

# Heart rate recovery, cardiac rehabilitation and erectile dysfunction in males with ischaemic heart disease

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## ABSTRACT

**Objective:** Heart rate recovery (HRR) is a recognised marker used in clinical practice for assessing the risk of sudden cardiac death. Physical exercise leads to an improvement in HRR and has a proven beneficial effect on erection quality (EQ) related to the activity of the autonomic nervous system in men with ischaemic heart disease (IHD). This paper evaluates the relationship between HRR and EQ in patients with IHD and erectile dysfunction (ED) who underwent cardiac rehabilitation.

**Methods:** The main analysis was based on the Mann–Whitney U test, Wilcoxon signed-rank test, Spearman correlation coefficient, Pearson's chi-square test, chi-square test, with the Yates correction and (if possible) parametric tests were used. This prospective, non-randomised intervention study included 124 men with IHD and ED [International Index of Erectile Function (IIEF-5) scores of  $\leq 21$ ]. Of these, 89 patients underwent a 6-month cardiac rehabilitation phase III programme, whereas 35 did not. The results of the participants' total IIEF-5 scores and their HRR, demographic and clinical data were analysed.

**Results:** The results of the 89 rehabilitated patients (mean age: 60.44 $\pm$ 9.29 years) and 35 controls (mean age: 61.43 $\pm$ 8.81 years) were analysed. In the rehabilitated patients, the mean baseline IIEF-5 score was 13.15 $\pm$ 5.76 (95% CI: 11.93–14.36) and HRR was 16.49 $\pm$ 7.68/min (95% CI: 14.88–18.11). After cardiac rehabilitation, the parameters of ED and HRR improved significantly and were significantly higher than those of the controls; the mean IIEF-5 score of the rehabilitated group increased to 15.36 $\pm$ 6.51 (95% CI: 13.99–16.73), while HRR increased to 21.40 $\pm$ 7.25/min (95% CI: 19.88–22.93). A significant correlation was found between  $\Delta$ HRR and  $\Delta$ EQ ( $r=0.409791$ ) as a result of the 6-month cardiac training programme.

**Conclusion:** Cardiac rehabilitation assessed by HRR has a sizable effect on autonomic balance in patients with IHD and ED, which plays a significant role in the mechanism of erection improvement. (*Anatol J Cardiol* 2016; 16: 256-63)

**Keywords:** cardiac rehabilitation, heart rate recovery, erectile dysfunction, ischaemic heart disease

## Introduction

Chronotropic response, as observed during subsequent phases of an exercise stress test, is the result of dynamic changes in the behaviour of both the sympathetic and parasympathetic subsystems of the autonomic nervous system. Heart rate recovery (HRR) after a treadmill stress test occurs due to the gradual deactivation of the sympathetic nervous system and the reactivation of the parasympathetic nervous system. Therefore, most problems with HRR are likely the result of both vagus nerve dysfunction and sympathetic hyperactivity (1, 2). A single parameter, HRR, measured as the difference between the peak heart rate and the heart rate measured after 60 s in the recovery phase of the stress test, shows the dynamics of this

process. This parameter is a recognised marker used in clinical practice for assessing the risk of sudden cardiac death (3).

From a physiological perspective, autonomic activity also affects many other processes, including penile erection in men. Gradual domination of the parasympathetic nervous system over the sympathetic nervous system leads, through the synthesis of nitrogen monoxide and cyclic guanosine-5'-monophosphate (GMP), to relaxation of muscles in the corpora cavernosa and to an increased inflow of blood, which causes erection and allows sexual intercourse (4).

Many pathological conditions that may result in autonomic dysfunction can thus affect erectile function and result in erectile dysfunction (ED) (5, 6). Ischaemic heart disease (IHD) is one of the disorders in which ED is an explicit effect of the dysfunction of the autonomic nervous system and damage to the vascu-

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lar endothelium (4, 7, 8). Disorders in autonomic regulation of the circulatory system lead to a less pronounced decrease in HRR for patients who discontinue exercising and are associated with total and cardiovascular mortality and morbidity in patients with IHD (9). Treating IHD requires multiple stages, one of which is cardiac rehabilitation. Physical training, a core component of cardiac rehabilitation programmes, leads to an improvement in HRR due to its sympatholytic and parasympathicotonic activity and has a proven beneficial effect on erection quality (EQ) related to the activity of the autonomic nervous system in men with IHD (1, 3, 10). Given the common denominator, i.e. the tone of the autonomic nervous system, the relationship between HRR and EQ in patients with IHD and ED who have undergone cardiac rehabilitation is interesting (1, 9, 11), yet there are no available sources on this subject. Therefore, the aim of this study was to assess the relationship between HRR and the severity of ED in patients with IHD and ED who have undergone cardiac rehabilitation.

## Methods

This is a prospective, non-randomised intervention study. We analysed 124 men being treated for IHD who scored  $\leq 21$  points on the initial International Index of Erectile Function (IIEF-5) test. All patients were in NYHA class I or II. The study group consisted of 89 patients (mean age:  $60.44 \pm 9.29$  years) who were to be subjected to a cardiac rehabilitation programme, while the control group consisted of 35 patients (mean age:  $61.43 \pm 8.81$  years) who did not undergo cardiac rehabilitation. As the beneficial influence of cardiac rehabilitation has already been documented, no typical randomisation was performed (12). All patients were encouraged to enrol in rehabilitation, as preventing the subjects from participating in cardiac rehabilitation would have been unethical. However, some of the 124 patients initially screened did not agree to participate due to distance from the facility and the 'bother' of having to attend exercises daily, which explains the resulting disproportion in the size of the study groups. The 2 groups were statistically equivalent with respect to all measured parameters, with the exception of left ventricular end-diastolic diameter (LVEDD).

All patients gave their informed consent to participate in the trial and completed the initial and final IIEF-5 tests (all categories). All patients had had the same sex partner for a long time. Pharmacological treatment as per IHD treatment standards was administered to all patients in the study group and the control group. Treatment for IHD included non-pharmacological protocols aimed at eliminating cardiovascular disease risk factors and pharmacological treatment employing acetylsalicylic acid and/or other antiplatelet medication and coronary artery disease medication (short-acting nitrate, beta-adrenergic blockers and calcium antagonists) and hypolipidaemic agents (statins and fibrates). According to the European Society of Cardiology Guidelines, all patients additionally received angiotensin-con-

verting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) (13).

The exclusion criteria included the following: chest pain after sexual intercourse or during physical activity; presence of benign prostatic hyperplasia or prostatic cancer; anatomical penile abnormalities; abdominal aortic surgery; cerebrovascular events; severe pelvis and/or vertebral column trauma; psychiatric disorders, especially depression; ventilatory failure or obstructive and restrictive lung diseases; anaemia; any hormonal treatment; any severe conduction abnormalities or conduction disorders estimated by 24-h ECG measurement before entering the study; any neurological and/or orthopaedic impairments and necessity of dosage modifications of drugs with proven negative effect on erection or drugs affecting the chronotropic response during the study.

The inclusion and exclusion criteria were assessed by a therapeutic team in charge of cardiac rehabilitation (a medical doctor with vast clinical and scientific experience and 2 physiotherapists). The team analysed the subjects' files and results of additional tests. In questionable cases, additional specialists were consulted. All patients received instructions on the research methodology and the idea behind the project and gave their written informed consent.

Baseline assessment of leisure-time physical activity prior to the start of the cardiac rehabilitation programme was conducted over the course of a week using the Framingham questionnaire (14). The clinical characteristics of the patients are presented in Table 1 and it includes data from medical history, biochemical findings and echocardiography parameters such as LVEDD, ejection fraction (EF) and left atrial dimension collected at baseline. Echocardiography was routinely performed before cardiac rehabilitation in all patients. The exercise programme was carried out over 6 months and included endurance trainings on cycle ergometers [ER-900, ERGOLINE (GmbH CoKG 72457, Bitz)], general gym or outdoor exercises and some resistance training.

The duration of the rehabilitation programme was consistent with the European Society of Cardiology guidelines (12). A physical examination and treadmill stress test were carried out before and after the rehabilitation cycle. The initial stress test allowed for individual assessment of the maximum heart rate for each subject.

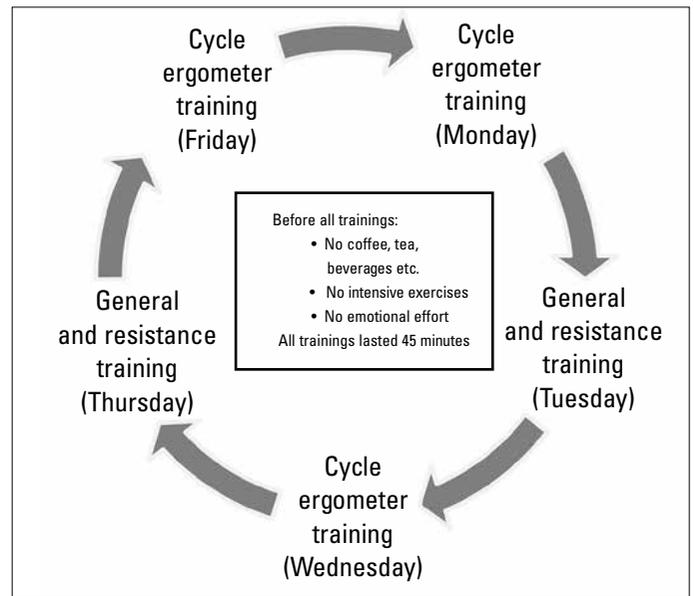
A diagram of cardiac rehabilitation is presented in Figure 1. During the exercises on cycle ergometers, the peak load of the initial exercises was established at 40%–70% of the maximum load reached during the initial cardiac stress test and was increased by no more than 10 W for each of the 12 intervals, each time at the point when the patient showed proper adaptation to the exercise. Heart rate was monitored continuously and blood pressure was measured automatically at the beginning and end of each interval.

During the gym exercises, patients worked out at no higher than the 13<sup>th</sup> fatigue level on the 15-point Borg scale. During

**Table 1. Clinical characteristics of the study groups (patients with ischaemic heart disease and erectile dysfunction)**

Description	Study group	Control group	Statistical significance
Numerical amount	89	35	
Age, years	60.44±9.29	61.43±8.81	0.588
BMI, kg/m <sup>2</sup>	28.72±4.70	27.08±2.43	0.052
Myocardial infarction	62 (67.83%)	19 (54.29%)	0.157
Hb concentration, g%	14.23±1.12	14.60±0.79	0.074
eGFR <sup>***</sup> , mL/min/1.73 m <sup>2</sup>	77.08±11.95	81.03±11.89	0.099
TC, mg %	214.62±49.89	214.60±41.10	0.999
TG, mg %	171.18±101.61	169.07±77.42	0.912
LDL-C, mg %	125.86±42.37	136.32±39.03	0.243
HDL-C, mg %	50.42±15.05	46.73±11.56	0.223
PCI	62 (69.66%)	27 (77.14%)	0.541
<b>Number of patients with erectile disorders</b>			
Light (17–21 p.)	29 (32.58%)	9 (25.71%)	0.799
Moderate (12–16 p.)	30 (33.71%)	11 (31.43%)	
Mid-serious (8–11 p.)	8 (8.99%)	4 (11.43%)	
Serious (0–7 p.)	22 (24.72%)	11 (31.43%)	
<b>Echocardiography parameters</b>			
LVEDD, mm	52.93±5.37	55.49±3.72	0.011*
EF, %	57.00±7.03	54.97±7.18	0.153
LA, mm	37.70±3.61	38.66±3.49	0.181
<b>Drugs</b>			
Beta-blockers	84 (94.38%)	33 (94.29%)	0.999
ACEI/ARB	56 (62.92%)	28 (80.00%)	0.106
Statins/fibrates	79 (88.76%)	28 (80.0%)	0.247
CCB	13 (14.61%)	9 (25.71%)	0.232
Antiplatelet drugs	88 (98.88%)	33 (94.29%)	0.192
Diuretics	22 (24.72%)	6 (17.14%)	0.503
<b>CVD risk factors</b>			
Hypertension	52 (58.43%)	26 (74.29%)	0.150
Diabetes type 2	16 (17.98%)	9 (25.71%)	0.472
Lipid disorders	55 (61.80%)	22 (62.86%)	0.923
Smoking habits	48 (53.93%)	20 (57.14%)	0.902
BMI ≥25	67 (75.28%)	22 (62.86%)	0.245
Low leisure-time physical activity**	88 (98.88%)	35 (100.00%)	0.999

Data are presented as mean ± standard deviation or percentage.  
 \*p<0.05, \*\*<1000 Kcal/week, \*\*\*MDRD formula: CrCl (mL/min/1.73 m<sup>2</sup>)=186×(0.742 if female)×Scr<sup>-1.153</sup>×age<sup>-0.0203</sup>. T-test for independent samples, Pearson's chi-square test, chi-square test, with the Yates correction  
 ACEI - angiotensin-converting enzyme inhibitor; ARB - angiotensin receptor blocker; BMI - body mass index; CABG - coronary artery bypass surgery; CCB - calcium channel blocker; CrCl - creatinine clearance rate; EF - ejection fraction; eGFR - estimated glomerular filtration rate measured by MDRD; Hb - haemoglobin; HDL-C - high-density lipoprotein cholesterol; LA - left atrial dimension; LDL-C - low-density lipoprotein cholesterol; LVEDD - left ventricular end-diastolic dimension; p. - points; PCI - percutaneous coronary intervention; Scr - serum creatinine; TC - total cholesterol; TG - triglyceride



**Figure 1. Methodology of cardiac rehabilitation. (1) Cycle ergometer training:** the load on cycle ergometers was increased at 4-min intervals until halfway through the training, when the patients achieved their peak; the load was then declined to the initial values, interrupted by 2-min recovery periods, with a maintained load of 0–5 W. Training began with a 2-min-long warm-up and finished with a 3-min-long rest phase (no load). (2) General and resistance training: the 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 resistance movements for different groups of muscles. All exercises were performed in series of 12–15 repetitions.

general rehabilitation exercises, heart rate was continuously monitored using a Polar S720i heart rate monitor (0.2-Hz sampling rate) (Polar Electro Oy, Kempele, Finland). Cardiac rehabilitation was performed as per the recommendations of the European Society of Cardiology (12, 15). The control group, which was not subjected to cardiac rehabilitation, received, as part of their health-promoting education, information about the importance of maintaining an active lifestyle, with individual recommendations concerning the type, intensity and amount of leisure-time physical activity.

An abridged IIEF-5 questionnaire was used for determining ED. It contained 5 questions, with answers scored from 0 to 5 points and summed to a total score on a 25-point scale. ED was diagnosed if the total score in the questionnaire was ≤21 points (16, 17). None of the patients reported taking phosphodiesterase type 5 (PDE5) in order to improve sexual function.

The International Index of Erectile Function is a widely used, multi-dimensional self-reporting instrument for the evaluation of male sexual function. It has been recommended as a primary endpoint for clinical trials of ED and for diagnostic evaluation of ED severity (18). The validity and sensitivity of the abridged scale were evaluated by analysing patients with ED from 4 placebo-controlled trials of sildenafil as well as by analysing a control group of men without ED (16, 19).

In the group of patients with IHD who were subjected to cardiac rehabilitation, the IIEF-5 test was administered twice, at

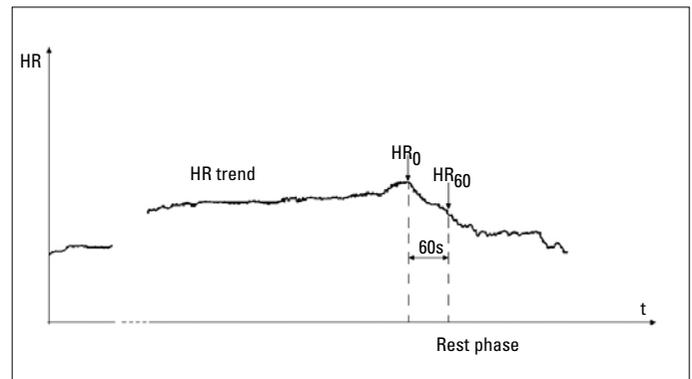
the beginning and at the end of the programme. In the control group, the test was also performed twice, at the beginning and end of a 6-month interval that corresponded to the rehabilitation programme. The analysed parameter was the total score (EQ) in the IIEF-5 questionnaire. The initial value  $EQ_1$ , end value  $EQ_2$  and  $\Delta EQ$  (the difference between  $EQ_2$  and  $EQ_1$ ) were assessed. The credibility of the data from the IIEF-5 questionnaire was verified by comparing the test score between the initial test and the control test, which was given at least 7 days later, in 32 randomly selected patients.

An electrocardiographic stress test was performed after thorough evaluation of the patient's clinical condition. The patients displayed no conditions that would be an absolute or relative contraindication to exercise. The 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. The cardiac stress tests were always performed in the morning after a night's rest. Prior to testing, the patients were asked to refrain from strenuous exercise, avoid emotional situations and not use any stimulants. All patients were also informed about how the test worked, why it was being done and how they could end it, i.e. with specific instruction provided on the reasons for ending the test that were based on their reported symptoms. All test participants had had a cardiac stress test in their medical history before doing the initial stress test as part of the study. A modified Bruce protocol was used to perform all tests. All patients achieved at least 70% of their maximum heart rate and stopped the test when their subjective feeling of fatigue made continuation of the test impossible. After finishing the test, the recovery period began. The treadmill slowed gradually and continued working so that the patient continued the exercise at a metabolic cost of 2 metabolic equivalents (MET). The recovery period lasted for at least 5 min, and during this time, the patient's electrocardiography tracings, well-being and arterial blood pressure normalisation were observed, with measurements taken every 60 s. The test was considered over when the feeling of fatigue lessened and the patient declared that he/she was ready to leave the lab. In all patients, cardiac stress testing was carried out twice (study group: at the beginning and end of the cardiac rehabilitation programme; control group: at a 6-month interval corresponding to the duration of the cardiac rehabilitation programme). The process of HRR adaptation was assessed by analysing initial  $HRR_1$ , final  $HRR_2$  and  $\Delta HRR$ , i.e. the difference between initial and final HRR (Fig. 2).

All results were obtained by applying non-invasive research methods within a project that was approved by the Local Bioethics Committee (95/WIM/2005, KB-433/2010). All patients signed an informed consent form for participation in the study.

### Statistical analysis

The study results were statistically analysed. The data are expressed as mean $\pm$ SD; 95% confidence intervals were assigned for the means of the analysed quantities. Student's



**Figure 2. Heart rate during the exercise stress test. Point HR0 indicates the beginning of a rest phase, which started when the maximum heart rate was reached during the treadmill exercise test. Point HR60 indicates the moment of measurement of heart rate recovery (HRR), which was 60 s after the beginning of the rest phase**

t-test was used for testing the significance of mean differences within 2 subgroups (for independent samples). For dependent samples, the same test was used for testing the impact of the selected factors on the behaviour of the analysed parameters. Levene's test was used for testing the hypothesis of equality of group variances within the population. The result of the test determined the appropriate formula for the t-test. Spearman's rank correlation coefficient ( $r$ ) was used to measure the strength of the relationship between variables, and correlation graphs of the analysed variables were used for visual assessment of the linearity of the relationship between them. The significance of Spearman's correlation coefficient was tested by classical statistics, with Student's t-distribution. The Mann-Whitney U test, Wilcoxon signed-rank test and Spearman correlation coefficient were used for non-normally distributed variables. Correlation between 2 dichotomous variables was determined using the chi-square test, with the value of  $p=0.05$  set as the level of statistical significance. All calculations were made using the STATISTICA statistical package (data analysis software system), (STATISTICA v.10; StatSoft, Inc, Tulsa, Oklahoma, USA).

### Results

The clinical parameters of the study group and the control group were similar. No statistically significant differences were found in any of the analysed parameters, except for LVEDD, which was significantly lower in the study group. However, the mean values for both groups remained within the normal range. The clinical characteristics of the study groups are presented in Table 1.

None of the patients in the study group reported stenocardial complaints as a result of the cardiac training. The exercise stress test was ended when patients were sufficiently fatigued and were no longer able to continue the test. Coronary pain did not appear in any of the patients. During the study period, symptoms of angina were absent in everyday functioning for all patients.

The mean  $EQ_1$  in the study group was  $13.15\pm 5.76$  (95% CI:  $11.93-14.36$ ) and it was not significantly different from that in the

control group. EQ<sub>2</sub> assessed after the cardiac rehabilitation programme in the study group was 15.36±6.51 (95% CI: 13.99–16.73), significantly higher than EQ<sub>1</sub>. In the control group, EQ<sub>2</sub> was 12.43±5.75 (95% CI: 10.45–14.40), which was not significantly different from EQ<sub>1</sub>. The mean ΔEQ in the study group was 2.21±1.32 (95% CI: 1.94–2.49) and it was significantly higher than that in the control group. Mean EQ<sub>1</sub>, EQ<sub>2</sub> and ΔEQ in the study group and the control group are presented in Figure 3.

EQ<sub>1</sub> in the study group showed significant correlations for 2 factors: age (r=–0.715) and estimated glomerular filtration rate (eGFR) (r=–0.385). Body mass index (BMI), echocardiographic parameters (both LVEDD and EF), haemoglobin concentration and lipid concentration [total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglyceride (TG)] were not significantly correlated to EQ<sub>1</sub>.

Among the analysed dichotomous parameters (type of invasive treatment, myocardial infarction, diabetes, hypertension, excess weight or obesity, lipid disorders and pharmacotherapy with ACEIs and/or ARBs, β-blockers, calcium channel blockers, diuretics and statins and/or fibrates), a significantly lower EQ<sub>1</sub> was found in patients with diabetes or those who were receiving treatment with ACEIs and/or ARBs.

ΔEQ in the study group was significantly related only to age (r=–0.525) and EQ<sub>1</sub> (r=0.492). BMI, echocardiographic parameters (LVEDD and EF), haemoglobin concentration and lipid concentration (TC, LDL-C, HDL-C and TG) showed no statistically significant relationship to ΔEQ. Among the analysed dichotomous parameters, only diabetes resulted in a significantly lower ΔEQ.

Mean HRR<sub>1</sub> in the study group was 16.49±7.68/min (95% CI: 14.88–18.11) and it was not significantly different from that in the control group. HRR<sub>2</sub> assessed after the cardiac training programme in the study group was 21.40±7.25/min (95% CI: 19.88–22.93) and it was significantly higher than HRR<sub>1</sub>. In the control group, HRR<sub>2</sub> was 17.11±3.46/min (95% CI: 15.91–18.32) and it was not significantly different from HRR<sub>1</sub>. Mean ΔHRR in the study group was 4.91±3.99/min (95% CI: 4.07–5.75) and it was significantly higher than that in the control group. Figure 3 presents mean HRR<sub>1</sub>, HRR<sub>2</sub> and ΔHRR in the study group and the control group.

HRR<sub>1</sub> in the study group was not significantly related to age, eGFR, BMI, echocardiographic parameters (LVEDD and EF), haemoglobin concentration and lipid concentration (TC, LDL-C, HDL-C and TG). Among the analysed dichotomous parameters, a significantly lower HRR<sub>1</sub> was again determined by diabetes.

ΔHRR in the study group was significantly related to age (r=–0.297) and HRR<sub>1</sub> (r=–0.362) and it was not significantly related to eGFR, BMI, echocardiographic parameters (LVEDD and EF), haemoglobin concentration and lipid concentration (TC, LDL-C, HDL-C and TG). Among the analysed dichotomous parameters, the occurrence of myocardial infarction and smoking resulted in a significantly lower ΔHRR.

Among the parameters describing HRR (HRR<sub>1</sub> and ΔHRR) and ED severity (EQ<sub>1</sub> and ΔEQ) in the study group, only ΔHRR and ΔEQ were significantly related (r=0.409791), which can be credited to the 6-month cardiac training programme. Figure 4 presents a graph of the linear correlation between ΔHRR and ΔEQ.

The credibility test conducted on the data from the IIEF-5 questionnaire showed no significant differences between the initial and control scores (16.53±3.47 vs. 16.75±3.25).

## Discussion

The present study was conducted among patient with vascular disorders, which predispose patients to development of ED (4, 20). The study results showed significant increase in HRR in patients subjected to cardiac rehabilitation. Significantly lower ΔHRR was observed among older patients, smokers and those who had myocardial infarction in the past, while significantly lower HRR<sub>1</sub> was observed in patients with diabetes. EQ

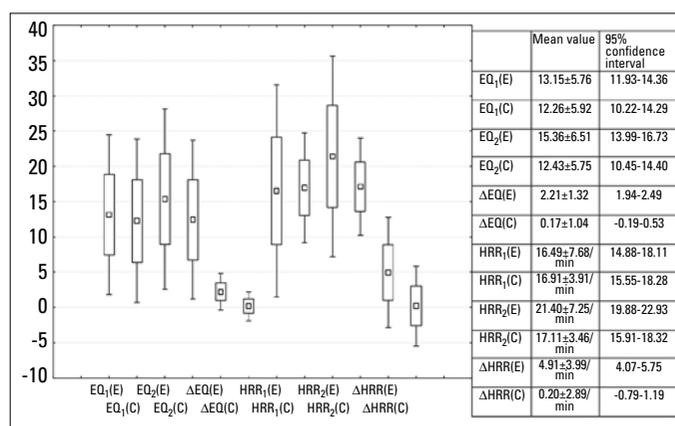


Figure 3. Erectile dysfunction intensity (EQ) and heart rate recovery (HRR) before (1) and after (2) cardiac rehabilitation in the study (E) and control (C) groups (mean, mean±SD and 95% confidence interval)

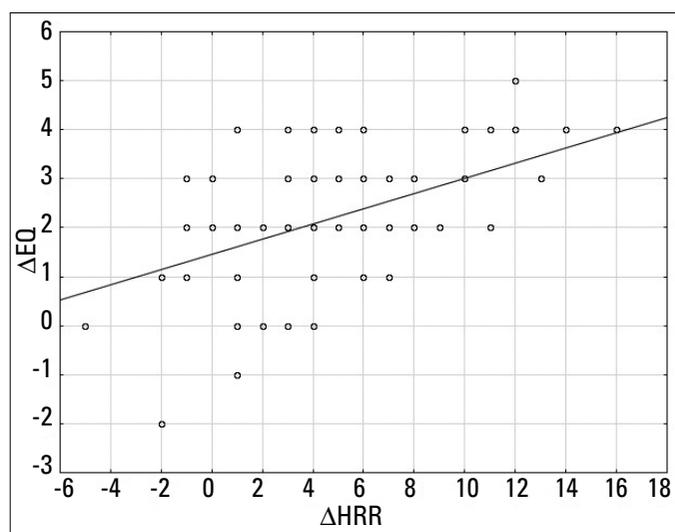


Figure 4. Correlation between ΔEQ and ΔHRR (Additionally regression line is visible)

was negatively correlated with age and was worse in patients with diabetes. Cardiac rehabilitation improved the IIEF-5 score; however, the change in EQ due to training was negatively related to age and initial EQ. In the literature, the risk of sexual disorders among men with IHD is 39%–65% (7, 20). Furthermore, autonomic dysfunction is among the known etiologic factors of ED (7). For patients suffering from IHD, both vascular disorders and autonomic dysfunction occur simultaneously. In clinical practice, assessment of the functioning of the autonomic nervous system is performed indirectly using heart rate variability analysis (20, 21). However, a review of published research shows that heart rate variability analysis alone does not allow practitioners to observe the dynamic response of the autonomic system to exercise stress (7). Therefore, we used the exercise stress test to analyse autonomic balance, as it allows for simultaneous assessment of the cardiovascular and autonomic pathologies.

HRR, when assessed in the first minute of the recovery period of an exercise stress test, is considered a marker of autonomic nervous system activity, and abnormal values result due to vagal dysfunction and sympathetic hyperactivity (1, 2, 22). In the analysed group of patients, significantly lower HRR<sub>1</sub> was observed in patients with diabetes mellitus type 2. Higher sympathetic activity can be observed as a result. HRR may also be affected by other risk factors. Data from the study by Lin et al. (23) show that HRR is inversely related to several risk factors, such as concentration of CRP, cholesterol, TGs and HDL-C, even in healthy children. Moreover, according to Brinkworth et al. (24) reduction of excess body weight, another risk factor for cardiovascular diseases, leads to an improvement in HRR. Finally, regular cardiac training during cardiac rehabilitation has a proven effect on autonomic tone and thus significantly improves HRR.

This effect was observed in our study group in which participation in a 6-month cardiac rehabilitation programme led to a significant increase in HRR that was not observed in the control group. An analogous effect was observed by MacMillan et al. (25) in a group of patients with IHD who had been subjected to only a 3-month-long phase II cardiac rehabilitation programme. It appears that the absolute value of HRR, as well as the change in HRR due to regular physical activity, depends on various factors that have a proven effect on autonomic activity. From among patients with IHD and ED analysed within our study group, significantly lower  $\Delta$ HRR was determined by myocardial infarction and smoking. Both of these factors are related to autonomic imbalance and sympathetic hyperactivity (26, 27). Additionally,  $\Delta$ HRR was also negatively related to age and HRR<sub>1</sub>. A negative relationship between the change in HRR adaptation dynamics and age indicates lower efficiency of cardiac training in modification of autonomic activity in elderly patients. It was also found

that patients who started training with the lowest HRR achieved the most improvement as a result of cardiac rehabilitation.

Furthermore, we found no negative effects of training on cycle ergometers on sexual function. The most recent clinical trials do not confirm the presence of any positive correlation between riding a bike and ED. Thus, the rehabilitation equipment used in most cardiac rehabilitation facilities around the world is safe and does not carry the risk of intensifying ED.

When analysing erection mechanisms, it is impossible not to notice the complicated cooperation between the autonomic nervous system and the vascular system. Observations made in groups of men with ED indicate that physical activity may have a beneficial effect on endothelium activity and may simultaneously improve autonomic balance. Recognised methods of analysing autonomic activity also indicate a relation between ED and autonomic imbalance. Lee et al. (28) specifically demonstrated that heart rate variability parameters were different between a group of patients with ED and a control group of healthy men. Moreover, Chen et al. (29) made an observation of the effect of functional disorders on ED, specifically that there exists a significant effect of cardiac sympathetic hyperactivity and severity-dependent cardiac vagal impairment in patients with non-organic ED. In the analysed group of patients in that study, the erection process, which is dependent on cooperation between the nervous system and the vascular system, was significantly negatively related to the age of the men in the study group. The relationship between the autonomic nervous system, age and EQ is probably the result of the age-related progression of risk factors and their long-term detrimental effect on the blood vessels responsible for erection, as previously observed by both Blanc et al. (30) in a rehabilitated population of men and by Feldman et al. (31) in the Massachusetts Male Aging Study. Another significant factor with a proven effect on ED prevalence as well as on EQ of the analysed group of patients is diabetes, due to its multi-directional negative effect on the human body and consequently the erection process.

Leisure-time physical activity has a proven beneficial effect on improving EQ in men. An observation by Derby et al. (32) confirmed the influence of men's physical activity on ED and stressed that it remains the only factor whose positive modification, even in mid-life, may reduce the risk of ED. Leisure-time physical activity also figures into physical capacity; both these factors, according to an observation by Agostini et al. (33), are related to ED. Intensification of physical activity in the study group, as part of the cardiac rehabilitation treatment, had a beneficial effect on EQ assessed using the IIEF-5 questionnaire. No such effect was observed in the control group. Cardiac rehabilitation-induced change in EQ in men with IHD and ED was found to be negatively related to age and initial EQ. Again, age determined a lower efficacy of the cardiac rehabilitation treatment, as confirmed by Ruzić et al. (34), who showed that the effectiveness of cardiac rehabilitation in men after myocardial infarction was related to age, with the largest

effects observed for men aged 30–39 years. A secondary, indirect effect of age is on the relation between initial EQ (measured at the start of the programme) and the change in it due to rehabilitation. Patients with lower initial EQ were able to achieve more improvement than those with a higher initial EQ because of cardiac training. However, this effect was most pronounced for younger patients without atherosclerosis, indicating there is an indirect effect of age on EQ and the effectiveness of cardiac rehabilitation.

A combined analysis of the relation between ED and HRR and autonomic system activity was carried out by Dođru et al. (7). They showed significant differences in HRR between the groups of patients with and without ED. In the group of men with ED, a positive correlation was shown between scores in the IIEF-5 test and HRR. It proves the significant role that autonomic nervous system dysfunction plays in the pathogenesis of ED.

In the analysed group of patients with IHD and ED, no significant relationships between  $HRR_1$  and  $EQ_1$  were found. However, the significant positive relationship between the training-induced change in EQ ( $\Delta EQ$ ) and the change in HRR dynamics ( $\Delta HRR$ ) appears interesting. This relationship shows the significant role of improvement in autonomic balance, leading to improvement in EQ, in patients with IHD and ED who have been subjected to cardiac rehabilitation. Use of a recognised parameter related to autonomic balance confirms observations of other authors that there are significant relationship between EQ and activity in both sub-systems of the autonomic nervous system.

### Study limitations

A possible study limitation is the difference in the number of participants between the study groups: 89 patients received cardiac rehabilitation and 35 did not, and there was lack of randomisation. The control group included patients who either refused to undergo cardiac rehabilitation programme or those for whom such treatment was contraindicated. For ethical reasons, cardiac rehabilitation was offered to all patients who required rehabilitation for medical reasons.

### Conclusion

In patients with IHD and ED subjected to cardiac rehabilitation, enhancement of autonomic balance assessed using HRR plays a significant role in the mechanism of improvement in EQ.

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