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| SEDES22 | **KU LEUVEN**  **GROEP BIOMEDISCHE WETENSCHAPPEN**  FACULTEIT BEWEGINGS- EN REVALIDATIEWETENSCHAPPEN |

**Effects of Aerobic Interval Training versus Moderate Continuous Training on exercise capacity, muscle strength and physical activity in patients with Coronary Artery Disease**

door Matthias Loeckx en Tomas De Mol

Masterproef aangeboden tot het behalen van graad van master in de revalidatiewetenschappen en kinesitherapie

o.l.v.

Prof. Dr. L. Vanhees, promotor

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**Contributes to the Saintex-CAD study**

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**WOORD VOORAF**

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Deelname aan dit 2-jarige proces van het begeleiden van de trainingen tot het uitschrijven van de resultaten heb ik als zeer verrijkend voor mijn individuele ontwikkeling ervaren. Ik hoop de verworven inzichten en vaardigheden in mijn latere carrière nog te kunnen gebruiken.

Leuven, 23 april 2014, M.L.

**SITUERING**

Deze Master thesis is uitgevoerd binnen het onderzoeksdomein van de Afdeling Cardiovasculaire & Respiratoire Revalidatie van het Departement van Revalidatiewetenschappen van de Faculteit van Bewegings- en Revalidatiewetenschappen aan de Katholieke Universiteit Leuven. Deze onderzoeksgroep gaat de effecten na van fysieke activiteit en inspanning op de primaire en secundaire preventie. De grote onderzoeksdomeinen van Professor Dr. L. Vanhees zijn: 1) Het effect van cardiale revalidatie en inspanning en de verklarende mechanismen van adaptatie; 2) De rol van fysieke activiteit en fysieke fitheid in de primaire, secundaire en tertiaire preventie; 3) De veiligheid van inspanning tijdens cardiale revalidatie en de rol van de cardiovasculaire screening voor preventie van ernstige cardiale voorvallen tijdens inspanning.

Onze masterproef kadert binnen een groter multicenter project tussen het UZ Leuven en het UZ Antwerpen, SAINTEX-CAD genaamd. “SAINTEX-CAD” staat voor Study on Aerobic INTerval EXercise training in Coronary Artery Disease patients. Binnen deze studie worden twee verschillende trainingsmodaliteiten met elkaar vergeleken, namelijk Aerobe Interval Training (AIT) en Matig Continue Training (MCT), en dit op parameters zoals het aëroob uithoudingsvermogen, de levenskwaliteit, de vaatfunctie en de veiligheid van deze trainingen.1,2

Tientallen jaren geleden werd verplichte wekenlange bedrust voorgeschreven als remedie tegen hartziekten. De evolutie van de geneeskunde bracht alsmaar meer wetenschappelijk bewijs met zich mee dat deze rust niet aangewezen is. Vandaag de dag wordt regelmatige fysieke activiteit dan ook gepromoot als belangrijk onderdeel binnen het multidisciplinair behandelingsprogramma voor hartpatiënten. Naast beweging staan medicatie, rookstop, voedingscontrole en stress management, voorop in het revalidatieprogramma van een doorsnee hartpatiënt.1

Het is aangetoond dat patiënten met een hoger aëroob uithoudingsvermogen, hogere spierkrachtwaarden en een hoger niveau van fysieke activiteit een verminderd risico op cardiale mortaliteit hebben.3,4,5 Binnen deze studie wordt nagegaan of trainingen met intervalcomponenten aan hoge intensiteit of trainingen van een eerder continu karakter aan matige intensiteit een verschillend effect hebben op deze drie grote pijlers. Voor zover wij weten zijn er nog geen studies gedaan over het effect van MCT en AIT op de combinatie van uithoudingsvermogen, spierkracht en fysieke activiteit bij patiënten met coronair vaatlijden.

Indien zou blijken dat intervaltraining een groter effect heeft op het aërobe uithoudingsvermogen, spierkracht en niveau van fysieke activiteit, dan zou dit aanleiding kunnen geven tot een kortere revalidatieduur en een snellere re-integratie van de patiënten in het maatschappelijke leven.

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**Effects of Aerobic Interval Training versus Moderate Continuous Training on exercise capacity, muscle strength and physical activity in patients with Coronary Artery Disease**

**Effects of Aerobic Interval Training versus Moderate Continuous Training on exercise capacity, muscle strength and physical activity in patients with Coronary Artery Disease**

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**ABSTRACT**

**Background**—Exercise training increases peak aerobic capacity (peak VO2), muscle strength and physical activity (PA), which all strongly predict the incidence of cardiovascular diseases and all-cause mortality. It is still not known which characteristics of exercise training are the most appropriate to maximize these training effects. The objective is to investigate if aerobic interval training (AIT) is superior to moderate continuous training (MCT) in improving peak VO2, muscle strength and PA.

**Methods and results**—In this clinical trial one hundred Coronary Artery Disease (CAD) patients were randomized to either MCT at 70-75% of the peak heart rate or AIT at 90-95% of peak heart rate, three times a week, for twelve weeks. Peak VO2 (with maximal graded exercise test on a cycle-ergometer), muscle strength (with Jamar hand-held dynamometer and Biodex) and PA (with sensewear) were measured before and after the training program. Peak VO2, peak heart rate, peak workload, resting heart rate and isokinetic flexion strength (60°/sec) improved significantly and to a similar extent after both exercise interventions. Peak VO2, isokinetic extension strength at 180°/s and active energy expenditure correlated significantly, except for relation between changes in active energy expenditure and changes in isokinetic extension strength at 180°/s which was weak and not significant.

**Conclusion**—Exercise training induced significant increases in peak VO2 and isokinetic flexion strength. Training effects were equal for AIT or MCT intervention. No significances in PA were found.

**Keywords**—Coronary artery disease, exercise capacity, muscle strength, physical activity, interval training

**Introduction**

Coronary artery disease (CAD) is the progressive narrowing of arteries that are responsible for supplying oxygen to the myocardium, caused by atherosclerosis.1 Atherosclerosis is the process in which fatty substances (e.g. cholesterol) accumulate in the wall of the arteries.2 CAD is the most prominent cause leading to death with a percentage of 12.8 in accordance to the World Health Association.3 In Belgium, CAD was responsible for a total cost of 3.5 billion Euros in 2004.4

Exercise based cardiac rehabilitation acts as a cornerstone in a multidimensional intervention for CAD patients, with a reduction in total and cardiac mortality of 20% to 32% compared with usual medical care.5,6 Exercise based cardiac rehabilitation also leads to greater reductions in systolic blood pressure, self-reported rates of smoking, triglyceride levels and total cholesterol levels, compared to usual care in patients with CAD.7 It might serve as an educational setting for the adjustment of patients’ activity patterns.8

Despite the importance of this treatment strategy, there is still debate concerning the optimal training characteristics that should be used in exercise training programs for CAD patients. The most commonly used training mode is the continuous training at moderate intensity (MCT). Recently, aerobic interval training (AIT) has been introduced as an alternative training mode in cardiac patients, in which bouts of high intensity loads are being incorporated.9 Small studies investigated the effects of AIT and MCT in CAD patients and conflicting results were found.8, 10,11,12 Recently, nine studies comparing AIT and MCT in CAD patients were extensively reviewed by Pattyn et al.13 They found that AIT improved peak aerobic capacity (peak VO2) 1.60 ml/min/kg more than MCT in patients with CAD.13,14 As peak VO2 is an independent predictor of survival in both healthy subjects and in individuals with CAD, this 1.60 ml/kg/min larger improvement after AIT is of clinical relevance.15 In addition, AIT has also been proved to have a superior effect over the traditional MCT regarding endothelial function, left ventricle morphology and function (e.g. ejection fraction).16 While some authors stated that higher intensity exercise is linked to a more common occurrence of adverse effects,17 AIT seems to be safe in CAD patients.18

In general, CAD patients have an impaired peak VO2 and a faster occurrence of muscle fatigability.19 This lower peak VO2 is associated with a decreased muscle strength, which is caused by a lower activity of local muscular enzymes and by a smaller cross-section of the muscle.19 After 3 months of exercise-based cardiac rehabilitation, including a combination of endurance training and moderate resistance training, peak VO2, isometric and isokinetic leg strength and endurance were significantly improved compared to baseline values.20

Thomaes et al.21 proved that patients who followed a 3 month cardiac rehabilitation program had an increase in peak VO2, muscle strength and diameter. They also showed that knee extensor muscular endurance was the best predictor for the relative change in peak VO2.21 Maximal knee extensor isometric strength has also been shown to be positively related to the exercise capacity in CAD patients.22 On the other hand, Sumide et al.23 found that higher values of muscle strength do not always result in better exercise tolerance. To our knowledge, no previous study investigated the effects of AIT versus MCT on muscle strength.

Persons of advanced age and people who endure health condition problems are less likely to participate in moderate or vigorous PA due to physical or psychosocial barriers.24 Lower levels of PA result in a further progression of CAD and an associated lowering of the cardiorespiratory fitness.25 This cardiorespiratory fitness is shown to have a greater influence on the incidence of CAD and cardiovascular disease risk factors than physical activity (PA).26

The main objective of our study was to compare the effects of AIT and MCT in patients with CAD on exercise capacity parameters, muscle strength and PA.

**Methods**

*Participants*

One-hundred CAD patients, aged between 40 and 75 years, were included in the Saintex study between February 2011 and December 2012.27 All patients were investigated in the cardiac rehabilitation center of the UZ Leuven Gasthuisberg. Patients with CAD were defined as having a history of myocardial infarction (MI), coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) and patients had a left ventricular ejection fraction (LVEF) of at least 40%. Further inclusion conditions were an optimal medical treatment of the patients, stable pharmacotherapy and normal symptoms. Exclusion criteria were significant illness during the last 6 weeks, recent CABG (<30 days), severe ventricular arrhythmia with functional or prognostic significance, myocardial ischemia, hemodynamic deterioration, exercise-induced arrhythmia or another heart disease that limits exercise tolerance, co-morbidities that influence a one year prognosis, functional and mental disability, a habit of regular vigorous exercise, acute chronic inflammatory disease, glomerular filtration rate (GFR) <25ml/min/1.73m², hemoglobin<10g/dl, severe chronic obstructive pulmonary disease (COPD) (FEV1<50%) and participation in another clinical trial. After screening, eligible and interested subjects were randomized in 2 groups (AIT and MCT) on a 1:1 basis, using an online randomization procedure. Subjects signed a written consent form prior to participation in accordance with the Declaration of Helsinki. The study was approved by the local ethics committee.

*Measurements*

*Cardiopulmonary exercise test.*A maximal graded exercise test until exhaustion on a cycle-ergometer was performed before the exercise intervention and after 12 weeks. The test protocol started with a load of 20 Watts, and workload increased by 20 Watts every minute. Heart rate (HR) and a twelve lead-ECG were continuously recorded during the test, and blood pressure was measured every 2 minutes and at the end of the test. Breath-by-breath gas exchange was measured continuously, providing ventilation (Ve), oxygen uptake (VO2) and carbon dioxide production (VCO2). Peak VO2 was defined as the mean VO2-value reached during the last full bout of 30 seconds of the exercise test. The criteria of Binder et al.28 for a maximal exercise test were used. The patient’s weight was measured with a Tefal progress sensitive computer.

*Muscle strength*. The Jamar hand-held dynamometer (Saehan corp., Korea) was used to measure maximal hand grip strength. Patients were seated with the upper arm parallel to the body, the elbow flexed at 90° and the wrist positioned neutral. Patients were instructed to develop a maximal contraction during 3 seconds. Instructors encouraged the subjects to perform the strength test with maximal effort. The test was repeated 3 times for each hand alternatively, with a break of 10 seconds between the measurements. The average of the 3 attempts was used for analysis. The Jamar dynamometer has shown to be valid for measuring hand grip strength.29

The Biodex system 3 PRO (Biodex medical systems, USA) was used to measure the patient’s isokinetic extension and flexion strength, and the maximal isometric extension strength. The patient had to sit upright on the Biodex chair with back support, with the hip joint in a 90° flexion-angle. The patients’ trunk and legs were firmly stabilized using straps around the chest, hips and the legs. To avoid any compensation, the subjects were instructed to hold their hands on their thighs during their maximal efforts. The instructor vocally encouraged each subject in a standardized way to complete every part of the test to the maximum. The subject started with isometric knee extension at 60° during 5 seconds, repeated 4 times and interrupted by 30 seconds of rest. The highest value, corrected for weight, was used in the analyses. After 1 minute of rest, an isokinetic test with an angular velocity of 60°/sec was performed, consisting of 4 knee extension and flexion movements as fast as possible. After a rest period of 30 seconds, the same procedure was repeated at an angular velocity of 180°/sec. The average of the 4 repetitions at each angular speed was used in the analyses.

Muscle strength was measured before and after the 12 weeks intervention period.

*Sensewear.* The sensewear bodymonitor (Bodymedia) is an armband enabling a continuous collection of data about energy expenditure.30 In particular, the amount of steps, the duration and intensity of activity (sedentary, moderate, vigorous), total energy expenditure, active energy expenditure and average level of PA expressed as average metabolic equivalent, were determined.

The Sensewear was given to the patients at the beginning and at the end of the exercise training intervention. The device was worn during the day at the upper dominant arm during seven consecutive days. In a population of COPD patients, Van Remoortel et al.31 concluded that the sensewear armband is a valid monitor to measure standardized PA.

*Exercise intervention*

The exercise training took place 3 times a week for 12 weeks (see figure 1). Each training session was performed on a cycle ergometer and was supervised by educated physiotherapist. The AIT group started with a ten-minute warming up (60-70% peak HR), then cycled four times a 4-minute interval at high intensity (90-95% peak HR) while each interval was separated by a 3 min active pause interval at 50-70% of peak HR. The total exercise time in the AIT group was 38 minutes.

The MCT group started with a 5-min warming up, followed by 37 minutes of cycling at moderate intensity (70-75% of peak HR), and ended with 5 min cool-down. Each session of the MCT group had a duration of 47 minutes. Both programs were isocaloric9.

HR was continuously monitored during training to assure patients trained within their target HRs. The Borg 6-20 scale was taken to evaluate the patients’ rate of perceived exertion. Apart from the exercise training, patients had the possibility to attend six multi-disciplinary educational sessions.

An overview can be seen in figure 1, where the study design and intervention programs are outlined.

**Figure 1.** Flowchart of the study design and intervention program



CAD, coronary artery disease; CABG, Coronary artery bypass graft; MI, myocardial infarction; PCI, percutaneous coronary intervention; n, number; AIT, aerobic interval training; MCT, moderate continuous training; CPET, cardiopulmonary exercise testing; Peak HR, peak heart rate; min, minutes.

*Statistical analysis*

Analyses were performed using SAS Software version 9.3 (SAS Institute Inc., Cary, North Carolina). Baseline data for AIT and MCT were compared using an ANOVA for the numerical variables and a chi-square test for categorical variables. Pathology groups were defined as follows: AMI included patients undergoing AMI or AMI+PCI; CABG group included patients undergoing CABG, AMI+CABG or AMI+PCI+CABG; PCI group included patients only undergoing PCI. As pathology differed significantly between groups, an ANCOVA with pathology as covariate was used to measure the changes before and after the intervention (follow up effect), between the groups (group effects), and the interaction effects (follow up x group effects). Pearson correlation coefficients were calculated between exercise capacity parameters, PA parameters and muscle strength outcomes. Statistical significance was set at p < 0.05.

**Results**

Table 1 shows the baseline characteristics of all included patients. Pathology differed significantly between groups and was therefore used as a covariate in further analysis. For the other baseline values, no significant differences were found.

**Table 1.** Baseline values of the AIT and the MCT group

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variables** | **AIT** | **MCT** | | **Significance** |
| |  | | --- | | **General** | |  |  | |  |
| Sample size | 50 | | 50 |  |
| Age (years) | |  | | --- | | 57.0 ± 8.74 | | | 59.9 ± 7.96 | Ns |
| Sex (% male) | 46 (92%) | | |  | | --- | | 46 (92%) | | Ns |
| Height (cm) | |  | | --- | | 172 ± 7.15 | | | |  | | --- | | 173 ± 8.53 | | Ns |
| Weight (kg) | |  | | --- | | 86.5 ± 15.4 | | | |  | | --- | | 83.8 ± 12.3 | | Ns |
| **Pathology** |  | |  | p = 0.014 |
| Post-AMI | |  | | --- | | 33 (66%) | | | |  | | --- | | 22(44%) | |  |
| Post-PCI | 4 (8%) | | 15 (30%) |  |
| |  | | --- | | Post-CABG | | 13 (26%) | | |  | | --- | | 13 (26%) | |  |
| **Medication** |  | |  |  |
| Clopidogrel | |  | | --- | | 15 (30%) | | | |  | | --- | | 16 (32%) | | Ns |
| Prasugrel | |  | | --- | | 23 (46%) | | | |  | | --- | | 24 (48%) | | Ns |
| Ace inhibitor | |  | | --- | | 36 (72%) | | | |  | | --- | | 37 (74%) | | Ns |
| Beta-blocker | |  | | --- | | 46 (92%) | | | |  | | --- | | 43 (86%) | | Ns |
| Statin | |  | | --- | | 49 (98%) | | | |  | | --- | | 50 (100%) | | Ns |
| Diuretics | |  | | --- | | 3 (6%) | | | |  | | --- | | 7 (14%) | | Ns |
| Vitamin K antagonists | |  | | --- | | 3 (6%) | | | |  | | --- | | 1 (2%) | | Ns |
| Oral anti-diabetics | |  | | --- | | 8 (16%) | | | |  | | --- | | 7 (14%) | | Ns |
| |  | | --- | | **Risk Factors** | |  | |  |  |
| History of hypertension | |  | | --- | | 34 (68%) | | | 22 (44%) | Ns |
| |  | | --- | | History of diabetes | | 13 (26%) | | 6 (12%) | Ns |
| Smoking | |  | | --- | | 39 (78%) | | | 39 (78%) | Ns |
| Alcoholic drinks/week | 4,00 ± 4.75 | | 3,80 ± 3.84 | Ns |
| Familial predisposition | |  | | --- | | 7 (14%) | | | 13 (26%) | Ns |
| **Social status** |  | |  | Ns |
| Working | |  | | --- | | 22 (44%) | | | 22 (44%) |  |
| Retired | |  | | --- | | 20 (40%) | | | 24 (48%) |  |
| Disability | |  | | --- | | 8 (16%) | | | 4 (8%) |  |
| |  | | --- | | **Education** | |  | |  | Ns |
| |  | | --- | | Primary school | | |  | | --- | | 4 (8%) | | | 2 (4%) |  |
| |  | | --- | | Trade/technical school | | |  | | --- | | 27 (54%) | | | 26 (52%) |  |
| |  | | --- | | High school | | |  | | --- | | 9 (18%) | | | |  | | --- | | 7 (14%) | |  |
| |  | | --- | | University or equivalent | | |  | | --- | | 10 (20%) | | | |  | | --- | | 15 (30%) | |  |

Data presented as mean ± SD or numbers and percentages. AIT, aerobic interval training; MCT, moderate continuous training; Ns, not significant; AMI, acute myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft;ACE,angiotensin-converting-enzyme. Statistical significance was set at p < 0.05.

Fifteen subjects dropped out during the 12 weeks of intervention. More specifically, there were nine drop outs for the AIT group and six for the MCT group (no significance).

As described in table 2, after 3 months of training there was a significant gain in peak VO2, peak HR and maximal load, while resting HR decreased significantly. Resting HR and maximal load differed between both intervention groups, with AIT showing higher values at all-time points. Participation to the exercise training induced a significant increase in peak VO2 (ml/kg/min) of 28.4% and 21.0% for respectively the interval and the continuous group. However, training effects were equal after both training interventions.

The overall trainings intensities differed significantly between the two intervention groups: AIT trained at 95 ± 13% of peak HR and MCT at 84 ± 10% of peak HR (p-group=0.001).

Isokinetic flexion strength (60°/sec) improved after 3 months of training, while for isometric extension strength and isokinetic flexion strength (180°/sec) a trend appeared.

None of the PA values changed significantly after 3 months of training.

Thus, our hypothesis concerning a superior effect of AIT to MCT in improving peak VO2, muscle strength and PA is rejected.

**Table 2.** Exercise capacity, muscle strength and PA at baseline and after 3 months of AIT or MCT

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Variables | AIT | | MCT | | F group | F follow-up | F interaction | |
|  | **Pre** | **Post** | **Pre** | **Post** |  |  |  |
| Exercise capacity | |  | | --- | |  | |  |  |  |  |  |  |
| Peak VO2 (ml/min) | 1865 ± 501 | 2366 ± 536 | 1894 ± 455 | 2263 ± 503 | 1.44ns | 35.84\*\*\* 35.8435.84\*\*\* | 0.89ns |
| Peak VO2 (ml/kg/min) | |  | | --- | | 21.8 ± 5.49 | | |  | | --- | | 28.0 ± 6.22 | | 22.9 ± 5.76 | |  | | --- | | 27.7 ± 6.64 | | |  | | --- | | 0.00ns | | |  | | --- | | 38.91\*\*\* | | |  | | --- | | 0.58ns | |
| Maximal load (watt) | |  | | --- | | 162 ± 39.2 | |  | | 207 ± 46.9 | |  | | --- | | 163 ± 42.1 | | |  | | --- | | 202 ± 45.8 | | |  | | --- | | 4.48\* | | |  | | --- | | 20.11\*\*\* | | |  | | --- | | 0.01ns | |
| peak HR (b.p.m.) | |  | | --- | | 139 ± 21.2 | |  | | 147 ± 19.7 | |  | | --- | | 136 ± 21.2 | | |  | | --- | | 141 ± 21.2 | | |  | | --- | | 3.66α | | 4.45\* | |  | | --- | | 0.31ns | |
| RER peak | 1.21 ± 0.10 | 1.21 ± 0.09 | 1.20 ± 0.11 | |  | | --- | | 1.22 ± 0.06 | | |  | | --- | | 0.00ns | | 1.02ns | |  | | --- | | 0.46ns | |
| Resting HR (b.p.m) | 68.7 ± 11.5 | 65.4 ± 10.4 | 64.1 ± 10.5 | |  | | --- | | 60.9 ± 10.1 | | |  | | --- | | 8.23\*\* | | 4.28\* | |  | | --- | | 0.00ns | |
| Body weight (kg) | 86.6 ± 15.4 | 85.9 ± 15.5 | 83.9 ± 12.3 | 82.9 ± 12.0 | 0.74ns | 0.34ns | 0.01ns |
| Muscle strength |  |  |  |  |  |  |  |
| Hand grip right (kg) | 41.7 ± 8.89 | 43.9 ± 10.1 | 40.9 ± 8.95 | |  | | --- | | 40.1 ± 8.19 | | |  | | --- | | 2.72ns | | |  | | --- | | 0.26ns | | |  | | --- | | 1.09ns | |
| Hand grip left (kg) | 39.3 ± 9.46 | 41.8 ± 10.1 | 38.9 ± 8.80 | |  | | --- | | 38.8 ± 7.80 | | |  | | --- | | 0.98ns | | |  | | --- | | 0.68ns | | |  | | --- | | 0.85ns | |
| Isometric ext (Nm) | 177 ± 42.8 | 195 ± 34.4 | 177 ± 46.1 | |  | | --- | | 185 ± 43.1 | | |  | | --- | | 0.65ns | | |  | | --- | | 3.65α | | |  | | --- | | 0.54ns | |
| Isokinetic ext at 60°/s (Nm) | 162 ± 44.2 | 170 ± 35.1 | 162 ± 45.7 | |  | | --- | | 167 ± 43.5 | | 0.06ns | 1.07ns | 0.03ns |
| Isokinetic flex at 60°/s (Nm) | 102 ± 29.3 | 113 ± 25.5 | 102 ± 29.7 | |  | | --- | | 114 ± 28.8 | | |  | | --- | | 0.00ns | | |  | | --- | | 6.37\* | | |  | | --- | | 0.05ns | |
| Isokinetic ext at 180°/s (Nm) | 104 ± 26.0 | 108 ± 26.5 | 104 ± 28.8 | |  | | --- | | 113 ± 31.4 | | |  | | --- | | 0.36ns | | |  | | --- | | 2.17ns | | |  | | --- | | 0.34ns | |
| Isokinetic flex at 180°/s (Nm) | 88.7 ± 23.1 | 96.5 ± 21.3 | 89.3 ± 28.7 | |  | | --- | | 96.5 ± 25.0 | | |  | | --- | | 0.02ns | | |  | | --- | | 3.75α | | |  | | --- | | 0.01ns | |
| PA |  |  | |  | | --- | |  | |  |  |  |  |
| Steps (per week) | 54850 ±17286 | 48982 ± 15871 | 53849 ± 32429 | |  | | --- | | 54224 ± 25262 | | |  |  | | --- | --- | | 0.01ns |  | | |  | | --- | | 0.41ns | | |  | | --- | | 0.60ns | |
| Moderate PA (hours/7days) | 10.8 ± 6.30 | 9.72 ± 5.86 | 11.1 ± 8.18 | |  | | --- | | 10.9 ± 6.38 | | |  | | --- | | 0.08ns | | |  | | --- | | 0.31ns | | |  | | --- | | 0.16ns | |
| Vigorous PA (hours/7days) | 0.22 ± 0.45 | 0.20 ± 0.26 | 0.21 ± 0.28 | |  | | --- | | 0.32 ± 0.49 | | |  | | --- | | 0.38ns | | |  | | --- | | 0.56ns | | |  | | --- | | 0.96ns | |
| Total energy expenditure (kcal/7days) | 15481 ± 3537 | 14314 ± 3425 | 15505 ± 3801 | |  | | --- | | 14954 ± 3677 | | |  | | --- | | 0.00ns | | |  | | --- | | 1.92ns | | |  | | --- | | 0.26ns | |
| Active energy expenditure (kcal/7days) | 3682 ± 2461 | 3205 ± 1776 | 3654 ± 2644 | |  | | --- | | 3522 ± 1840 | | |  | | --- | | 0.00ns | | |  | | --- | | 0.61ns | | |  | | --- | | 0.21ns | |
| Average MET (MET) | 1.61 ± 0.30 | 1.55 ± 0.25 | 1.58 ± 0.29 | |  | | --- | | 1.61 ± 0.28 | | 0.00ns | |  | | --- | | 0.14ns | | |  | | --- | | 0.73ns | |
| PA duration (hours) | 11.1 ± 6.50 | |  | | --- | | 9.92 ± 5.91 | | 11.3 ± 8.33 | |  | | --- | | 11.2 ± 6.71 | | |  | | --- | | 0.09ns | | |  | | --- | | 0.27ns | | |  | | --- | | 0.19ns | |
|  |  |  |  |  |  |  |  |

Values are mean ± SD or F-values. Pre, before intervention; post, after intervention; AIT, aerobic interval training; MCT, moderate continuous training; peak VO2: peak oxygen uptake; HR, heart rate; b.p.m., beats per minute; RER peak, peak respiratory exchange ratio; ext, extension strength; flex, flexion strength, Nm, Newton meters; PA, physical activity; MET, average metabolic equivalent; \*\*\*P<0.001; \*\*p<0.01; \*p<0.05; αp=0.06; ns: not significant. Statistical analyses are performed by ANCOVA (adjusted for pathology).

The correlations between exercise capacity and PA (table 3A and B), exercise capacity and muscle strength (table 3C and D) and muscle strength and PA (table 3E and F) are shown in table 3. Figure 2 (A and B) shows the relation between peak VO2, isokinetic extension strength at 180°/s and active energy expenditure. These parameters are outlined as specific values of respectively; exercise capacity, muscle strength and physical activity. All three parameters correlated significantly, except for the correlation between changes in active energy expenditure and changes in isokinetic extension strength at 180°/s which was weak and not significant (r=0.195; p=0.129). Moderate correlations were found for peak VO2 and isokinetic extension strength at 180°/s and its changes.

Relative peak VO2 correlated significantly with all the PA parameters except for the correlation with total energy expenditure (r=0.107; p=0.128). However, changes in total energy expenditure had a moderate and significant correlation with changes in relative peak VO2 (r=0.322; p=0.008). All correlations between relative peak VO2 and muscle strength parameters (see table 3C) were significant and moderate/strong, except for the correlation with hand grip strength which was weak (but still significant). Only changes in isokinetic extension strength at 180°/s had a moderate and significant correlation with changes in relative peak VO2. Other correlations in table 3D were shown to be weak and not significant. Correlations between parameters of PA and muscle strength and its changes are variable and outlined in table 3E-F.

**Figure 2A-B.** Correlations between exercise capacity, muscle strength and PA

r=0.180\*

r=0.253\*

r=0.412\*\*\*

r=0.195ns

r=0.333\*\*\*

r=0.574\*\*\*

Values are Pearson correlation coefficients. peak VO2: peak oxygen uptake; Δ, changes; ext, extension strength; ns, not significant; \*\*\*p<0.001; \*p<0.05.

**Table 3A-B-C-D-E-F.** Correlations after 3 months of AIT or MCT

**B)** Correlations between changes in exercise capacity and PA

**A)** Correlations between exercise capacity and PA

|  |  |
| --- | --- |
| Variables | Relative peak VO2 (ml/kg/min) |
| Steps (per day) | 0,231\*\* |
| Moderate PA(hours/7days) | 0,411\*\*\* |
| Vigorous PA (hours/7days) | 0,334\*\*\* |
| Total energy expenditure (kcal) | 0,107ns |
| Average MET (MET) | 0,372\*\*\* |
| Active energy expenditure (kcal) | 0,333\*\*\* |
| PA duration (hours) | 0,418\*\*\* |

|  |  |
| --- | --- |
| Variables | Δ Relative peak VO2 (ml/kg/min) |
| Δ Steps (per day) | 0.149ns |
| Δ Moderate PA(hours/7days) | 0.269\* |
| Δ Vigorous PA (hours/7days) | 0.303\* |
| Δ Total energy expenditure (kcal) | 0.322\*\* |
| Δ Average MET (MET) | 0.144ns |
| Δ Active energy expenditure (kcal) | 0.253\* |
| Δ PA duration (hours) | 0.283\* |

**C)** Correlations between exercise capacity and muscle strength  **D)** Correlations between changes in exercise capacity and muscle strength

|  |  |
| --- | --- |
| Variables | Relative peak VO2 (ml/kg/min) |
| Hand grip right (kg) | 0,228\*\* |
| Hand grip left (kg) | 0,344\*\*\* |
| Isometric Ext (Nm) | 0,507\*\*\* |
| Isokinetic Ext at 60°/s (Nm) | 0,552\*\*\* |
| Isokinetic Flex at 60°/s (Nm) | 0,563\*\*\* |
| Isokinetic Ext at 180°/s (Nm) | 0,574\*\*\* |
| Isokinetic Flex at 180°/s (Nm) | 0,582\*\*\* |

|  |  |
| --- | --- |
| Variables | Δ Relative peak VO2 (ml/kg/min) |
| Δ Hand grip right (kg) | 0,082ns |
| Δ Hand grip left (kg) | 0,095ns |
| Δ Isometric Ext (Nm) | 0,016ns |
| Δ Isokinetic Ext at 60°/s (Nm) | 0,030ns |
| Δ Isokinetic Flex at 60°/s (Nm) | 0,126ns |
| Δ Isokinetic Ext at 180°/s (Nm) | 0,412\*\*\* |
| Δ Isokinetic Flex at 180°/s (Nm) | 0,141ns |

**E)** Correlations between muscle strength and PA

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Variables | Hand grip right (kg) | Hand grip left (kg) | Isometric Ext (Nm) | Isokinetic Ext at 60°/s (Nm) | Isokinetic Flex at 60°/s (Nm) | Isokinetic Ext at 180°/s (Nm) | Isokinetic Flex at 180°/s (Nm) |
| Steps (per day) | -0,048ns | 0,025ns | 0,108ns | 0,119ns | 0,187\* | 0,093ns | 0,229\*\* |
| Moderate PA (hours/7days) | -0,017ns | 0,103ns | 0,259\*\* | 0,303\*\*\* | 0,284\*\*\* | 0,212\* | 0,289\*\*\* |
| Vigorous PA (hours/7days) | 0,099ns | 0,083ns | 0,187\* | 0,240\*\* | 0,192\* | 0,269\*\* | 0,243\*\* |
| Total energy expenditure (kcal) | 0,279\*\*\* | 0,335\*\*\* | 0,115ns | 0,215\* | 0,200\*\*\* | 0,204\* | 0,173\* |
| Average MET (MET) | 0,067ns | 0,105ns | 0,289\*\*\* | 0,329\*\*\* | 0,308\*\*\* | 0,271\*\* | 0,283\*\*\* |
| Active energy expenditure (kcal) | 0,065ns | 0,179\* | 0,227\*\* | 0,276\*\*\* | 0,270\*\* | 0,180\* | 0,281\*\*\* |
| PA duration (hours) | -0,010ns | 0,106ns | 0,262\*\* | 0,307\*\*\* | 0,287\*\*\* | 0,220\*\* | 0,294\*\*\* |

**F)** Correlations between changes in muscle strength and PA

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Variables | Δ Hand grip right (kg) | Δ Hand grip left (kg) | Δ Isometric Ext (Nm) | Δ Isokinetic Ext at 60°/s (Nm) | Δ Isokinetic Flex at 60°/s (Nm) | Δ Isokinetic Ext at 180°/s (Nm) | Δ Isokinetic Flex at 180°/s (Nm) |
| Δ Steps (per day) | -0,038ns | -0,032ns | 0,039ns | 0,176ns | 0,150ns | 0,090ns | 0,150ns |
| Δ Moderate PA (hours/7days) | 0,160ns | 0,110ns | 0,198ns | 0,190ns | 0,082ns | 0,219ns | 0,166ns |
| Δ Vigorous PA (hours/7days) | 0,247α | 0,233β | 0,141ns | 0,209ns | -0,080ns | 0,310\* | 0,064ns |
| Δ Total energy expenditure (kcal) | 0,116ns | 0,082ns | 0,039ns | 0,126ns | 0,083ns | 0,168ns | 0,154ns |
| Δ Average MET (MET) | 0,206ns | 0,053ns | 0,220ns | 0,258\* | 0,039ns | 0,216ns | 0,121ns |
| Δ Active energy expenditure (kcal) | 0,160ns | 0,133ns | 0,194ns | 0,231β | 0,082ns | 0,195ns | 0,154ns |
| Δ PA duration (hours) | 0,175ns | 0,125ns | 0,198ns | 0,194ns | 0,072ns | 0,231β | 0,164ns |

Values are Pearson correlation coefficients; peak VO2: peak oxygen uptake; kcal, kilocalories; MET, metabolic equivalent; average MET, average metabolic equivalent; PA, physical activity; Δ, change; Ext, extension strength; Flex, flexion strength; Nm, Newton meters; ns, not significant; \*\*\*p<0.001; \*\*p<0.01; \*p<0.05; αp=0.06; βp=0.07.

**Discussion**

After following 3 months of AIT and MCT, significant improvements were found for peak VO2, peak HR, maximal load, isokinetic flexion strength (at 60°/sec) and resting HR. These improvements were similar for both intervention groups. In addition, peak VO2, isokinetic extension strength and active energy expenditure correlated significantly. However, the correlation between changes in active energy expenditure and changes in isokinetic extension strength at 180°/s had no significance.

These results were in contrast with several studies who found a significantly greater increase in peak VO2 in AIT compared to MCT in CAD patients.8,9,10,11 This can be the consequence of the different intensities at which patients exercised in the studies. In Rognmo’s study10, the moderate intensity group exercised at 60-70% of the peak HR, which is lower than the training intensity of the MCT group in our study (70-75% of peak HR). Intensities of the AIT group were comparable with our AIT group. Therefore there is a greater difference in intensity in AIT vs MCT, which could induce a significantly greater improvement of peak VO2 in the study of Rogmno.

Peak VO2 correlated moderately and significantly with muscle strength and changes in isokinetic extension strength at 180°/s. Thomaes et al.21 supported these findings by indicating significant correlations between muscular parameters (including isokinetic extension strength at 180°/s (r=0.68; p<0,01)) and baseline peak VO2. Change in peak VO2 was significantly correlated with change in isokinetic extension strength at 180°/s (r=0,16; p<0,05). Knee extensor endurance (r=0.69) and its response (r=0.32) after training were retained as strongest muscular predictors in explaining peak VO2 change in patients with CAD. Although, in our study no measures of muscle endurance were obtained, it’s likely that an increase in endurance strength took place regarding the improving results on the successive maximal exercise tests.

Remarkably, there was a significant training effect for isokinetic flexion at 60°/s and a trend for isokinetic flexion at 180°/s, while no effect for the isokinetic knee extensors was found. Cycling includes a repeated extension and flexion movement, while more power output is produced during the extension phase. Seat height, pedaling rate, fatigue, power output, physical condition and shoe-pedal interface are factors altering the muscular activation pattern during cycling.32 Cycling with a higher seat will induce a diminished knee angle, which will lead to a higher relative hamstrings (knee flexors) activation compared to the quadriceps (knee extensor) muscles. During the exercise sessions, patients were possibly seated higher than their optimal position, so a significant isokinetic knee flexors strengthening was induced while isokinetic knee extensor strength remained unchanged.

Both exercise capacity and muscle strength are inversely associated with mortality in both healthy and diseased populations.33 In CAD patients, being less mobile, having fear of movement, being ill, lying in bed and sarcopenia are some of the underlying causes of a decline in muscle strength.19 It is important to intervene in this vicious cycle where post-operative CAD patients are less active and become less mobile. Including patients in gradually exercise trainings programs with appropriate guiding and multidisciplinary support to overcome these problems, is essential.

No significant effects on PA for both intervention groups were found, which means that there was no transfer effect from the higher amount of exercise training during the sessions to an increase in leisure-time PA. These findings are in discrepancy with those of Weinstein et al.34 who found a significant increase in PA after a 10-week intervention program in patients with pulmonary arterial hypertension.

A significant relationship was found between an increase in vigorous PA and isokinetic extension strength at 180°/s. Goodpaster et al.35 constructed a randomized control trial to investigate the influence of regular PA on muscle strength and muscle fat infiltration. They proved that PA prevents the loss of knee extension strength, which is known to be a common risk in an advancing aged population.35

*Strength and limitations*

This study is strengthened by the combination of measurements of exercise capacity, PA and muscle strength and correlations between these parameters after an AIT or MCT intervention, in a large study group of CAD patients.

On the other hand, this study has some limitations. The adaptable height of the bicycle seat and position of the handle-bars could have been potential confounders for changes in muscle strength during exercise training. In addition, the irregularity in pedaling rate from 60 to 90 rounds per minute could also have altered the muscular activation pattern, the change in power output and the amount of work that was produced.

*Future research*

More intensive research in a large CAD population group is needed for a better understanding of the optimal guidelines concerning programs for CAD patients and for further clarification of the relationship between exercise capacity, muscle strength and PA.

**Conclusions**

Exercise based cardiac rehabilitation is a keystone in the multidisciplinary treatment of patients with CAD. After an AIT or MCT intervention of 12 weeks, patients with CAD significantly increased exercise capacity and isokinetic flexion strength, but not PA. Changes were similar after both interventions. Peak VO2, isokinetic extension strength at 180°/s and active energy expenditure correlated significantly, except for relation between changes in active energy expenditure and changes in isokinetic extension strength at 180°/s which was weak and not significant.

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All original papers must be arranged in sections under the headings and in the order indicated below (begin each on a separate page):   * **Title page**   + The title page should carry the full title of the paper, consisting of no more than 20 words (only common abbreviations should be used if absolutely necessary); titles should be clear and brief, conveying the message of the paper   + **Manuscripts should have no more than 10 authors.  In cases where there are more than 10 authors, the corresponding author will be contacted and asked to amend.**   + All authors’ names: the full first name, middle name/initial (optional) and last name of each author should appear; if the work is to be attributed to a department or institution, its full name and location should be included. **Persons listed as authors should be those who substantially contributed to the study's conception, design, and performance.**   + The affiliations of all the authors; when authors are affiliated to more than one institution, their names should be connected using a,b,c. 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**Populaire samenvatting**

Het progressief vernauwen van kransslagaders noemen we coronair vaatlijden. Vandaag is dit met 12,8% de meest voorkomende doodsoorzaak volgens de Wereldgezondheidsorganisatie.

Onderzoek heeft aangetoond dat deelname aan cardiale revalidatie de kans op overlijden vermindert met 20-32% bij hartpatiënten. Onderbouwde trainingsprogramma’s zijn een fundamenteel onderdeel binnen dit revalidatieproces. Echter, welke trainingskarakteristieken het meest effect hebben in deze patiëntenpopulatie is nog onduidelijk.

Daarom onderzochten we of Aerobe Interval Training (AIT, 90-95% van maximale hartslag) efficiënter is dan Matig intense Continue Training (MCT, 70-75% van maximale hartslag). Dit zou kunnen leiden tot een kortere revalidatieduur met bijhorend minder kosten en een snellere re-integratie in de maatschappij.

Honderd patiënten met coronair vaatlijden werden gelijk verdeeld over een AIT en MCT groep. Gedurende 3 maanden trainden ze 3x/week op een fietsergometer. De maximale inspanningscapaciteit, spierkracht (handknijpkracht en kracht van bovenbenen) en fysieke activiteit werden gemeten voor en na de 3 maanden interventie.

Uit de resultaten bleek dat beide groepen significant verbeterden in maximale inspanningscapaciteit en in één parameter van de spierkracht, maar dat fysieke activiteit onveranderd bleef. AIT en MCT hadden dezelfde effecten. Maximale inspanningscapaciteit, spierkracht en fysieke activiteit bleken onderling gerelateerd te zijn en hebben elk een effect binnen het revalidatieproces in deze patiëntenpopulatie.