

A Combined and Intensive Exercise Model Improves Physical Capacity in Cardiac Patients

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Received date: September 09, 2017; Accepted date: September 21, 2017; Published date: September 25, 2017

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Abstract

Objective: We have measured the effect of combined strength and high intensity endurance training on physical capacity and lipid profile in patients with heart and coronary diseases. We wanted to see whether cardiac patients were able to increase training intensity to improve strength without losing endurance capacity.

Methods: Thirty heart-operated subjects participated in an intervention period of 10 weeks. The age of the participants was between 52-72 years. The Resistance-Interval group (RE-INT) practiced four times a week with two intensive endurance (spinning) sessions and two strength training sessions. The endurance training consisted of intervals where the heart rate reached >90% of maximum heart rate. Strength training was performed in three series with a load of 8-12 repetition maximum (RM). The subjects in the control group (CON) performed two to three sessions per week according to a national program specialized for coronary patients (called "Ullevaal model"). We had a randomized controlled trial.

Results: Maximal leg strength increased in both groups during the intervention, but the increase was higher in the RE-INT group (from 107.9 ± 8.1 kg to 162.0 ± 8.4 kg) compared to the CON group (from 110.8 ± 8.9 to 125.4 ± 9.5) (p<0.001). Strength in chest press, the maximal oxygen uptake and the concentration of high density-lipoprotein (HDL) protein increased in both groups during the test period. However, no differences were observed between the RE-INT and CON group. Low density-lipoprotein (LDL), blood pressure and body weight did not change during the intervention period in any of the groups.

Conclusion: Cardiac patients were able to increase training intensity, strength and maximal oxygen uptake during a period of 10 weeks. We found that combined training has an effective impact on the increase in leg strength. The increase in muscle strength can be vital for the everyday quality of life in cardiac patients.

Keywords: Cardiac patients; Combined exercise model; Muscle strength; Maximal oxygen uptake; Lipid profile

Introduction

Heart disease is one of the most common diseases in the western world with an increase in the number of annual heart surgeries [1]. Since the 1980s, physical activity has been recognized as an important part of rehabilitation for these patients and different training programs have been suggested with documented positive effects [2-4].

Recent studies have shown that high intensive endurance training has a positive effect on oxygen uptake and lipid profile [5-7]. There has been an increased interest in including strength training in coronary rehabilitation, also in programs including overweight patients [8,9]. Resistance training increases the performance of endurance activities such as walking and alike. This is highly relevant for elderly subjects with risks for disabilities and is an important component of physical functioning [10]. The effect of resistance training has been shown to be more pronounced in older subjects (>60 years), probably related to the increased loss of muscle strength with age [11].

Previously strength training has not been recommended for people with high blood pressure [12], but one may argue the opposite. For instance, sarcopenia, the age-associated loss of skeletal muscle, is a major concern for this group and is further associated with increased risk of inactivity and associated implications and requirement of health care [13-15]. Additionally, increased leg strength has been well documented to improve quality of daily life situations [16]. Kazior and co-workers found improvements in muscle mitochondrial function and increased hypertrophy when a combined training model consisting of both strength and endurance was applied compared to a model with resistance exercise only [17]. In general, resistance training claims to be beneficial for inflammatory profiles and able to lower the risk of cardiovascular diseases [18].

Implementation of strength training in cardiac rehabilitation could be crucial considering that >80% of these patients are overweight [10,19]. Volume and distribution of fat combined with reduced muscle mass often increase cardiovascular risks [20]. Strength training stimulates muscle mass compared to aerobic training, which might result in decreased fat mass by an increase in resting metabolic rate [8,19,21,22]. Strength training has also been shown to improve lipid profiles, which is a risk factor in cardiovascular diseases [9].

Interestingly, combined exercise models of endurance and strength training has been shown to impair the gain in strength [23], whereas others have seen improvement in strength when performing combined training [24]. Development in strength and muscle mass volume is of clinical interest since this can reduce risks of falling accidents and increase the ability to handle daily activities [25].

We wanted to test if a combination of strength training and high intensity endurance training increased muscle strength in cardiac patients. Additionally, we were interested to monitor several other parameters such as lipid profiles, systolic and diastolic blood pressure and maximal oxygen uptake to identify any potential differences between the resistance-Interval (RE-INT) group, and the control group (CON).

Materials and Methods

Experimental design

Participants were recruited from an independent association (The Cardio Club, Fredrikstad, Norway; <http://cardioclub.no/>) for previously heart-operated patients. All participants received oral and written information about the research project, test procedures and risk factors. Written consents were collected. The experimental design was approved by the Regional Ethics Committee of Southern Norway (protocol number: 2012/1103-1, Chairman: prof. Dr. Med Stein A Evensen, date of approval: 01.10.2012), and complied with the standards set by the Declaration of Helsinki. There is no conflict of interest to report.

	CON group (n=15)	RE-INT group (n=15)
Age (years)	65 (2)	62 (2)
Height (cm)	170.0 (3.2)	176.5 (2.3)
Male/Female	12/3	15/0
Data are mean		

Table 1: Physical characteristics of the cardiac patients.

The Resistance-Interval (RE-INT) group, were set to perform both strength and high intensity interval endurance training during the intervention period, while the control (CON) group continued with their normal training protocol, as described below.

Initially, ten subjects were excluded for medical reasons by our cardiologist (Head Cardiologist at the Department of Thoracic and Cardiovascular Surgery, Østfold Hospital, Norway). Seven of the participants wanted to continue their normal training program consisting of endurance training two to three times a week, and were for that reason included in the CON group. The remaining 23 participants were randomly assigned based on VO₂max and weight into two groups of 15 subjects (Table 1). The seven subjects with a preference of training method did not differ in regards to the parameters used for randomization, and the groups are for that reason considered properly randomized. Age, gender, weight (Table 2) and medication were not different between the two groups. The age of the participants was 50-72 years. Two of the participants experienced discomfort during training but were allowed to continue in the program after medical examination. Three participants in the CON group dropped out for reasons not related to the study itself.

	CON group (n=15) Pre-post Mean (SEM)	RE-INT group (n=13) Pre-post Mean (SEM)
Weight (kg)	82.4 (4.7)-81.3 (4.6)	89 (5.1)-89.3 (5.2)
BMI	28.2 (1.1)-27.7 (1.3)	28.3 (1.3)-28.8 (1.3)
Training sessions	26 (3)	40 (1)
Data are mean and SEM in parentheses		

Table 2: Body weight and BMI before and after the intervention.

Training protocol

The RE-INT group trained two endurance sessions and two strength training sessions per week (Table 2). Strength and endurance were performed on different days. During the first week participants performed only one strength training session and two endurance training sessions. Endurance training consisted of spinning arranged as pyramid training, with intervals of 2-3-4-5-4-3-2 min with one min rest between the intervals. Heart rate was measured by using heart rate monitors (Polar RS400/RS800CX, Kempele, Finland) at each training session. During the intervals >90% of maximum heart rate was devised. A heart rate of >90 % HR_{max} corresponds to 17-18 on the Borg scale [26,27]. Strength training was performed with three sets of eight exercises (leg press, leg curl, leg extension, chest press, pull down, crunch, 2 back activities). The load was 12 RM during the first two weeks, 10 RM during week 3-6 and 8 RM during week 7-10. The training was performed in Life Fitness training machines (Brunswick, Chicago, USA) at Friskis & Svettis Fitness Center, Fredrikstad, Norway. Training adherence was 98% (SEM 0.9) in the RE-INT group during the intervention period.

The CON group continued with their normal Cardio Club fitness program, consisting of two to three sessions per week according to a national standard program (The Ullevaal Model) specialized for coronary patients [4]. This training model consists of warming up, 2 to 3 intervals of step, running or other exercises in six minutes duration with increasing intensity with a heart rate of 85-90 % of HF_{max} at the end. The intensity was 16-17 on the Borg scale (80-90% of max heart rate). The interval exercise was followed by 10-15 min stretching. Each session lasted for 45-55 min and the training adherence was 82% (SEM 2.8) during the intervention period.

Training intensities were adjusted if necessary by employing the Borg scale of perceived intensity. If the heart rate were below 85-90% of HF_{max}, higher intensities were suggested. Exclusion criteria during the intervention were sickness, injury, or other reasons that made the participants fail to conduct training in a satisfactory manner.

Maximal oxygen uptake

Prior to the randomization, all 30 participants performed a preliminary maximal oxygen uptake test. The cardiologists wanted to ensure that all participants could go through intensive endurance test through controlled conditions. All participants conducted VO₂max measurements (mixing chamber, Jaeger Oxycon Pro, Hoechberg, Germany) on a bike (Ergo-line ELG 55 Bitz, Germany). The pre-test of VO₂max was performed one week before the intervention and a VO₂max test less than one week after the last training session. The VO₂max started at a workload of 50 W and increased by 15 W every 30 s until exhaustion. The VO₂, respiratory exchange ratio (RER), heart rate and rate of perceived exertion (Borg scale) were measured during

the 2 last min of each workload. Capillary blood samples (ABL 700 series Bergman Diagnostika, Radiometer Copenhagen) were collected within 1 min after finishing the test to confirm that the patients had reached exhaustion.

	CON group (n=15) Pre-post AV (SEM)	RE-INT group (n=13) Pre-post AV (SEM)
Total cholesterol mmol/L	3.9 (0.2)-4.1 (0.2)	4.6 (0.3)-4.4 (0.2)
HDL mmol/L	1.3 (0.1)-1.4 (0.1)	1.4 (0.1)-1.5 (0.1)
LDL mmol/L	2.2 (0.2)-2.1 (0.2)	2.5 (0.2)-2.3 (0.2)
Triglycerider mg/dl	1 (0.1)-1.2 (0.2)	1.3 (0.1)-1.2 (0.1)
Hemoglobin mg/dL	14.4 (0.2)-14.7 (0.2)	14.4 (0.3)-14.3 (0.4)
Blood pressure systolic (mmHg)	140.5 (4.2)-132.1 (3.3)	133.2 (2.7)-132 (3.9)
Blood pressure diastolic (mmHg)	78.2 (2.6)-79.7 (2.3)	86.6 (2.5)-81.2 (2.3)
Data are mean and SEM in parentheses		

Table 3: Effect of the intervention on circulating lipids and blood pressure.

Test of maximal strength in leg press and chest press

Prior to the pre-test all participants went through a training session with the test machines to get familiar to the test-procedure. Blood pressure was on a normal level and no preliminary strength test was performed prior due to the randomization [12]. All participants performed chest and leg press with one repetition maximum (1RM) before and after the intervention period. Tests were performed in Life Fitness training machines after a general warm up. The load was increased until participants were unable to lift the weight. Participants were given three attempts to fulfil the highest load and one minute rest between the attempts.

Blood samples

Venous blood samples were collected in the fasting state (≥ 12 h) prior to and after the intervention period. The final samples were collected 2-3 days after the intervention period (Table 3). Serum triglycerides, serum-total cholesterol, serum-HDL and serum-LDL were analyzed by the Siemens Advia 1650 automatic analyzer (Østfold Hospital Trust, Fredrikstad, Norway).

Blood pressure

Blood pressure was measured using an ERKA D-83646 blood pressure gauge (Produsent, Bad Tölz, Germany Calmeyer Medizintechnik GmbH) before and after the intervention period following general procedures. The participants relaxed 10 min prior to and during the examination with the arm positioned at the level of the right atrium. Three measurements were taken at intervals of one min, and the average value was calculated to represent the patient's blood pressure. Additional readings were done if the measurements differed with >5 mm Hg.

Statistics

Data are presented as mean values with respectively SEM values. Two ways ANOVA was used to compare data for the two groups obtained before and after the training intervention. A P value <0.05 was considered significantly different.

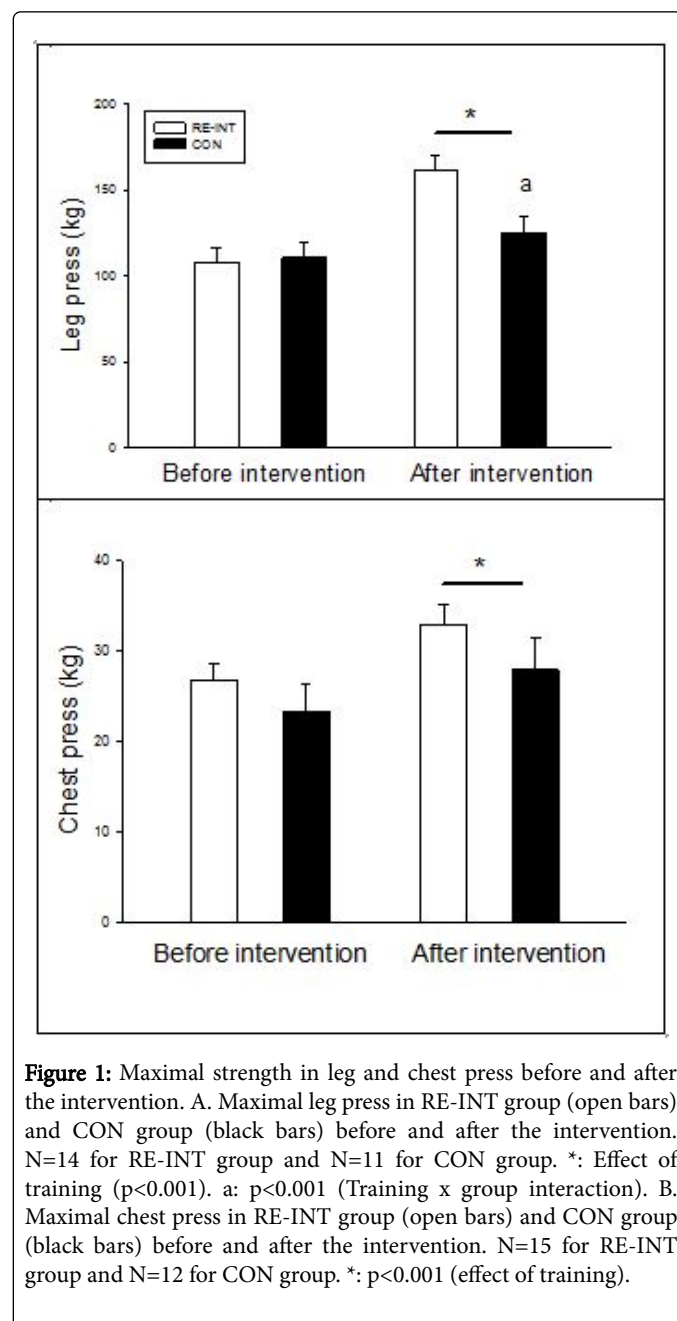


Figure 1: Maximal strength in leg and chest press before and after the intervention. A. Maximal leg press in RE-INT group (open bars) and CON group (black bars) before and after the intervention. N=14 for RE-INT group and N=11 for CON group. *: Effect of training ($p < 0.001$). a: $p < 0.001$ (Training x group interaction). B. Maximal chest press in RE-INT group (open bars) and CON group (black bars) before and after the intervention. N=15 for RE-INT group and N=12 for CON group. *: $p < 0.001$ (effect of training).

Results

Maximal leg strength increased in both groups during the intervention (Figure 1A). The maximal load in leg press increased from 107.9 ± 8.1 kg to 162.0 ± 8.4 kg (50.1%) in the RE-INT group, and from 110.8 ± 8.9 kg to 125.4 ± 9.5 kg (13%) in the CON group. The observed increase in leg strength for the RE-INT group was

significantly larger compared to the increase in leg strength for the CON-group ($p < 0.001$).

Maximal strength in chest press increased from 26.7 ± 2.0 kg to 32.9 ± 2.2 kg (23.2%) in RE-INT group and from 23.3 ± 3.0 kg to 27.9 ± 3.4 kg (19.7%) in the CON group (Figure 1B). There were no differences in increase between the groups.

Maximal oxygen uptake increased from 30.9 ± 1.0 to 32.4 ± 1.2 ml/kg/min (5%) in the RE-INT group ($p < 0.01$), and from 29.7 ± 1.3 to 30.9 ± 1.2 ml/kg/min (4%) ($p < 0.05$) during the 10 week intervention (Figure 2A). There were no differences in increase of the maximal oxygen uptake between the groups.

The power increased from 228.3 ± 98 watt to 249.0 ± 94 watt (9.1%) in the RE-INT group, and from 206.3 ± 54 watt to 216.2 ± 72 watt (4.9%) in the CON-group (Figure 2 B). There were no differences in the increase between the groups.

The concentration of high density lipoprotein (HDL) increased from 1.37 ± 0.3 mM to 1.47 ± 0.9 mM (7.4%) in the RE-INT group, and from 1.29 ± 0.5 mM to 1.39 ± 0.6 mM (8.2%) in the CON-group (Figure 3). There was no difference in increase between the groups.

Body weight, concentration of low density lipoprotein (LDL) and the systolic and diastolic blood pressure did not change significantly during the intervention period in any of the groups.

Discussion

The main finding in this study is that a combined exercise model consisting of strength training and high intensive endurance training increases leg strength in cardiac patients compared to a control group performing endurance training only. This suggests that strength training successfully can be included in an intensive endurance training program for cardiac patients.

The increase in leg strength (Figure 1A) in our study was considerably larger compared to other studies [28-30]. Also, hypertrophy has been shown in subjects using a similar combined exercise program [31]. Such increase in leg strength is of large clinical relevance as sarcopenia is predominant in cardiac patients [11].

However, others have shown that a combination of strength and endurance training can impair improvements [23]. Adaptations in strength have also been reported to be compromised when combined training is performed compared to strength training only [32,24].

The large increase in leg strength in the RE-INT group was surprising and it can be speculated that the high intensity endurance training on cycle has contributed in a positive manner. Furthermore, exercise at different days may be favourable since the participants always performed training in a recovered state which reduces the possibility of interference or inhibition in combined training. Improvement in physical capacities will normally be affected by different variables like volume and intensity [33]. The total volume in our training protocol differed between the two groups. The CON group practiced two or three training session per week ($N=25$) while the RE-INT group practiced four training sessions a week ($N=39$). This might reflect the differences in results. The intensity in the training was at a high level in the RE-INT group which practiced heavy load strength training (6-12 RM) which normally results in muscular hypertrophy (>85% of 1RM) combined with >90% intensity in spinning training. The CON group practiced submaximal circuit training which

normally results in minor hypertrophy compared with heavy load training.

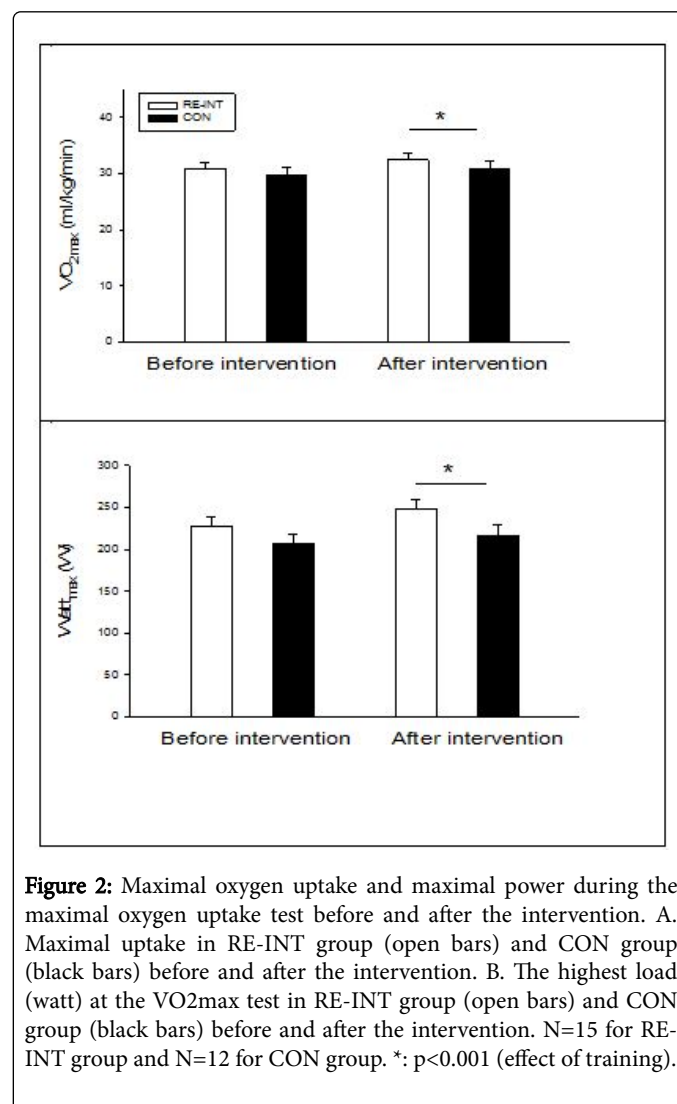


Figure 2: Maximal oxygen uptake and maximal power during the maximal oxygen uptake test before and after the intervention. A. Maximal uptake in RE-INT group (open bars) and CON group (black bars) before and after the intervention. B. The highest load (watt) at the VO_{2max} test in RE-INT group (open bars) and CON group (black bars) before and after the intervention. $N=15$ for RE-INT group and $N=12$ for CON group. *: $p < 0.001$ (effect of training).

We found the percentage increase in arm strength to be much lower compared to the increase in leg strength. This is in line with a previous report using subjects of the same age [34]. In a previous study conducted by our group we noticed that upper body muscles seem to respond differently compared to leg muscles considering different loads [35]. Furthermore, other studies confirmed that leg muscles increased more in cross-sectional area with high training volume compared to lower training volume, whereas no differences were observed in the upper body muscles [33,36].

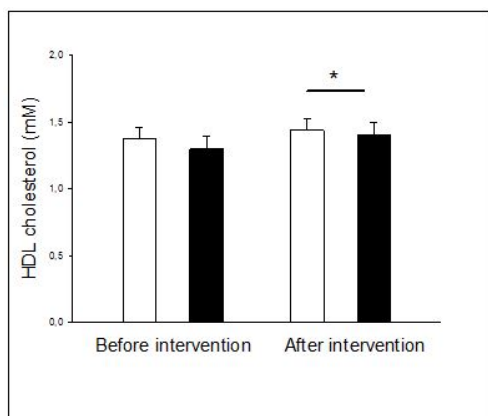


Figure 3: HDL cholesterol and total cholesterol before and after the intervention. A. HDL cholesterol in RE-INT group (open bars) and CON group (black bars) before and after the intervention. N=14 for RE-INT group and N=12 for CON group. *: Effect of training ($p < 0.05$). B. Total cholesterol in RE-INT group (open bars) and CON group (black bars) before and after the intervention. N=15 for RE-INT group and N=12 for CON group. Int: Interaction (Time \times training; $p < 0.02$).

In older subjects, the decrease in leg strength is normally larger than the decrease in arm strength [37]. The reason for the larger decrease in leg strength is unclear, but has large implications on mobility and independent life [38]. Older people accumulate extracellular fat in muscle tissue, which is associated with decline in strength and muscle quality [39]. In the present study all, except four subjects, had a BMI > 25, and were categorized as overweight or obese. Additionally as reported earlier 80% of patients participating in cardiac rehabilitation are overweight [19,40]. Others have shown that an increase in strength is impaired by accumulation of extracellular fat in muscles [41].

Endurance training has been recommended for cardiac patients [42]. In our study we found that the maximal oxygen uptake increased equally in both groups. The endurance training in the RE-INT group (two sessions a week) was very intensive with strenuous levels at the Borg Scale (17-18). The CON group performed two-three sessions a week with submaximal intensity. The reason for the small increase in maximal oxygen uptake in both groups is not obvious. In other studies an increase in maximal oxygen uptake caused by 10 weeks of high intensity endurance training is normally reported to be as much as 10% [43-45]. In our study heart rate was related to maximal heart frequency when maximal oxygen uptake was tested. Several of the participants used β -blockers and all used medication to reduce blood pressure, making data difficult to interpret. The subjects in the present study had a maximal oxygen uptake of about $30 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, which is lower than the Norwegian population in the same age group [46,47].

In both groups we noticed a significant increase ($p < 0.001$) in maximum work load (watt) by exhaustion. According to Vikmoen and co-workers, hypertrophy is important to gain a stronger effect in cycling performance [48]. Furthermore, improved cycling economy has been observed after addition of heavy strength training in trained cyclists [49-51].

Both groups had an increase in leg strength after the intervention. This may explain the equal increase related to the improvements in

work load. However, this was an unexpected result regarding the different training programs between the two groups.

In the present study, all participants, except one had a HDL concentration > 1 mmol/L before the intervention, but in both groups we still observed an increase in HDL after the intervention period. Some studies have reported elevated HDL after endurance training [52]. Many of the participants in the present study used statins, which makes it difficult to interpret data on lipids. However, the participants in the present study did not show any decrease in LDL during the intervention period (Table 3).

The blood pressure did not change during the intervention period (Table 3). It is worth to note that all participants used 3-4 different medicines to reduce blood pressure and risk factors for heart diseases. Neither systolic nor diastolic blood pressure decreased during the study and medication was not changed. Strength training is not recommended for subjects with high blood pressure [12]. However, our data show that strength training, under controlled circumstances, can be conducted successfully in cardiac-operated patients without complications.

Conclusion

Importantly, cardiac patients are able to perform high intensity strength and endurance training. Inclusion of strength training increased leg strength substantially even when conducted in combination with endurance training. The increase in muscle strength, especially leg strength, is important for quality of everyday life in cardiac risk populations.

References

1. Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, et al. (2010) Heart disease and stroke statistics--2010 update: a report from the American Heart Association. *Circulation* 121: e46-e215.
2. McCartney N (1998) Role of resistance training in heart disease. *Med Sci Sports Exerc* 30: S396-402.
3. Yung LM, Laher I, Yao X, Chen ZY, Huang Y, et al. (2009) Exercise, vascular wall and cardiovascular diseases: an update (part 2). *Sports Med* 39: 45-63.
4. Nilsson BB, Hellesnes B, Westheim A, Risberg MA (2008) Group-based aerobic interval training in patients with chronic heart failure: Norwegian Ullevaal Model. *Phys Ther* 88: 523-535.
5. Jensen J, Rustad PI, Kolnes AJ, Lai YC (2011) The role of skeletal muscle glycogen breakdown for regulation of insulin sensitivity by exercise. *Front Physiol* 2: 112.
6. Wojtaszewski JF, Nielsen JN, Richter EA (2002) Invited review: effect of acute exercise on insulin signaling and action in humans. *J Appl Physiol* 93: 384-392.
7. Marzolini S, Oh PI, Thomas SG, Goodman JM (2008) Aerobic and resistance training in coronary disease: single vs. multiple sets. *Med Sci Sports Exerc* 40: 1557-1564.
8. Marzolini S, Oh PI, Brooks D (2012) Effect of combined aerobic and resistance training versus aerobic training alone in individuals with coronary artery disease: a meta-analysis. *Eur J Prev Cardiol* 19: 81-94.
9. Kraemer WJ, Ratamess NA, French DN (2002) Resistance training for health and performance. *Curr Sports Med Rep* 1: 165-171.
10. Ades PA, Ballor DL, Ashikaga T, Utton JL, Nair KS (1996) Weight training improves walking endurance in healthy elderly persons. *Ann Intern Med* 124: 568-572.
11. Collamati A, Marzetti E, Calvani R, Tosato M, D'Angelo E, et al. (2016) Sarcopenia in heart failure: mechanisms and therapeutic strategies. *J Geriatr Cardiol* 13: 615-624.

12. Cardoso CG Jr, Gomides RS, Queiroz AC, Pinto LG, da Silveira Lobo F, et al. (2010) Acute and chronic effects of aerobic and resistance exercise on ambulatory blood pressure. *Clinics* 65: 317-325.
13. Burton LA, Sumukadas D (2010) Optimal management of sarcopenia. *Clin Interv Aging* 5: 217-228.
14. Johnson ML, Robinson MM, Nair KS (2013) Skeletal muscle aging and the mitochondrion. *Trends Endocrinol Metab* 24: 247.
15. Montero-Fernández N, Serra-Rexach JA (2013) Role of exercise on sarcopenia in the elderly. *Eur J Phys Rehabil Med* 49: 131-143.
16. Bindawas SM, Al Snih S, Ottenbacher AJ, Graham J, Protas EE, et al. (2015) Association Between Lower Extremity Performance and Health-Related Quality of Life in Elderly Mexican Americans. *J Aging Health* 27: 1026-1045.
17. Kazior Z, Willis SJ, Moberg M, Apró W, Calbet JA (2016) Endurance exercise enhances the effect of strength training on muscle fiber size and protein expression of Akt and mTOR. *PLoS One* 11: e0149082.
18. Silveira Mm, Bouffleur Fj, Basso Bc, Alves Ca, Duarte T, et al. (2015) Positive effects of resistance training on inflammatory parameters in men with metabolic syndrome risk factors. *Nutrición hospitalaria: Organó oficial de la Sociedad española de nutrición parenteral y enteral* 32: 792-798.
19. Audelin MC, Savage PD, Ades PA (2008) Changing clinical profile of patients entering cardiac rehabilitation/secondary prevention programs: 1996 to 2006. *J Cardiopulm Rehabil Prev* 28: 299-306.
20. Després JP (1997) Visceral obesity, insulin resistance, and dyslipidemia: contribution of endurance exercise training to the treatment of the plurimetabolic syndrome. *Exerc Sport Sci Rev* 25: 271-300.
21. Pratley R, Nicklas B, Rubin M, Miller J, Smith A, et al. (1994) Strength training increases resting metabolic rate and norepinephrine levels in healthy 50- to 65-yr-old men. *J Appl Physiol* 76: 133-137.
22. Westcott WL (2012) Resistance training is medicine: effects of strength training on health. *Curr Sports Med Rep* 11: 209-216.
23. Hickson RC (1980) Interference of strength development by simultaneously training for strength and endurance. *Eur J Appl Physiol Occup Physiol* 45: 255-263.
24. Häkkinen K, Alen M, Kraemer WJ, Gorostiaga E, Izquierdo M (2003) Neuromuscular adaptations during concurrent strength and endurance training versus strength training. *Eur J Appl Physiol* 89: 42-52.
25. Warburton DE, Gledhill N, Quinney A (2001) Musculoskeletal fitness and health. *Can J Appl Physiol*, 26: 217-237.
26. Astrand Po, Rodahl K (2003) Textbook of work physiology: physiological bases of exercise, Champaign, Ill, Human Kinetics.
27. Borg GA (1974) Perceived exertion. *Exerc Sport Sci Rev* 2: 131-153.
28. Kraemer WJ, Adams K, Cafarelli E, Dudley GA, Dooly C, et al. (2002a) American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. *Med Sci Sports Exerc* 34: 364-380.
29. Jones TW, Howatson G, Russell M, French DN (2016) Effects of strength and endurance exercise order on endocrine responses to concurrent training. *Eur J Sport Sci* 17: 326-334.
30. Giuliano C, Karahalios A, Neil C, Allen J, Levinger I, (2017) The effects of resistance training on muscle strength, quality of life and aerobic capacity in patients with chronic heart failure - A meta-analysis. *Int J Cardiol* 227: 413-423.
31. Kūusmaa M, Schumann M, Sedliak M, Kraemer WJ, Newton RU, et al. (2016) Effects of morning vs. evening combined strength and endurance training on physical performance, muscle hypertrophy, and serum hormone concentrations. *Appl Physiol Nutr Metab* 41: 1285-1294.
32. Häkkinen K, Komi PV, Alén M (1985) Effect of explosive type strength training on isometric force- and relaxation-time, electromyographic and muscle fibre characteristics of leg extensor muscles. *Acta Physiol Scand* 125: 587-600.
33. Rønnestad BR, Egeland W, Kvamme NH, Refsnes PE, Kadi F, et al. (2007) Dissimilar effects of one- and three-set strength training on strength and muscle mass gains in upper and lower body in untrained subjects. *J Strength Cond Res* 21: 157-163.
34. Sousa N, Mendes R, Abrantes C, Sampaio J, Oliveira J (2013) A randomized 9-month study of blood pressure and body fat responses to aerobic training vs. combined aerobic and resistance training in older men. *Exp Gerontol* 48: 727-733.
35. Hanssen KE, Kvamme NH, Nilsen TS, Rønnestad B, Ambjørnsen IK, et al. (2013) The effect of strength training volume on satellite cells, myogenic regulatory factors, and growth factors. *Scand J Med Sci Sports* 23: 728-739.
36. Paulsen G, Mykkestad D, Raastad T (2003) The influence of volume of exercise on early adaptations to strength training. *J Strength Cond Res* 17: 115-120.
37. Janssen I, Heymsfield SB, Wang ZM, Ross R (2000) Skeletal muscle mass and distribution in 468 men and women aged 18-88 yr. *J Appl Physiol* 89: 81-88.
38. Thomas DR (2007) Loss of skeletal muscle mass in aging: examining the relationship of starvation, sarcopenia and cachexia. *Clin Nutr* 26: 389-399.
39. Delmonico MJ, Harris TB, Visser M, Park SW, Conroy MB, et al. (2009) Longitudinal study of muscle strength, quality, and adipose tissue infiltration. *Am J Clin Nutr* 90: 1579-1585.
40. Ades PA, Savage PD, Toth MJ, Harvey-Berino J, Schneider DJ (2009) High-calorie-expenditure exercise: a new approach to cardiac rehabilitation for overweight coronary patients. *Circulation* 119: 2671-2678.
41. Kraemer WJ, Volek JS, Clark KL, Gordon SE, Puhl SM (1999) Influence of exercise training on physiological and performance changes with weight loss in men. *Med Sci Sports Exerc* 31: 1320-1329.
42. Hirai DM, Musch TI, Poole DC (2015) Exercise training in chronic heart failure: improving skeletal muscle O₂ transport and utilization. *Am J Physiol Heart Circ Physiol* 309: H1419-1439.
43. Bacon AP, Carter RE, Ogle EA, Joyner MJ (2013) VO₂max trainability and high intensity interval training in humans: a meta-analysis. *PLoS One* 8: e73182.
44. Bækkerud FH, Solberg F, Leinan IM, Wisløff U, Karlsen T, et al. (2016) Comparison of Three Popular Exercise Modalities on VO₂max in Overweight and Obese. *Med Sci Sports Exerc* 48: 491-498.
45. Rønnestad BR, Hansen J, Vegge G, Tønnessen E, Slettaløkken G (2015) Short intervals induce superior training adaptations compared with long intervals in cyclists-an effort-matched approach. *Scand J Med Sci Sports* 25: 143-151.
46. Loe H, Rognum Ø, Saltin B, Wisløff U (2013) Aerobic capacity reference data in 3816 healthy men and women 20-90 years. *PLoS One* 8: e64319.
47. Loe H, Nes BM, Wisløff U (2016) Predicting VO₂peak from Submaximal-and Peak Exercise Models: The HUNT 3 Fitness Study, Norway. *PLoS One* 11: e0144873.
48. Vikmoen O, Ellefsen S, Trøen Ø, Hollan I, Hanestadhaugen M, et al. (2016) Strength training improves cycling performance, fractional utilization of VO₂max and cycling economy in female cyclists. *Scand J Med Sci Sports* 26: 384-396.
49. Barrett-O'Keefe Z, Helgerud J, Wagner PD, Richardson RS (2012) Maximal strength training and increased work efficiency: contribution from the trained muscle bed. *J Appl Physiol* 113: 1846-1851.
50. Sunde A1, Støren O, Bjerkaas M, Larsen MH, Hoff J (2010) Maximal strength training improves cycling economy in competitive cyclists. *J Strength Cond Res* 24: 2157-2165.
51. Louis J, Hausswirth C, Easthope C, Brisswalter J (2012) Strength training improves cycling efficiency in master endurance athletes. *Eur J Appl Physiol* 112: 631-640.
52. Slentz CA, Bateman LA, Willis LH, Shields AT, Tanner CJ, et al. (2011) Effects of aerobic vs. resistance training on visceral and liver fat stores, liver enzymes, and insulin resistance by HOMA in overweight adults from STRRIDE AT/RT. *Am J Physiol Endocrinol Metab* 301: E1033-1039.