after (Post) the period of 8 weeks

Parameters	Control group (n= 13)		Moderate group (n= 11)		Group differences
	Pre Mean ± SD	**Post Mean ± SD**	**Pre Mean ± SD**	**Post Mean ± SD**	**p-value**
Total Cholesterol	5,58 ± 1,2	5,78 ± 1,3	6,01 ± 1,2	5,75 ± 1,1	0,156
LDL	3,41 ± 1,2	3,47 ± 1,3*	3,90 ± 1,1	3,63 ± 1,2	0,03*

HDL	1,70 ± 0,5	1,58 ± 0,4*	1,58 ± 0,4	1,58 ± 0,3	0,09#
Triglycerides	1,05 ± 0,3	1,09 ± 0,2	1,17 ± 0,6	1,20 ± 0,6	0,660
Glucose	5,88 ± 1,0	5,98 ± 1,3	6,03 ± 1,6	6,22 ± 1,6	0,383
Hs-CRP	2,41 ± 2,3	2,20 ± 1,9	2,45 ± 3,8	1,78 ± 1,7	0,680
ST2	15,93 ± 2,4	16,94 ± 2,7	18,57 ± 8,6	20,05 ± 8,4	0,868

Values presented as mean ± SD., *p≤0.05, #0.05<p<0.1, SD (standard deviation)

4. Discussion

4.1 Notable findings in present study

The main finding in this study was that 8 weeks of moderate exercise induced a 6% increase in VO_{2max}. Furthermore moderate exercise in 8 weeks resulted in more favourable changes in several cardiovascular risk-factors such as LDL, Hs-CRP, one minute heart rate recovery, waist circumference and body fat. LDL is referred to as '' the bad cholesterol''. This is a possible sign of the health quality of life steadily improving with 8 weeks of moderate training.

4.2 Maximal oxygen uptake and heart rate recovery

It has previously been shown that even a small increase in VO_{2max} makes a substantial impact on survival (Kavanagh, Mertens et al. 2002). Also VO_{2max} is a strong cardiovascular mortality predictor (Blair and Brodney 1999). VO_{2max} measurements determine the level of aerobic capacity in individuals. (Saltin 1985). Thus the 6% increase in VO_{2max} observed in the present study might be of great importance for health. This change in VO_{2max} is a strong trend ($p< 0.1$). 6 % increase in the moderate group is exactly as one would expect of 8 weeks, it is good and not insignificant increase. Other studies also showed that VO_{2max} did not increase significantly after 8 weeks of moderate exercise (Helgerud, Hoydal et al. 2007).

This was partly expected, since a previous study of 12 weeks of moderate exercise in elders resulted in significant increase of VO_{2max} (Meredith, Frontera et al. 1989). Eight weeks of moderate exercise turned out to be a too short a period to achieve a significant increase in VO_{2max} in older men. In the present study, majority of participants in moderate exercise group increased their VO_{2max} slightly. Helgerud et al. show that high intensity exercise is required to achieve significant increase in VO_{2max} in 8 weeks of time period (Helgerud, Hoydal et al. 2007). However several studies have shown that intensity of exercise is crucial and that moderate exercise cannot be as effective as high intensity even if it lasts over longer periods (Thomas, Adeniran et al. 1984, Wenger and Bell 1986, Helgerud, Hoydal et al. 2007).

Since we know that many older people are not able to perform high intensity exercise, then moderate intensity could be another solution to improve the health. For some elders moderate intensity is also a good start to get in better shape first then increase to higher intensity if possible. The present study may show that moderate exercise should not be underestimated especially for the elderly who need a slow tempo in the beginning. None of the elderly gave up in the moderate group and that is a good sign.

Furthermore, no significant change was observed in HHR in comparison between two groups. Further, participants in the moderate group were looking forward to taking the test again to see the progress. The attendance throughout the training period and none of the participants in the moderate group withdrew from the project. Furthermore, none of the participants in moderate group gave up too early during the VO_{2max} measurements.

4.3 Weight and waist circumference

As expected, there were no significant changes in weight during the exercise period. Previous studies on moderate exercise achieved similar results (Meredith, Frontera et al. 1989, Young, Appel et al. 1999). Meredith et al. show that 12 weeks of moderate exercise did not affect the weight of both older and young adults. Participants who took part in our study were not instructed to any diet change. Food intake was not taken into account during the study. Thus control group was recommended to not change either their exercise or diet habits. This was done to unsure that the control group did not get large changes in their results or to achieve ʻʻ as ideal as possibleʼʼ controls. Within the control group there was a significant decrease in waist circumference. However, there was a non-significantly decrease in waist circumference in the moderate exercise group. Decreasing their waist circumference is a good sign, since a large waist circumference is risk factor of metabolic syndrome (Alberti, Zimmet et al. 2006, Alberti, Eckel et al. 2009, Stensvold, Slordahl et al. 2012) and used as a predictor of CVD (Dobbelsteyn, Joffres et al. 2001). Schjerve et al. also show that 3 months of moderate exercise had no significant effect on waist circumference (Schjerve, Tyldum et al. 2008). Usually due to aging, waist circumference increases in the elderly and is a health risk predictor (Racette, Evans et al. 2006). Williams et al. show that older athletes have smaller waist circumference compared to elders with no regular training background (Williams 1998). It is unknown why the control group slightly decreased in waist circumference. It may be that when people join the study they become more aware of fitness and quality of food and therefore change their habits.

4.4 Resting heart rate

As expected, in both groups there was no observed significant changes in resting HR. Meredith et al. found that 12 weeks of moderate exercise in elderly did not result in major changes in resting heart rate (Meredith, Frontera et al. 1989). Resting heart rate is measurement of heartbeat in one minute in a relaxed condition. This parameter can be measured to determine if a person has too slow heart beats (Bradycardia) or too rapid (Tachycardia) (Durham and Worthley 2002). A study has shown that people with low resting heart rate have a lower chance of developing CVD (Nauman, Janszky et al. 2011).

4.5 Body composition

As expected there was no indication of significant change in body fat, muscle mass and BMI after 8 weeks of moderate exercise. Meredith et al. also show similar results after 12 weeks of moderate exercise. While in that study, methods used to measure body composition were different (Meredith, Frontera et al. 1989). According to other studies, it is normal not to achieve great changes of body fat or weight in short timed exercise periods (Wilmore, Royce et al. 1970, Sidney, Shephard et al. 1977). However, Dumortier et al. show that 8 weeks of moderate exercise led to significant decrease in body fat in overweight patients with metabolic syndrome (Dumortier, Brandou et al. 2003). In that study they had 28 participants and thus higher statistical power. Another possible reason of significant decrease is different populations. Increasing of body fat is associated with aging (Brozek, Grande et al. 1963). Therefore 9.3 % decrease in body fat in the moderate group after 8 weeks of training notes a positive development even though it is not statistically significant. Longer periods of moderate exercise could possibly produce a significant decrease in body fat but we need more studies to confirm that. Most of the participants who took a part in our study did not exercise regularly before the pre-test.

4.6 Blood analyses

There was no any significant change in the values of LDL within the moderate group. Within this group there was a non-significant decrease by 7% in the values of LDL. This result shows no significant improvement in cardiovascular health, but at least it prevents deterioration and helps the level of LDL to remain stable. In the moderate group, one participant increased greatly in the values of LDL, while the most of the participants decreased slightly. Considering this fact, statistical analysis was done again without this particular participant who increased much. This analysis showed a decreasing trend in LDL in the moderate group without this participant. (These results are not shown in present study). It has not been examined as to why this participant increased greatly in the values of LDL. A possible explanation may be that this participant changed diet habits or the participant did not give blood in the fasted state.

Decrease in values of LDL is perceived as a positive impact of exercise on this cardiovascular biomarker. Another study also shows that regular exercise leads to decreasing LDL levels (Williams 1998). High levels of LDL are used as an indication for presence of several diseases such as CVD. Reduction of LDL is an indication of health improvement in older people (Williams 1998).

The reason for the observed 27% non-significant decrease in Hs-CRP in the moderate group could possibly be explained through the value contribution of one participant who had very high baseline Hs-CRP. And this participant probably contributes to the large decline in the moderate group. Probably this person has inflammation in the body at baseline, i.e. the participant had a cold. The results from other participants were more variable thus no significant decline was observed within the moderate group. Ballou et al have shown that concentration of Hs-CRP is increased in plasma due to aging (Ballou, Lozanski et al. 1996). Compared to LDL, Hs-CRP is even more crucial predictor of CVD (Ridker, Rifai et al. 2002). Non-significant change of Hs-CRP levels in moderate group was expected, since another similar study also achieved same result (Schjerve, Tyldum et al. 2008). Some other studies have shown that regular exercise decreases the levels of Hs-CRP (Petersen and Pedersen 2005, Troseid, Lappegard et al. 2009, Balducci, Zanuso et al. 2010). Possibly 8 weeks of moderate exercise is too short a period to achieve significant decrease in levels of Hs-CRP in older individuals. Two long term studies have also shown that regular exercise decreases levels of Hs-CRP significantly (Mattusch, Dufaux et al. 2000, Fallon, Fallon et al. 2001). Otherwise regular exercise has a reducing effect on low grade inflammation (Stensvold, Slordahl et al. 2012).

There were no-significant differences in values of total cholesterol neither between nor within the groups. Similar to LDL measurements, low values of total cholesterol are beneficial (Williams 1998). Total cholesterol represents both LDL and HDL. LDL makes up the majority, almost two of three part of total cholesterol content. Thus decrease in LDL values should affect values of total cholesterol. Elevated total cholesterol values are also associated with several diseases such as coronary heart disease and myocardial infarction (Rossouw, Lewis et al. 1990).

As expected, values of HDL remained the same within the moderate exercise group. Schjerve et al. show that 12 weeks of moderate exercise did not affect the values of HDL (Schjerve, Tyldum et al. 2008) There was a trend in the values of HDL between the groups. This result is neither positive nor negative for health. HDL is associated with several CVD such as Coronary heart disease (CHD), high levels of HDL is favourable and decreasing the risk of CHD (Durstine and Haskell 1994). In some cases lower values of HDL can also be associated with metabolic syndrome (Alberti, Eckel et al. 2009, Stensvold, Slordahl et al. 2012). In another study, values of HDL also remained the same after 2 months of low intensity exercise on patients with metabolic syndrome (Dumortier, Brandou et al. 2003). Surprisingly within the control group there was a significant decrease in the values in HDL from baseline to post period. This development was not expected. It is unknown if higher values of HDL in the control group is an indication of improved health condition or may several participants did not fast before blood sampling.

No significantly difference occurred in the values of Triglycerides both between and within groups. Elevated plasma levels of triglycerides are risk factor of CHD.(Austin, Rodriguez et al. 2000).

Ahmad et al. notes that low levels ST2 protein are favourable and ST2 is a novel cardiovascular biomarker that has previously been shown to change slightly after exercise training (Ahmad, Felker et al. 2012). Thus this effect is considered to be individual. The levels of ST2 are elevated in patients with heart failure and used as a predictor of this disease (Ky, French et al. 2011, Ahmad, Felker et al. 2012, Ahmad, Fiuzat et al. 2012). This is due to the fact that high level of ST2 increase the probability of myocardial stress (Shah and Januzzi 2010).

Our results matching partly with these facts, since two of the participants in the moderate group decreased highly in ST2 compared to the majority. Otherwise, there was no observed significant change both within and between the groups.

High levels of glucose combined with other risk factors are associated with metabolic syndrome and diabetes mellitus 2 (Alberti, Eckel et al. 2009, Stensvold, Slordahl et al. 2012, Tang, Pei et al. 2013).

All participants were asked to fast before the blood samples. A non-fasted state will cause false elevated results. As unexpected there was a non-significant increase by 3.2 % in levels of glucose. This increase was sensational although this change was neither significant or a trend. Similar results were obtained after 12 weeks of moderate exercise training (Schjerve, Tyldum et al. 2008). This increase may be an indication of increased food intake due to exercise or that some of the participants did not fast even though they were instructed to do so. King et al have previously shown that moderate exercise has only limited effect on appetite. They showed that exercise only delayed hunger short time period after session (King, Wasse et al. 2013).

4.7 Limitations

Results of VO_{2max} tests are considered to be credible, but the number of participants in the study was low. In other word, the statistical power is low. Otherwise we have standardized methods that we trust.

Participants in the control group have some changes that were not expected. Observed improvements in control group suggest that participants changed their lifestyle habits despite the fact they were encouraged to continue as before. It is possible that more statistically significant differences would have been observed between the two groups had the statistical power been greater.

5. Conclusion

Eight weeks of moderate exercise caused a significant decrease of body fat within the moderate exercise group. Since body fat increases due to aging this decrease is considered to be beneficial for their health. Further there was a trend towards increase in VO_{2max}; this was expected and even if the change were not significant this is an important improvement. VO_{2max} is the most crucial parameter analysed in present study and is a strong mortality predictor. These findings show that 8 weeks of moderate exercise improves to some extent cardiovascular risk factors and quality of life in older men.

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Appendix

A. BORG SCALE

6 No exertion at all

7 Extremely light

8

9 Very light

10

11 Light

12

13 Somewhat hard

14

15 Hard (heavy)

16

17 Very hard

18

19 Extremely hard

20 Maximal exertion