· Advances in Medical Sciences · Vol. 58(1) · 2013 · pp 50-57 · DOI: 10.2478/v10039-012-0073-z

The influence of endurance training intensity on dynamics of post-exertional heart rate recovery adaptation in patients with ischemic heart disease

Kałka D[1,2], Domagała Z[3]*, Kowalewski P[4], Rusiecki L[1], Wojcieszczyk J[5], Kolęda P[1], Marciniak W[6], Adamus J[6], Janocha A[7], Pilecki W[1]

1 Department of Pathophysiology, Wroclaw Medical University, Wroclaw, Poland
2 Center of Cardiac Prevention and Rehabilitation 'Creator' in Wroclaw, Wroclaw, Poland
3 Department of Normal Anatomy, Wroclaw Medical University, Wroclaw, Poland
4 Dietrich Bonhoeffer Klinikum Neubrandenburg, Germany
5 Department of Physiotherapy in Conservative and Operative Medicine, University School of Physical Education in Wrocław, Wroclaw, Poland
6 Ostrobramska Medical Center, Health Care Facility, Magodent, Warsaw, Poland
7 Department of Physiology, Wroclaw Medical University, Wroclaw, Poland

* CORRESPONDING AUTHOR:
Department of Anatomy,
Wroclaw Medical University,
Chalubinskiego 6a,
50-367 Wroclaw, Poland
Tel: +48717841340
Fax/Tel +48717840079
e-mail: zygmunt.domagala@am.wroc.pl (Zygmunt Domagala)

Received 09.07.2012
Accepted 31.12.2012
Advances in Medical Sciences
Vol. 58(1) 2013· pp 50-57
DOI: 10.2478/v10039-012-0073-z

ABSTRACT

Purpose: The intensity of post-exertion heart rate recovery, evaluated in the first minute of the recovery period (HRR_{60}), is considered to be a strong predictor of risk for cardiac death. Intensification of physical activity performed as part of cardiac rehabilitation (CR) increases the HRR_{60} value in ischemic heart disease (IHD) patients. In this context, the impact of endurance training intensity (ETI) on change in HRR_{60} intensity seems to be an interesting issue.

Material/Methods: The study group consisted of 251 patients who were subjected to a CR cycle. 45 patients of this group participated in CR twice. The control group consisted of 35 patients who were not subjected to any CR. ETI was estimated by the training work. In all patients an exertion test on a treadmill was performed twice within six months, analyzing the initial and final HRR_{60} value and ΔHRR_{60}.

Results: After a six-month observation, there was a statistically significant increase in the HRR_{60} value (17.98±8.33/min vs. 22.72±7.72/min, $p<0.01$) in the test group, which was not observed in the control group. Mean ΔHRR_{60} value in the test group was statistically significantly greater than in the control group. In the subgroup subjected to the two CR cycles, only the first cycle led to a statistically significant increase in the mean HRR_{60} value.

Conclusions: A six-month CR cycle significantly increased the HRR_{60} value, while cardiac training intensity did not affect the exertion-evoked change in its intensity. Continuation of the CR cycle beyond 6 months no longer significantly affected the change in the HRR_{60} value.

Key words: cardiac rehabilitation, heart rate recovery, endurance training

INTRODUCTION

Heart rate changes associated with taking and cessation of physical activity are a result of permanent cooperation between the parts of the autonomic nervous system. Double neural control, based on reciprocal feedback inhibition of both parts of the autonomic nervous system, increases the body's regulatory abilities, better adapts it to the environment and helps to maintain homeostasis.

The increase in heart rate that supplements exercise is due to combination of sympathetic activation and parasympathetic

withdrawal [1]. The rapid post-exercise decrease in heart rate is thought to be predominantly due to parasympathetic reactivation [1,2].

Observations of double neural control indicated that a simple parameter – the difference in the uppermost heart rate and the heart rate measured after sixty seconds during the recovery phase of the exertion test (HRR_{60}) – objectifies the dynamics of post-exercise heart rate recovery adaptation. Disorders in autonomic regulation of the circulatory system's function results in less pronounced decrease of heart rate after exercise cessation and is associated with total and cardiovascular mortality and morbidity in apparently healthy subjects, in patients with coronary artery disease or in patients with diabetes [3].

Physical training, which is a fundamental component of cardiac rehabilitation (CR) programs, improves physical performance and modifies the process of rapid elimination of fatigue changes after finishing exertion [4]. Post-exertion heart rate recovery adaptation also fits into the latter concept.

It is deemed that modification in autonomic balance is one of the reasons why physical exertion has a beneficial impact on reduction in death rate with patients suffering from circulatory-vascular diseases. HRR is one of the simplest and the best tools to assess the modification. [5-7]

A majority of research which analyses a relation between HRR and cardiac rehabilitation cycles is concentrated on differentiated programs of early rehabilitation or comparing different rehabilitation methods with reference to their effectiveness and costs. In this context, the problem of the impact of cardiac trainings' intensity on change in HRR_{60} intensity seems to be interesting.

The aim of this study was the assessment of the influence of the endurance training on change in HRR_{60} value in a group of patients treated invasively due to ischemic heart disease (IHD).

MATERIAL AND METHODS

We analyzed 286 patients (80 females and 206 males), treated due to IHD. Participants were randomized into two groups. The study group consisted of 251 patients (mean age 61.39±9.69) who were subjected to a CR cycle. 45 patients of this group (mean age 59.3±7.45) participated in CR twice, without rest in between cycles. The control group consisted of 35 patients (mean age 62.91±6.76) who were not subjected to any CR. The project was approved by the Local Bioethics Committee (Resolution No. 95/WIM/2005).

Inclusion criteria are presented in *Tab. 1*. In all patients pharmacological treatment according to IHD treatment standards was applied. The criterion for exclusion of the patient from the observation was a necessary dosage adjustment of medicines affecting chronotropic reaction, carried out during the six-month observation.

Table 1. **Inclusion criteria.**

Inclusion Criteria	
1	No previous history of clinically significant pulmonary disease
2	No significant deviations in the initially performed resting spirometry test
3	Absence of any neurological and orthopedic disorders
4	No clinical symptoms of thyroid gland disorders
5	Absence of any stenocardial symptoms provoked by the cardiac training
6	Laboratory tests: a) no anemia b) no deviations from the norm in thyrotropic hormone plasma levels

Intensity of leisure-time physical activity (LTPA) prior to the CR cycle was assessed using the Framingham questionnaire. In all patients the leading rhythm was the sinus rhythm. 24-hour ECG Holter monitoring allowed to classify all patients in the test group and the control group to an appropriate group from 1 to 4a according to Lown and Wolf classification. The clinical characteristics of the study groups are outlined in *Tab. 2*.

A cardiac stress test (ECG treadmill test) was performed after a thorough evaluation of the patient's current clinical status, always after obtaining the patient's consent for the test. Tests were carried out on a treadmill (Challenger, USA; ECG Cardio system for cardiac stress testing, Perfekt MD Rozinn Electronics, New York, USA) in a dedicated room with appropriate ambient temperature and adequate ventilation. The cardiac stress tests were always performed in the morning, after a night's rest. For all test participants, the initial cardiac stress test was not the first test of this kind in their lives. Modified Bruce protocol was used for performing all tests. The cardiac stress test was carried out as a *symptom-limited* test. All patients achieved at least 70% of maximum pulse and the reason for test termination was a subjective feeling of fatigue that made the continuation of the test impossible. Each cardiac stress test was ended with at least a 5-minute *recovery* period during which patients continued the exertion of a metabolic cost of 2 MET. During this time, the patient's ECG record, well-being and arterial blood pressure normalization were observed (measurement was taken every 60 seconds). The test was terminated when the feeling of fatigue was gone and the patient declared that he/she was ready leave the lab. In all patients, cardiac stress testing was carried out twice (in the test group, at the beginning and end of the CR cycle, and in the control group with a six-month interval corresponding to the duration of the CR cycle).

The process of heart rate recovery (HRR) adaptation was assessed by analyzing the initial and final HRR_{60} value and

Table 2. **The clinical characteristics of the study groups.**

	Test group (n=251)	Control group (n= 35)	Statistical significance (p)
Males	180 (71.71%)	26 (74.29%)	NS (p=0.9071)
Females	71 (28.29%)	9 (25.71%)	NS (p=0.9071)
Age, years	61.39±9.69	62.91±6.76	NS (p=0.3718)
BMI (kg/m2)	28.00±4.98	26.44±2.59	NS (p=0.0717)
Myocardial infarction	165 (65.73%)	20 (57.14%)	NS (p=0.4192)
Hemoglobin concentration (g%)	14.09±1.25	14.48±0.74	NS (p=0.0710)
TC (mg%)	215.36±45.37	218.26±44.71	NS (p=0.7243)
LDL-C (mg%)	128.83±39.73	135.91±39.24	NS (p=0.3343)
HDL-C (mg%)	48.88±14.40	48.96±11.42	NS (p=0.9753)
TG (mg%)	165.37±94.55	166.98±69.71	NS (p=0.9230)
Echocardiography parameters:			
LVEDD (mm)	52.78±5.77	53.97±3.10	NS (p=0.2328)
EF (%)	56.51±7.68	56.11±3.28	NS (p=0.7709)
LA (mm)	38.25±4.20	38.29±3.18	NS (p=0.9584)
IMLK (g/m2)	97.06±24.21	100.09±18.08	NS (p=0.4780)
IHD treatment:			
PTCA	184	29	NS (p=0.3139)
CABG	67	6	NS (p=0.3139)
Drugs:			
Beta-blockers	237 (94.42%)	35 (100%)	NS (p=0.2398)
ACEI	151 (60.16%)	17 (48.57%)	NS (p=0.2622)
ARB	32 (12.75%)	6 (17.14%)	NS (p=0.6515)
Statins	203 (80.87%)	24 (68.57%)	NS (p=0.1436)
Fibrates	43 (17.13%)	5 (14.28%)	NS (p=0.8567)
Ezetimibe	6 (2.39%)	0 (0%)	NS (p=0.9999)
Calcium blockers	41 (16.33%)	9 (25.71%)	NS (p=0.2580)
Diuretics	59 (23.51%)	12 (34.29%)	NS (p=0.2403)
Antiplatelet drugs	243 (96.81%)	34 (97.14%)	NS (p=0.6804)
α1-adrenergic blockers	21 (8.37%)	3 (8.57%)	NS (p=0.9999)
CVD risk factors:			
Hypertension	163 (64.94%)	23 (65.71%)	NS (p=0.9210)
Diabetes – type 2	45 (17.93%)	6 (17.14%)	NS (p=0.9029)
Lipid disorders	163 (64.94%)	21 (60.00%)	NS (p=0.7015)
Smoking habits	132 (52.59%)	20 (57.14%)	NS (p=0.7452)
BMI >25	174 (69.32%)	20 (57.14%)	NS (p=0.2106)
Inadequate leisure-time physical activity*	250 (99.60%)	35 (100.00%)	NS (p=0.9999)
Mean week intensity of leisure–time physical activity	432.84±198.46	442.57±169.83	NS (p=0.7836)

** < 1000 Kcal/week*

BMI – body mass index; TC – total cholesterol; LDL– low density lipoprotein C; HDL – high density lipoprotein; TG – triglyceride; LVEDD - left ventricular end-diastolic dimension; EF - ejection fraction; LA - Left atrial dimension; PTCA - percutaneous transluminal coronary angioplasty; CABG - coronary artery bypass surgery; ACEI - angiotensin-converting-enzyme inhibitor; ARB - angiotensin receptor blockers; IMLK-left ventricular mass index; CVD – cardiovascular disease; NS – not significant.

ΔHRR_{60} being the difference in HRR_{60} values of the final and initial trial.

The cycle of physical trainings was carried out over six months and it included exertion trainings on cycle ergometers, general rehabilitation exercises and elements of resistance training. The CR training sessions took place five days a week (alternately two days of general rehabilitation and resistance exercises and three days of bicycle training on ERGOLINE ER 900 cycle ergometer (GmbH CoKG 72457, Bitz)).

In the applied training (which lasted 45 minutes at a time), the loads on cycle ergometers were increased at 4-minute intervals until halfway through the training, when they achieved their peak, and then they were declined to their initial values, interrupted by 2-minute recovery periods with a maintained load of 0-5 W. Training started with 1.5 min. time of warm – up.

The peak load of the initial trainings was established at 40–70% of the load achieved during the initial cardiac stress test and it was increased not more than by 10 W for each interval every 12 endurance trainings on the cycle ergometer by the proper adaptation of patients for exertion (subjective assessment and declining trend of heart rate increment on the exertion peak).

Intensity of endurance training (EIT) was estimated according to formula (*Tab. 3*). The initial and final training work, the growth of the work and mean training work were analyzed. Moreover the influence of CR cycle length on the HRR_{60} value was analyzed.

The general rehabilitation training consisted of relaxation, stretching, balance and skill exercises performed in groups. Exercises at the gymnasium were supplemented by elements of resistance training that included 8–10 various resistance exercises involving different groups of muscles. All exercises were performed in series consisting of 12–15 repetitions. During the activities, the 13th fatigue level, according to the 15-level Borg scale, was not exceeded. The intensity of the exercises at the gymnasium was established individually, taking into account continuous heart rate monitoring by means of a Polar S720i heart rate monitor. Cardiac rehabilitation was performed according to the recommendations of the European Society of Cardiology [8].

The control group – not subjected to any CR – received, as part of health-promoting education, information about the necessity to maintain an active lifestyle, with individual recommendations concerning the type, intensity and desired dose of LTPA.

All patients of the study group and the control group underwent earlier stage 1 CR, and 161 patients of the study group and 31 of the control group stage 2 CR in a health resort hospital or an outpatient clinic.

Statistical analysis

The basic measure of central tendency used in this study is the arithmetic mean. Standard deviation was used to describe the dispersion of values within variables. Student's t-test was used for testing the significance of mean differences within two subgroups (both for independent and dependent samples). Levene's test was used for testing the hypothesis of equality of group variances in the population. The result of the test determined using a proper formula of the *t* test. Pearson correlation coefficient *r* was used for measuring the strength of the linear relationship between the variables,

Table 3. **Training work formulas.**

Title	formula	abbreviations
endurance training intensity	$W[kJ] = P[W] \times t[s]$	W – work; P – load; t-time
Δ training work	$\Delta W = W^{fin} - W^{init}$	fin – final; init - initial
mean training work	$\overline{W} = \frac{W_1+W_2+\cdots+W_n}{n}$	n – number of trainings

Table 4. **Mean values of training work.**

	Mean value	Interval values	Pearson coefficient value [ΔHRR_{60} versus training work]
General Training Work	78.23±20.08 KJ	33.6 KJ – 140.0 KJ	-0.065 NS
Initial Training Work	66.46±18.18 KJ	33.6 KJ - 126.0 KJ	-0.072 NS
Final Training Work	89.05±23.18 KJ	33.6 KJ - 159.6 KJ	-0.072 NS
Δ Training Work	22.59±11.85 KJ	-8.4 KJ - 58.8 KJ	-0.030 NS

NS-not significant; HRR – heart rate recovery

and correlation graphs of the analyzed variables were used for the visual assessment of the linearity of the relationship between variables. The significance of Pearson correlation coefficient *r* was tested by classical statistics with Student's t-distribution. The value of $p<0.05$ was taken as the level of statistical significance.

RESULTS

All results were obtained as a result of applying non-invasive research methods within the scope of the project.

Comparative analysis of initial HRR60 values showed no statistically significant differences between the study and the control group (NS, p=0,598443). In both groups, the initial HRR60 value was not significantly associated with age, BMI, gender, presence of hypertension, type 2 diabetes, lipid disorders, echocardiographic parameters (LVEDD and EF), HGB concentration, value of eGFR-MDRD, intensity of leisure-time physical activity (LTPA) prior to the CR cycle, and applied pharmacotherapy.

Completion of stage 2 of CR did not significantly affect the initial HRR60 value in the study group (16.93±8.42/min vs 17.11±7.58/min, NS) and the control group (17.20±6.50/min vs 19.10±6.71/min, NS).

As a result of the CR cycle, there was a significant increment in the HRR_{60} value (17.98±8.33/min *vs* 22.72±7.72/min, $p<0.01$) in the study group.

Such an effect was not observed in the control group, in which the initial and final HRR_{60} values did not differ statistically significantly. The ΔHRR_{60} value in the study group was statistically significantly greater than in the control group ($p<0.01$). The mean initial and final HRR_{60} values and the mean ΔHRR_{60} values for the study and control group are presented in *Fig. 1*.

The ΔHRR_{60} value in the study group was statistically significantly associated with the initial HRR_{60} value by the Pearson coefficient of -0.595 ($p<0.01$). The graph of the linear relationship for this correlation is presented in *Fig. 2*.

The ΔHRR_{60} value in the study group was not statistically significantly associated with BMI, gender, presence of NT, type II diabetes, lipid disorders, echocardiographic parameters, HGB concentration, eGFR value, intensity of LTPA prior to the CR cycle and applied pharmacotherapy.

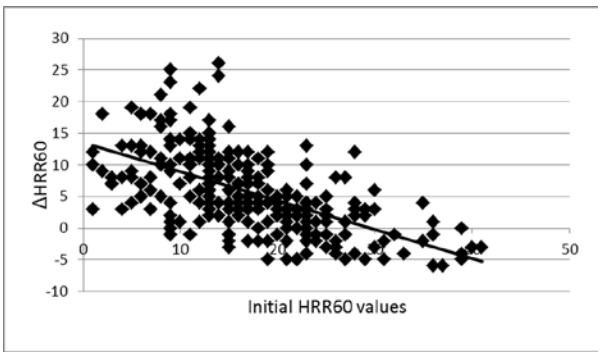
In the subgroup subjected to the CR cycle twice (45 patients), the first cycle led to a statistically significant increase in the mean of HRR_{60} value, whereas the following cycle did not change significantly the HRR_{60} value (*Fig. 3*).

The results of the mean training work, mean initial training work, mean final training work and mean increment (delta) of training work are presented in *Tab. 4*. All work values are not associated with ΔHRR_{60} value.

DISCUSSION

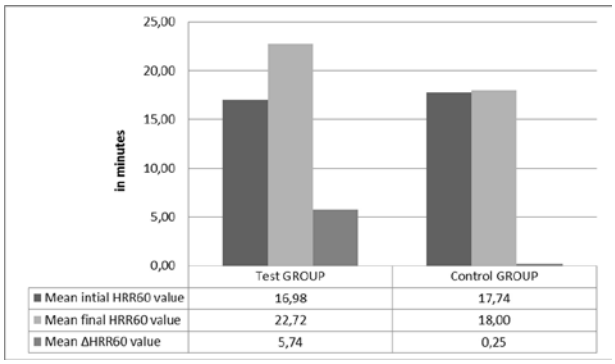
The chronotropic reaction observed during subsequent periods of the cardiac stress test is a result of dynamically

Figure 2. **The graph of the linear relationship between the ΔHRR_{60} value and the initial HRR values.**



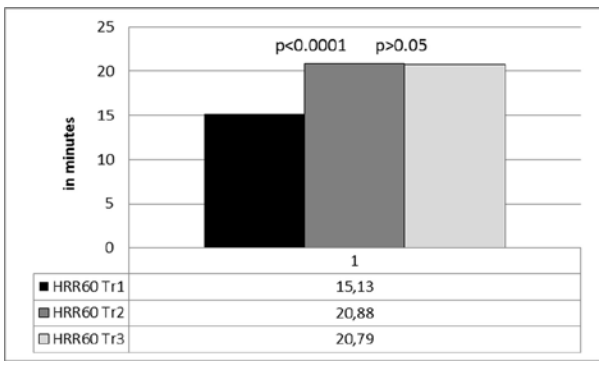
HRR – heart rate recovery

Figure 1. **The mean initial and final HRR_{60} values and the mean ΔHRR_{60} values for the study and the control group.**



HRR – heart rate recovery

Figure 3. **The depicting change of HRR_{60} value in the first and second CR cycle.**



Tr1-first treadmill test; Tr2-second treadmill test; Tr3-third treadmill test

occurring changes of both parts of the autonomic nervous system [1,2]. According to Arai *et al*. [5], the heart's response to exercise reflects the rapid parasympathetic weakness in the early phase of physical exertion until the anaerobic threshold, and then the HR acceleration above this threshold. This is a result of a gradual increasing in the sympathomimetic activity. In turn, the heart rate recovery adaptation that takes place during the recovery phase is a result of rapid reactivation of the parasympathetic system and of a gradual disabling of the sympathetic system activity. Therefore, HRR disorders are most likely not just a result of vagus nerve disorders, but also an effect of excessive parasympathetic system activity [5,9]. Molecular mechanisms regulating the function of the parasympathetic system may also be involved in this process. It was shown that a variation in the DNA code (the acetylcholine receptor subtype M2 locus) may be responsible for the variability exhibited in HRR in healthy individuals [10].

A repeated physical training, as a result of interaction between two parts of the autonomic system, leads not only to resting bradycardia and lowered frequency in heart action during exertion, but also to improvement in post-exertion heart restitution [5,6,11,12]

Although the mechanism through which physical training reduces mortality in IHD patients is not precisely known, one of the hypotheses involves the impact of effort on autonomic balance. Thus, the intensity of post-exertion heart rate recovery adaptation assessed in the first minute of the recovery period of the cardiac stress test (HRR_{60}) is useful in assessing the risk of death due to cardiovascular causes [13-17].

In many studies published to date, a beneficial impact of CR on change in the HRR_{60} value was proven. Soleimani *et al.* [18] proved that the number of training sessions was considered an an independent predictor of mean post-training HRR_{60} ($r=0.626$; $r^2=0.392$; $p<0.0001$). Tsai *et al.* [7], Tiukinhoy *et al.* [19] and MacMillan *et al.* [20] stated a statistically significant improvement in HRR_{60} value in CR groups.

The HRR_{60}-modifying CR impact was also observed in the own 251-patient test group. In this group, CR led to a statistically significant increase in HRR_{60} values, which was not observed in the non-rehabilitated control group.

Analysis of literature indicates substantial differences between initial HRR_{60} intensity presented by different populations of IHD patients. These values range from 4.15±3.74/min in the study by Tsai *et al*. [7] to 21.4±11.2 in the observation of Macmillan *et al*. [20] and to 22.1+/-8.7 in the study by Korzeniowska-Kubacka *et al*. [12]. Interestingly, all studies concerned the same period of rehabilitation treatment. A substantial improvement in HRR_{60} intensity, evoked even by a very short 5-unit training cycle (8.74±4.62/min vs. 11.63±6.66/min), indicates a possible impact of individually variable intensity of LTPA, presented prior to implementing CR, on the HRR_{60} value [7].

However, the observation carried out on the our study group of 251 IHD patients indicates that both in the study and control group, the participation in stage 2 CR (28-day stays) was not determining significantly the initial HRR_{60} value.

Apart from the different HRR_{60} value prior to rehabilitation treatment, the assessed papers and own studies also present differently-intense rehabilitation treatment effects. In the context of autonomic balance optimization, identification of factors which have an impact on the obtained improvement in HRR_{60} intensity seems to be an interesting aspect.

So far, it was proved that the number of training sessions is an independent predictor of mean post-training HRR_{60}. However, this effect was observed for rehabilitation cycles that consisted of a small number of training units (5 to 24) [18]. Unfortunately, with such scant data today we cannot precisely tell how long the training cycle should be to allow the achievement of optimal HRR_{60} intensity.

Due to the applied research methodology, a partial answer to this question is provided by our own study, in which two six-month CR cycles were implemented without a break. The first six-month CR cycle, analogical to the observation conducted for the entire test group, led to a statistically significant increase in the mean HRR_{60} value. However, continuation of the CR in accordance with the same model no longer led to a further improvement in the HRR_{60} intensity. Therefore, extension of training duration over 6 months allows to maintain the obtained results, however it does not increase them any further.

In the analysis of the modifying impact of rehabilitation exercises (carried out according to many schedules) on vagus nerve tension, a question arises whether the obtained effects might be dependent on intensity of the applied cardiac training.

Moholdt *et al*. [22] compared the impact of various CR models on HRR_{60} in 107 patients after myocardial infarction. They analyzed the effects evoked by classical CR and AIT (aerobic interval treadmill) rehabilitation, in which exercises lasted 4x4 minutes and led to obtaining 85-95% of max HR. It was considered that the new rehabilitation technique, compared to classical CR, does not affect significantly differently the change in the HRR_{60} value.

Importance of the impact of additional physical activity accompanying a CR cycle on HRR dynamics was examined by Sato *et al.* [11] HRR assessment was conducted on the day when the examination was initiated and after 2 weeks of CR. After termination of CR, the time of HRR changed only in the more active group $p<0.001$. This suggests a relationship between HRR dynamic improvement and the entire daily dose of physical activity.

In the analyzed group of 251 patients, ΔHRR_{60} was associated with statistically significantly negative Pearson's coefficient $r=-0.595$, only with the initial HRR_{60} intensity

This testifies to the statement that patients who start training with the lowest heart rate recovery adaptation dynamics achieve the greatest increment of it as a result of CR. A graph illustrating the linear relationship between ΔHRR_{60} and the initial HRR_{60} value is presented in *Fig. 2*.

The grade of HRR dynamic change (ΔHRR_{60}) is not affected by cardiac training intensity assessed by means of initial, final and mean cardiac training work or by the increment of their work within 6 months of a CR cycle.

Maintaining the beneficial effect of CR also seems to be a key issue. It was analyzed by Giallauria *et al*. [23] who observed a group of 44 patients after myocardial infarction subjected to a three-month CR. As might be expected given other observations concerning the positive effects of physical activity, maintaining HRR_{60} improvement also required further continuation of the cardiac training.

Studies performed on populations of IHD patients using different training procedures complement the knowledge about the process of post-exertion heart rate restitution. Evidence supporting the beneficial modification of autonomic balance within CR, resulting in a reduction of the sudden cardiac death risk, encourage the use of this type of therapy in IHD patients. In the aspect of maintaining the continuity of the positive effects of physical activity modification, resulting in reducing the sudden cardiac death risk, it is essential that the patients participate in CR programs (with secure training intensity adjusted to their ability), with particular emphasis on the group of patients presenting initially lowest HRR_{60} values.

CONCLUSIONS

Six-month CR cycle significantly increased the HRR_{60} value, however cardiac training intensity did not affect the exertion-evoked change in its intensity. Continuation of the CR cycle beyond 6 months no longer significantly affected the change in the HRR_{60} value. The greatest benefits of the applied rehabilitation treatment were achieved by patients who were initially characterized by the greatest performance impairment of post-exertion heart rate recovery adaptation.

ACKNOWLEDGEMENTS

Conflict of interest: The authors do not declare any conflicts of interest.

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