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Effect of very short-term inpatient cardiac rehabilitation programs in acute myocardial infarction patients treated with primary percutaneous coronary intervention

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Abstract

Background: Exercise-based rehabilitation is an important part of treatment patients following acute myocardial infarction (MI). However, data are scarce on the efffects of very short-term exercise programs in patients with acute MI treated with primary percutaneous coronary intervention (pPCI). The aim of the study was to evaluate the effects of very short-term exercise training on cardiopulmonary exercise testing (CPET) parameters in patients suffering acute MI treated with pPCI.

Methods: We studied 40 consecutive patients with MI treated with pPCI reffered for rehabilitation to our institution. The study population consisted of 39 men and 1 women (age 50,60±8,40 years, left ventricular ejection fraction 53,05±6,74 %), who participated in 3-week clinical cardiac rehabilitation program. The program consisted of cycling for 7 times/week, and daily walking for 45 min at intensity of 70-80% of the individual maximal heart rate**.** All patients performed symptom-limited CPET on a bicycle ergometer with a ramp protocol of 10w/min. The CPET also performed after cardiac rehabilitation programs.

Results: After 3 weeks of exercise-based cardiac rehabilitation program improved exercise tolerance as compared to baseline (peak workload 111,50±15,07 vs 129,00±12,77 watts, respectively, p<0,001), as well as peak respiratory exchage ratio (1,02±0,10 vs 1,08 ± 0,13, respectively, p<0,05). Peak systolic blood pressure, heart rate, peak and after 1 minute of rest were also improved. Most importantly, peak VO2 (18,17±3,30 vs 20,64±3,27 ml/kg/min, respectively, p<0,001), peak VCO2 (1,65±0,28 vs 1,96±0,25 ml/kg/min, respectively, p<0,001), peak ventilation (48,61±10,70 vs 57,27±9,85 L/min, respectively, p<0,001) and peak oxygen pulse (14,16±2,62 vs 60.18±14.19 ml/beat, respectively, p<0,05) were also improved. No major adverse cardiac events were noted during the rehabilitation program.

Conclusion: Very short-term exercise training in patients with acute MI treated with pPCI is safe and improves functional capacity, as well as test duration, work load and heart rate response.

Key Words cardiac pulmonary exercise testing, exercise training, cardiac rehabilitation, myocardial infarction

Background

Cardiovascular prevention and rehabilitation critically depend on physical activity and exercise training. [1, 2] Exercise-based rehabilitation leads to reduction in all-cause mortality and the risk of reinfarction. Also, it modulates other risk factors and improves exercise-based capacity and quality of life after myocardial infarction (MI).[3, 4] Aerobic exercise consists of three major components, that include intensity, duration and frequency of exercise sessions. [3, 5] The intensity of exercise training prescription is a key issue in cardiac rehabilitation program. It has not been universaly shown that exercise-based rehabilitation leads to improvement in exercise capacity and reduction in the incidence of cardiac events in patients following acute MI. [1, 6]

Cardiopulmonary exercise testing (CPET) using ramp incremental protocol is the gold standard for exercise intensity assessment and prescription in patients with cardiovascular disease. It has been advocated that this test should be performed, where available, in patients before and after cardiac rehabilitation (CR) program,[7, 8,

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[9] in order to quantify exercise capacity, chronotropic and inotropic responses to exercise, as well as to detect presence and severity of arrhythmias and inducible myocardial ischemia.[10]

Aerobic exercise training in cardiac patients is usually performed using the constant work-rate (CWR) exercise.[5] The exercise intensity influences the metabolic and gas exchange responses to CWR. A number of studies have documented improvements in functional capacity after cardiac rehabilitation programs in patients with stable coronary artery disease and myocardial infarction who underwent percutaneous coronary intervention (PCI). Most studies have reported increase in peak VO_2, in the range of 14 to 31% after exercise training.[11] Almost all previous studies have investigated effects of exercise-based rehabilitation that lasted for at least six weeks. As to our knowledge, there are no studies that investigated effects of very short-term exercise programs in patients suffering acute MI treated with primary PCI (pPCI).

Therefore, the aim of our study was to evaluate effect of very short-term (3 weeks) exercise training on CPET parameters in patients suffering acute MI treated with pPCI.

Methods

Study population. We studied 40 consecutive patients admitted to the Institute for rehabilitation Belgrade for exercise-based rehabilitation program who met all of the following criteria: 1) previous acute MI treated with pPCI, 2). ability to perform a symptom-limited CPET, and 3) signed informed consent. Patients were exluded if they had previous MI or revascularization (other than for index event), unstable angina, significant provocable ischemia, complex ventricular arrhythmias, primary valvular disease, severe peripheral vascular disease, severe chronic obstructive pulmonary disease, neuromuscular disease or orthopedic limitation. Study design was approved by the Belgrade University School of Medicine Ethics Committee, and written information and consent were obtained from all patients prior to any study procedure.

Cardiac rehabilitation program. Patients took part in a comprehensive CR program seven times a week for a period of three weeks. The program included exercise training, information sessions, dietary counseling, psychosocial support and smoking cessation. There were two training sessions daily, each of 45 minutes duration. First training session was performed in the morning, which included warm up and cool-down period and a 30-min training phase (aerobic interval training consisting of 3 minutes exercise and 3 minutes rest on a cycle ergometer). The second session was performed in the afternoon, in which aerobic training included walking on the flat surface (continuous training) and walking up stairs (interval training). The training intensity was aimed to be between 60-80% of peakVO_2 as assessed by CPET.

Cardiopulmonary exercise testing. Symptom-limited CPET was performed on a bicycle ergometer (Ergometer DX1 and Ergometer AX1, Kettler, Ense-Parsit, Germany) with a ramp protocol of 10w/m (workload was increased by 10w/m). The aim was to achieve a maximal effort with a respiratory exchange ratio > 1,05. Blood pressure was measured manually at rest and every one-minute during the entire testing. The electrocardiogram and heart rate (HR) were monitored at rest and throughout exercise all the time. Breathe-by breath respiratory gas exchange parameters were measured by a computerized metabolic cart (Cardiovit AT 104 PC, Shiller, Baar, Switzerland). CPET was performed prior to the start of program and immediately after the end of three week exercise-based rehabilitation program. The following CPET parameters were measured: 1) peak VO_2 expressed in ml/kg/min and predicted percentage, 2) slope of minute ventilation vs. carbon dioxide production (VE/VCO_2), 3) peak respiratory exchange ratio (RER), defined as the peak VCO_2/peak VO_2ratio, 4) peak VCO_2, 5) peak oxygen pulse, defined as peak VO_2 divided by peak HR and expressed in ml/beat (O_2 pulse), 6) ventilatory anaerobic threshold detection (VAT), using the V-slope method, 7) maximum ventilation (VE max), 8) peak end-tidal CO_2 partial pressure, (PET CO_2), 9) peak HR, 10) HR recovery, 11) test duration, 12) peak work load , 13) peak systolic arterial blood pressure (SBP), and 14) peak diastolic blood pressure (DBP).

Echocardiography. Complete echocardiographic evaluations were performed using dedicated echocardiographic equipment (Vivid 3, General Electric, Little Chalfont, UK). Left ventricular ejection fraction (EF) was calculated using Simpson biplane method. Measurements were made just before the start and 3 weeks after the rehabilitation program.

Laboratory. Blood for biochemical analysis was drawn after 12 hours fasting period. The following serum parameters were measured: total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides, fasting glucose, urea, creatinine, sodium, potassium, red blood cells, a high-sensitivity C-reactive protein (hsCRP).

Measurements were made just before start and after termination of inpatient rehabilitation program using biochemical analyzer (Roche 902, Basel, Switzerland).

Statistical analysis. The data were entered into an electronic database (Access, Microsoft) and analyzed using the SPSS 16.0 software (SPSS Inc., Chicago, USA). Continuous variables were expressed as mean and standard deviations. Categorical variables were expressed as percentages. The variables tested prior to the start of program and immediately after the end of three-week exercise-based rehabilitation program were analyzed and compared using analysis of variance (ANOVA). Dichotomous variables were analyzed using the c^2test and Fisher's exact test, and continuous variables were analyzed using the *t*-test. The level of statistical significance was set a two tailed probability value of < 0,05.

Results

Demographic data and comorbidities. Basic demographic data for the patients included in the study are

Table 1. Baseline demographic data and comorbidities

Sex, male (%)	39/40 (97,5 %)
Age, years	50,60 ± 8,40
Diabetes, n (%)	8/40 (20 %)
Hypertension, n (%)	24/40 (60 %)
Hyperlipoproteinemia, n (%)	37/40 (92,5 %)
Obesity, n (%)	17/40 (42,5 %)
Smoking, n (%)	34/40 (85 %)
Family burden, n (%)	30/40 (75 %)

shown in Table 1. Briefly, the study population consisted of 39 men and 1 women, mean age of 50,60±8,40 years. More than two-thirds of patients suffered acute MI of the inferior wall. All patients had acute MI with ST segment elevation and received pPCI within 12 hours of typical chest pain. There were 34/40 (85%) of patients who actively smoke. Comorbidities are detailed in the Table 1. Patients received contemporary concomitant medical treatment, that is 40/40 (100%) patients were on dual antiplatelet therapy, 38/40 (95%) received beta-blockers, 31/40 (77,5%) were on angiotensin converting enzyme inhibitor or angiotensin receptor blocker, and 39/40 (97,5%) was on statin. Exercise-based rehabilitation program was started 34,2±10,9 days after acute MI.

CPET parameters. All CPET parameters were examined before and after completed CR programs (Table 2). After 3 weeks of exercise-based cardiac rehabilitation program improved exercise tolerance as compared to baseline (peak workload 111,50±15,07 vs 129,00±12,77 watts, respectively, p<0,001), as well as peak respiratory exchage ratio (1,02±0,10 vs 1,08 ± 0,13, respectively, p<0,05). Peak systolic blood pressure, heart rate, peak and after 1 minute of rest were also improved. Most importantly, peak VO2 (18,17±3,30 vs 20,64±3,27 ml/kg/min, respectively, p<0,001), peak VCO2 (1,65±0,28 vs 1,96±0,25 ml/kg/min, respectively, p<0,001), peak ventilation (48,61±10,70 vs 57,27±9,85 L/min, respectively, p<0,001) and peak oxygen pulse (14,16±2,62 vs 60.18±14.19 ml/beat, respectively, p<0,05) were also improved.

Interestingly, exercise electocardiography indicated the presence of ischemia in five patients (12,5%) before and one patients (2,5%) after CR program. There were no major adverse cardiac events during rehabilitation program.

Laboratory and clinical data. We noticed a statistically significant difference only at hsCRP values (7,27±5,73 vs 4,96 ± 5,50, respectively, p<0,01) comparing a start and three-week measurement.

There was significant differences in body mass index (28,82±4,41 vs 28,50±4,13, respectively, p<0,001). Left ventricular ejection fraction recorded no significant difference (53,05±6,74 vs 53,83±6,59, NS) before and after CR program (Table 3).

Discussion

Main finding of our study is that very short-term (three weeks daily, 21 training sessions) exercise training in patients with acute MI treated with pPCI is safe and improves functional capacity. Very short-term daily exercise training in these patients improves also peak work load and chronotropic parameters evaluated during CPET. This suggests that the effects of physical training depend on the total number of sessions regardless of the length of interval training.

Previuos studies indicated that values of peak VO_2 on entry in cardiac rehabilitation program are relatively low, particularly in women. It has been shown that peak VO_2 measured in 2896 patients prior to cardiac rehabilitation program, was higher in men than women:

Table 2. Cardiopulmonary exercise test parameters (at start and 3 weeks after exercise rehabilitation)

	start	3 weeks	p value start/3 weeks
Peak work load (W)	111,50 ± 15,07	129,00 ± 12,77	**< 0,001**
Test duration (min)	11,15 ± 1,87	12,9 ± 2,36	**< 0,001**
Peak SBP (mmHg)	167,50 ± 19,01	177,75 ± 16,09	**< 0,001**
Peak DBP (mmHg)	93,75 ± 11,13	97,25 ± 9,99	> 0,05
HR at rest (bpm)	74,40 ± 11,80	74,73 ± 10,20	> 0,05
Peak HR (bpm)	116,28 ± 15,82	124,90 ± 17,75	**< 0,001**
HR recovery 1 min (bpm)	18,73 ± 9,29	22,18 ± 9,11	**< 0,05**
Peak RER	1,02 ± 0,10	1,08 ± 0,13	**< 0,05**
VO2 at rest (ml/kg/min)	4,44 ± 0,95	4,72 ± 1,32	**< 0,05**
VO2 at VAT (ml/kg/min)	12,67 ± 2,27	13,65 ± 2,78	> 0,05
Peak VO2 (ml/kg/min)	18,17 ± 3,30	20,64 ± 3,27	**< 0,001**
Peak VCO2 (ml/kg/min)	1,65 ± 0,28	1,96 ± 0,25	**< 0,001**
Peak PET CO2 (mmHg)	38,07 ± 4,12	38,08 ± 3,64	> 0,05
VE/VCO2 slope	27,56 ± 3,60	26,66 ± 2,54	> 0,05
Peak oxygen pulse (ml/beat)	14,16 ± 2,62	14,90 ± 2,56	**< 0,05**
Peak VE (L/min)	48,61 ± 10,70	57,27 ± 9,85	**< 0,001**

Abbreviations: DBP, diastolic blood pressure; HR, heart rate; PET, peak end-tidal; RER, respiratory exchange ratio; SBP, systolic blood pressure; VE, ventilation; VAT, ventilatory anaerobic threshold.

Table 3. Laboratory and clinical data (at start and 3 weeks after exercise rehabilitation)

Laboratory	start	3 weeks	p value start/3 week
Glucose (mmol/L)	5,37 ± 0,66	4,89 ± 0,41	> 0,05
Total cholesterol (mmol/L)	3,93 ± 0,86	3,79 ± 0,68	> 0,05
LDL cholesterol (mmol/L)	2,32 ± 0,76	2,76 ± 0,81	> 0,05
HDL cholesterol (mmol/L)	0,84 ± 0,21	0,82 ± 0,20	> 0,05
Triglycerides (mmol/L)	1,74 ± 0,76	1,76 ± 0,71	> 0,05
Creatinine (μmol/L)	83,72 ± 13,23	83,75 ± 13,58	> 0,05
Urea (μmol/L)	6,32 ± 1,22	5,96 ± 1,60	> 0,05
RBCs (10^{12}/L)	4,59 ± 0,40	4,53 ± 0,38	> 0,05
Na (mmol/L)	142,08 ± 1,74	142,07 ± 1,69	> 0,05
K (mmol/L)	4,57 ± 0,29	4,65 ± 0,22	> 0,05
hsCRP (mg/L)	7,27 ± 5,73	4,96 ± 5,50	**< 0,01**
Clinical data			
BMI (kg/m^2)	28,82 ± 4,41	28,50 ± 4,13	**< 0,001**
LVEF (%)	53,05 ± 6,74	53,83 ± 6,59	> 0,05

(9,3±6,1 ml/kg/min vs 14,5±3.9 ml/kg/min; p<0,0001).[12] Previous studies have reported that in patients following acute MI, peak VO_2 and VO_2 at anaerobic threshold increase between 7% and 54% after a period of few weeks of exercise training.[3] Lack of improvement in exercise capacity after an exercise training program is a predictor of poor prognosis. The study authored by Savage et al, which included 385 patients in CR program, showed that 81 (21%) patients failed to improve peak VO_2 after termination of the program.13 Similarly, patients with peak VO_2 bellow 10ml/kg/min had a poor prognosis, and those above 18ml/kg/min had a good prognosis.[14] Therefore, the increase in peak VO_2, after exercise training might contribute to better survival in patients following MI. Our data demonstrate an increase of 13,5% in peak VO_2 and 7,7% of VO_2 at anaerobic threshold. It is worth emphasizing that VO_2 at anaerobic threshold is independent of patient´s motivation, and it is a good parameter to evaluate the training effect.[3]

In accordance with our findings is the results of one meta-analysis [15] which have reported an average increase in peak VO_2 of 2 to 22% following exercise training program. Study by Gremeaux et al. also used three week exerecise-training program, but with less frequent training sessions (3 days a week, total 15 sessions). This study showed marked improvement in peak VO_2 (+14,25%) and peak workload (+30,8%), after completion of the program as compared to baseline. [16] Similarly, Bjarnason et al. have showed in a study which included 262 patients with coronary artery disease[17] that the maximum exercise workload had improved significantly (105,3±32,3 vs. 123,9±37,3 watts, p<0,001) after a four week, three times per week, ambulatory CR program.

Six electronic databases were searched to identify studies investigating resistance training, coronary heart disease and physical function. Improvements in peak oxygen uptake (WMD: 0.61, 95% CI: 0.20-1.10), peak work capacity (SMD: 0.38, 95% CI: 0.11-0.64) and muscular strength (SMD: 0.65, 95% CI: 0.43-0.87) significantly favoured resistance training in combination with aerobic training over aerobic training only with moderate quality evidence. There was no evidence of a difference in effect when comparing resistance training and aerobic training. Resistance training in combination with aerobic training is more beneficial than aerobic training alone for improving physical function.[18]

Longer, but less intensive, exercise rehabilitation programs may also improve functional capacity following acute MI. In the study that included 94 patients following acute MI treated with pPCI, exercise sessions were prescribed for 3 months, 3 day a week (total of 36 sessions), and significant improvement in peak VO_2 was noted at the end of rehabilitation program as compared to baseline (20±4 vs. 14±4 ml/kg/min, p<0,001), as well as in peak workload (p<0.001).[19] Lavie and Milani[20] have reported that exercise training program can be also improve heart rate recovery (- 10 to 12%), peak anaerobic threshold (+10 to 15%), as well as metabolic parameters including total cholesterol (-5%), triglycerides (-15%), HDL–cholesterol (+5 to 10%), and LDL – cholesterol (-3%).[20] Our study showed modest improvements in metabolic parameters that failed to reach statistical significance.

Overall, 359 patients who have suffered acute MI, and were referred for CR after PCI from 2010 to 2015 and underwent an exercise tolerance test before and after phase II CR were included in this study. The patients were divided into two groups: obese group with body mass index (BMI) ≥25 kg/m^2 (n=170; age, 54,32±9,98 years; BMI, 27,52±2,92 kg/m^2) and non-obese group with BMI <25 kg/m^2 (n=189; age, 59,12±11,50 years; BMI 22,86±2,01 kg/m^2). There were significant changes in resting heart rate (HR_{rest}) before and after CR between the obese and non-obese groups (before CR, p=0,028; after CR, p=0,046), but other cardiopulmonary exercise capacity before and after CR was not different between the groups. HR_{rest} (p<0,001), maximal metabolic equivalents (METs, p<0,001), total exercise duration (TED, p<0,001), and maximal oxygen consumption (VO_{2max}, p<0,001) improved significantly in the obese and non-obese groups after CR. No difference in the change in the cardiopulmonary exercise capacity rate was detected between the groups. CR may improve functional capacity in patients who suffered AMI regardless of their obesity.[21]

A number of other CPET parameters may be inproved folllowing comprehensice exercise-based training program in patients with coronary artery disease. Heart rate recovery after 1 minute (HRR1) reflects parasympathetic activity after exercise training. HRR1 improves after 36 sessions (12 weeks, 3 times per week) exercise training, as reported by Dimopoulos et.al in a small study that included only 29 patients with heart failure who took part in a CR program.[22] Our study extends this data on patients following acute MI treated with pPCI as we also showed improvement in HRR1 following exercise-program, which indicates good training response and higher contribution to the autonomic nervous system. VE/VCO_2slope is also an important parameter for prognosis, expected to decrease after exercise training.[23] Patients with a VE/VCO_2 slope exceeding 55 had a 2 year mortality of 65% reported as reported by the study by Francis and co-authors.[14] For the reasons that are not clear, our data failed to show improvement in VE/VCO2 slope after training.

Study limitations. The major limitation of the present is relatively small number of patients.

Conclusions

Very short-term exercise training in patients with acute MI treated with pPCI is safe and improves functional capacity, as well as test duration, work load and heart rate response.

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Sažetak

Uticaj kratkih programa bolničke kardiološke rehabilitacije kod pacijenata sa akutnim infarktom miokarda lečenih primarnom perkutanom koronarnom intervencijom

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Uvod: *Rehabilitacija zasnovana na vežbanju je važan deo lečenja pacijenata nakon akutnog infarkta miokarda (IM). Međutim, veoma su oskudni podaci o efektima kratkoročnih programa fizičke aktivnosti kod pacijenata sa akutnim IM koji su lečeni primarnom perkutanom koronarnom intervencijom (pPCI). Cilj ovog rada je bio da se evaluiraju efekte kratkotrajnih programa fizičke aktivnosti na parametre kardiopulmonalnog testa opterećenja (KPTO) kod pacijenata nakon akutnog IM lečenih (pPCI).*

Metode: *Ispitivali smo 40 pacijenata sa IM lečenih pPCI-om koji su upućeni u našu ustanovu radi sprovođenja rehabilitacije. Studijska populacija se sastojala od 39 muškaraca i 1 žene (starosne dobi 50,60 ± 8,40 godina, ejekcione frakcije leve komore, 53,05 ± 6,74%), koji su učestvovali u 3 nedeljnom programu kardiološke rehabilitacije. Program se sastojao od vožnje bicikle 7 puta nedeljno i svakodnevnog hodanja u trajanju od 45 minuta na intenzitetu od 70-80% individualne maksimalne srčane frekvence. Svi pacijentima je urađen simptomima ograničen KPTO na biciklergometru po ramp protokolu od 10 W/min. KPTO je takođe rađen nakon sprovedenog programa kardiološke rehabilitacije.*

Rezultati: *Nakon 3 nedeljnog programa kardiološke rehabilitacije zasnovanog na vežbanju poboljšana je tolerancija na napor u poređenju sa polaznim nivoom (maksimalno radno opterećenje 111,50±15,07 vs 129,00±12,77 wati, p <0,001), kao i maksimalni odnos disajne razmene (1,02±0,10 vs 1,08±0,13, p <0,05). Maksimalna vrednost sistolnog krvnog pritiska, srčana frekvenca, maksimalna i 1 minut nakon odmora, takođe su poboljšani. Najznačajnije poboljšanje je zabeleženo kod maksimalne VO2 (18,17±3,30 vs 20,64±3,27 ml/kg/min, p <0,001), maksimalne VCO2 (1,65±0,28 vs 1,96± 0,25 p <0,001), maksimalne ventilacije (48,61±10,70 vs 57,27±9,85 L/min, p <0,001) i maksimalnog kiseoničnog pulsa (14,16±2,62 vs 60,18±14,19 ml/otkucaj, p <0,05). Tokom sprovođenja programa rehabilitacije nisu zabeleženi značajni neželjeni kardiološki događaji.*

Zaključak: *Kratkoročni fizički trening kod kod pacijenata sa akutnim IM koji su lečeni pPCI je pre svega bezbedan, poboljšava funkcionalni kapacitet, kao i trajanje testa, stepen opterećenja i reakciju srčane frekvence.*

Ključne reči: *kardiopulmonalni test opterećenja, fizički trening, kardiološka rehabilitacija, infarkt miokarda.*