The Influence of Increasing Physical Effort on the Concentrations of Selected Neurohormonal Factors in Patients with Heart Failure

Wpływ wysiłku fizycznego o wzrastającej intensywności na stężenie wybranych czynników neurohormonalnych u pacjentów z niewydolnością serca

Abstract

Background. The incidence of diagnosed cases of heart failure is increasing. There have been some studies exploring the influence of physical exercise on the course of heart failure, but the influence of physical effort on the concentrations of neurohormonal factors crucial for the pathogenesis of heart failure remains unknown.

Objectives. To investigate the influence of physical effort on the concentrations of the neurohumoral factors atrial natriuretic peptide, brain natriuretic peptide, endothelin-1, nitric oxide, von Willebrand factor (vWf), adrenaline, and noradrenaline in patients with heart failure.

Material and Methods. The study was carried out on 39 patients with diagnosed heart failure. The control group consisted of 25 healthy volunteers. In both groups the concentrations of the selected factors in blood serum were measured at baseline and directly after an exercise test.

Results. In the heart failure group the change in nitric oxide concentration during exercise significantly correlated with left atrium diameter, while in the control group it correlated with the duration and intensity of exercise. In the heart failure group the statistically significant change in vWf concentration after exercise significantly correlated with interventricular septum thickness, whereas in the control group it correlated with the patient’s body mass.

Conclusions. The decrease in vWf concentration seen in the group of HF patients seems to be significant marker of endothelial dysfunction. The lack of statistically significant differences in the concentrations of the other studied factors after physical exercise may suggest similarities between the two groups, which may justify the use of exercise in the rehabilitation and treatment of patients with heart failure (Adv Clin Exp Med 2010, 19, 2, 185–193).

Key words: heart failure, physical exercise, neurohormonal factors.
Heart failure (HF) is a complex of pathological changes resulting from impairment of heart function (systolic and/or diastolic), with typical hemodynamic and clinical symptoms. The incidence of diagnosed heart failure is currently increasing and the treatment of HF patients has become one of the most important problems of contemporary medicine. It is estimated that every second patient admitted to a cardiology ward is diagnosed with heart failure. This is a consequence of the longer life expectancy of patients with coronary artery disease, which constitutes the most important cause of HF [1]. In recent years, enormous progress has been made in the research of the pathophysiology of HF, including the discovery of molecular processes, genetic issues, and the impact on the whole circulatory system. The methods of HF treatment are developing rapidly.

One of the symptoms associated with HF and severely influencing patients’ quality of life is limited exercise tolerance. A large part of the patients give up physical activity, thus changing their lifestyle. In independent studies many authors have demonstrated that this is unfavorable as regular exercise positively influences the life quality of HF patients [2].

Adrenaline (ADR) and noradrenaline (NOr) are hormones of the catecholamine group. Stimulating the adrenergic receptors, NOr less strongly than ADR, they provoke the spasm of arterial vessels, except for coronary arteries, which they dilate. With their positive inotropic action they increase cardiac output. By narrowing the arteries and increasing cardiac output, they increase the systolic blood pressure. With their compensatory influence on the sympathetic nervous system, beneficial only in the first phase, they play an important role in the development of HF. Disorders in catecholamine secretion during exercise has been the subject of many studies [3].

Atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) are natriuretic peptides that are physiologically secreted by the left ventricular muscle (BNP) and by the muscles of both atria (ANP), whereas in HF their increased blood concentration is caused by excessive secretion by an overloaded left ventricle. This makes them good markers of HF [4].

Von Willebrand factor (vWf), the largest circulating particle in human plasma, plays an important role in hemostasis, being a carrier for factor VIIIc and taking part in blood platelet adhesion in the areas of defected vessel wall. Considering the fact that increased levels of vWf are found in patients with pulmonary hypertension and in patients with episodes of hypoxia (frequent in patients with HF), vWf can be an independent marker of endothelial dysfunction in this patient group [5].

Endothelin-1 (ET-1) is a peptide secreted mainly by endothelial cells. It plays a minor role in the function of the cardiovascular system in healthy persons, its role being much more important in pathological states (especially in HF), where it is one of the major vasoconstrictive agents and has a great influence on the remodeling of heart and vessels [6]. The main action of ET-1 consists of the strongest pressure-increasing action of all known hormones as a result of vessel constriction [7]. Many authors have shown that the level of ET-1 is increased in patients with HF [8–12].

Nitric oxide (NO) is one of the most active vasodilating substances produced by endothelial cells. It is characterized by local action throughout the whole vascular system and is a substance which antagonizes the vasoconstrictive action of ET-1 [8].

There have been reports on the influence of regular physical exercise (in terms of specially developed training programs) on patients with heart failure. The aim of this study was to evaluate the influence of a single physical effort of increasing intensity on the concentrations of ANP, BNP, ADR, NOR, ET-1, NO, and vWf as well as to study their correlations in HF patients. The undoubtedly crucial role of these factors in the etiopathogenesis of HF has been documented in many studies; nevertheless, their role in the pathophysiology of physical exercise in patients with heart failure is still unknown.
Material and Methods

The study was carried out on 39 patients aged 43–89 (mean: 64 ± 10) years, previously treated at the Department of Cardiology of Wroclaw Medical University, with diagnosed chronic HF (decreased ejection fraction EF < 50%) in NYHA classes I–III. Twelve of them were women aged 46–89 years and 27 were men aged 43–76 years. Twenty-three patients were NYHA class I/II and 16 were NYHA class III. The cause of heart failure was coronary artery disease (30 patients) or dilated cardiomyopathy (9 patients).

The patients included in the study did not have any concomitant diseases such as endocrine disorders, history of stroke, respiratory diseases, malignant neoplasm, other chronic inflammatory diseases, or musculoskeletal disorders that would make it impossible to perform an exercise test. The treatment of heart failure, which was consistent with contemporary ESC guidelines and comprised angiotensin convertase inhibitors or angiotensin II receptor antagonists, selected beta-blockers such as carvedilol, bisoprolol, metoprolol CR, diuretics thiazides and/or loop diuretics, as well as spironolactone and in selected cases digoxin, was continued.

The control group (CG) consisted of 25 healthy volunteers aged 22–75 (mean: 47 ± 17) years, 12 of whom were women aged 23–75 years and 13 were men aged 22–69 years, with normal heart structure and function in echocardiography.

All the patients had echocardiography using the GE Vingmed System V device with a 2.5-MHz multifrequency probe. In the M-mode presentation with the 2D picture control (according to ASE guidelines), the following parameters were measured: aortic diameter (Ao), left atrium diameter (LA), left ventricular end-diastolic diameter (LVD), interventricular septum thickness (IV) and posterior wall thickness (PW), as well as left ventricular end systolic diameter (LVS) [6]. The mass of the left ventricle (LVM) was calculated according to the formula postulated by the American Society of Echocardiography with the Devereux modification [7]. The left ventricular ejection fraction (EF) was determined using the modified biplane Simpson method. All the echocardiographic measurements were mean values calculated from three subsequent cardiac cycles.

The exercise test was performed on a treadmill using the modified Bruce protocol for HF patients and the standard Bruce protocol for the control group. The exercise was stopped upon reaching either the submaximal heart rate (calculated from the patient’s age), electrocardiographic ischemic changes, or clinical symptoms such as chest pain, decrease in systolic pressure, dyspnea, or fatigue. During the exercise test, heart rate and systolic and diastolic blood pressure were measured in one minute intervals. The exercise capacity was measured in metabolic equivalents (METs) and at the end of the exercise test the double product, DP, was calculated (maximal systolic blood pressure × maximal heart rate).

To measure the levels of the selected neurohumoral factors, blood samples were taken twice from each patient: at baseline and directly after termination of the exercise test. Their concentrations in blood serum was measured using isotope methods with ready-to-use kits, i.e. catecholamines (NOR and ADR); RIA kit from Biosource; vWF: Elisa kit from Diagnostica Stago, Mannheim, Germany; NO: Elisa kit from R&D Systems (the concentration was measured using an indirect method based on enzymatic transformation from nitrates into nitrites using the nitrate reductase enzyme); ET-1: immunoenzymatic kit from Biomedica, Austria; and ANP and BNP: radioimmunological RIA kit from Peninsula Laboratories Inc. Blood was taken from the patients according to the procedure required by the manufacturers of the respective kits. The study was carried out in accordance with the Helsinki Declaration after approval of Wroclaw Medical University Bioethics Committee was obtained.

The results were analyzed using STATISTICA version 5.0 software. The mean values and standard deviations of the examined variables were calculated. The normal distribution of the variables was verified with the Kolmogorov-Smirnov test and Snedecor’s $F$ test. For variables with a normal distribution, the statistical significance of differences was calculated using Student’s $t$ test for paired and unpaired variables. In the remaining cases, non-parametric tests were used, i.e. the Mann-Whitney $U$ test and the Wilcoxon matched pairs test. Then variance analysis was carried out (ANOVA). The NIR test and Tukey test were used for post-hoc analysis. The correlations were examined using Pearson’s $r$ and Spearman’s $r$ coefficients, respectively. The results were considered statistically significant with $p < 0.05$.

Results

The results are presented in the Tables 1–4. The parameters measured at baseline are marked with 0 and those measured after the exercise test are marked with 1. The following correlations were observed.

In the HF group, the change in NO concentration during the exercise test (ΔNO) signifi-
cantly correlated with left atrium diameter LA ($r = -0.4175, p = 0.013$).

In the control group (CG), the change in NO concentration during the exercise test ($\Delta$NO) correlated with the duration of exercise ($r = 0.4505, p = 0.024$) and with the number of METs reached during the exercise test ($r = 0.4526, p = 0.023$).

In the HF group, the change in vWf concentration during exercise ($\Delta$vWf) significantly correlated with interventricular septum thickness IV ($r = -0.3691, p = 0.029$) and in the control group (CG) with the patient’s body mass ($r = 0.4789, p = 0.015$).

**Discussion**

The advantages of an active lifestyle have been known for many years, both in healthy persons and in patients with cardiovascular diseases. However, patients with HF are advised to limit their physical activity (the so-called bed-armchair

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**Table 1.** Characteristics of the study groups. Age, height, weight, and cardiac ultrasound parameters: left atrium diameter (LA), left ventricular diastolic diameter (LVD), left ventricular systolic diameter (LVS), interventricular septum thickness (IV), posterior wall thickness (PW), left ventricular mass (LVM), right ventricle diameter (RV), and left ventricular ejection fraction (EF). Mean ± standard deviation, nst – lack of statistical significance

<table>
<thead>
<tr>
<th></th>
<th>HF patients (Chorzy z niewydolnością serca)</th>
<th>Control group (Grupa kontrolna)</th>
<th>Statistical significance (Istotność statystyczna)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64.1 ± 10.5</td>
<td>47.1 ± 17.1</td>
<td>$p = 0.00001$</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169.4 ± 9.8</td>
<td>170.3 ± 12.9</td>
<td>nst</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>81.4 ± 13.5</td>
<td>76.2 ± 10.2</td>
<td>nst</td>
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<tr>
<td>LA (mm)</td>
<td>45.5 ± 7.7</td>
<td>38.4 ± 4.0</td>
<td>$p = 0.00007$</td>
</tr>
<tr>
<td>LVD (mm)</td>
<td>59.5 ± 11.2</td>
<td>53.8 ± 4.4</td>
<td>$p = 0.019$</td>
</tr>
<tr>
<td>LVS (mm)</td>
<td>43.2 ± 12.6</td>
<td>31.8 ± 4.7</td>
<td>$p = 0.00005$</td>
</tr>
<tr>
<td>IV (mm)</td>
<td>13.3 ± 1.7</td>
<td>11.6 ± 1.0</td>
<td>$p = 0.00009$</td>
</tr>
<tr>
<td>PW (mm)</td>
<td>10.1 ± 1.8</td>
<td>10.0 ± 0.9</td>
<td>nst</td>
</tr>
<tr>
<td>LVM (g)</td>
<td>325.9 ± 112.1</td>
<td>243.1 ± 29.7</td>
<td>$p = 0.00006$</td>
</tr>
<tr>
<td>RV (mm)</td>
<td>25.9 ± 6.7</td>
<td>18.3 ± 3.1</td>
<td>$p = 0.000002$</td>
</tr>
<tr>
<td>EF (%)</td>
<td>36.1 ± 7.2</td>
<td>64.9 ± 4.5</td>
<td>$p = 0.000001$</td>
</tr>
</tbody>
</table>

**Table 2.** Exercise test parameters: heart rate (HR), systolic blood pressure (RRsyst), exercise duration, number of METs, double product (DP) after exercise. Mean ± standard deviation. Baseline results are marked with 0, the results after exercise with 1; nst – lack of statistical significance

<table>
<thead>
<tr>
<th></th>
<th>HF patients (Chorzy z niewydolnością serca)</th>
<th>Control group (Grupa kontrolna)</th>
<th>Statistical significance (Istotność statystyczna)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (l/min)</td>
<td>0 81.4 ± 13.5 120.1 ± 21.7</td>
<td>76.2 ± 10.2 143.4 ± 18.3</td>
<td>nst $p = 0.00003$</td>
</tr>
<tr>
<td>RR syst (mm Hg)</td>
<td>0 127.3 ± 17.2 152.6 ± 24.2</td>
<td>127.1 ± 14.9 184.7 ± 28.7</td>
<td>nst $p = 0.00001$</td>
</tr>
<tr>
<td>Exercise duration (min)</td>
<td>6.1 ± 3.0</td>
<td>8.7 ± 2.3</td>
<td>$p = 0.0004$</td>
</tr>
<tr>
<td>MET (l)</td>
<td>4.2 ± 2.1</td>
<td>9.4 ± 2.7</td>
<td>$p = 0.000001$</td>
</tr>
<tr>
<td>DP after exercise (l)</td>
<td>18420.72 ± 4730.19</td>
<td>26812.60 ± 6275.470</td>
<td>$p = 0.000001$</td>
</tr>
</tbody>
</table>
lifestyle) and they have been excluded from exercise rehabilitation programs for fear of aggravating their condition. Many authors have demonstrated in independent studies a beneficial effect of physical exercise in HF patients on the aerobic changes in muscles, which prevents muscle atrophy and explains the increase in physical capacity and higher quality of patients’ life [14]. The body mass reduction in this group through physical exercise, as shown by Evangelista et al., has a beneficial influence on quality of life and on the increase in physical capacity [15].

An interesting study was carried out by Yeh et al., who examined the influence of regular Tai Chi exercise on a group of 30 persons with HF. They observed an increase in quality of life and an increase in exercise tolerance with an increase in maximal oxygen consumption and a decrease in serum BNP concentration [16]. Not all authors agree with that. McKelvie et al. evaluated the effects of nine-month home exercise and expressed the opinion that the positive effects of physical effort last only as long as the effort itself and that they have no influence on the qual-

### Table 3. Blood serum concentrations of selected neurohormonal factors ANP, BNP, ET-1, NO, vWF, NOR, and ADR. Mean ± standard deviation. Baseline results were marked with 0, the results after exercise with 1

<table>
<thead>
<tr>
<th>Factor</th>
<th>HF patients (Chorzy z niewydolnością serca)</th>
<th>Control group (Grupa kontrolna)</th>
<th>Statistical significance (Istotność statystyczna)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANP (g/ml)</td>
<td>0.306 ± 0.236 0.411 ± 0.284</td>
<td>0.148 ± 0.138 0.147 ± 0.133</td>
<td>( p = 0.00352 ) ( p = 0.000051 )</td>
</tr>
<tr>
<td>BNP (g/ml)</td>
<td>0.649 ± 0.635 0.678 ± 0.517</td>
<td>0.517 ± 0.231 0.544 ± 0.206</td>
<td>nst nst</td>
</tr>
<tr>
<td>ET-1 (fmol/ml)</td>
<td>0.158 ± 0.179 0.180 ± 0.253</td>
<td>0.216 ± 0.104 0.199 ± 0.098</td>
<td>nst nst</td>
</tr>
<tr>
<td>NO (umol/ml)</td>
<td>27.2 ± 27.1 24.2 ± 23.0</td>
<td>23.1 ± 12.8 21.0 ± 10.7</td>
<td>nst nst</td>
</tr>
<tr>
<td>vWF (%)</td>
<td>79.9 ± 27.2 74.1 ± 24.9</td>
<td>62.3 ± 27.8 72.9 ± 30.3</td>
<td>( p = 0.0162 ) nst</td>
</tr>
<tr>
<td>Nor (nmol/l)</td>
<td>0.44 ± 0.18 0.33 ± 0.19</td>
<td>1.30 ± 1.59 2.00 ± 2.62</td>
<td>nst nst</td>
</tr>
<tr>
<td>ADR (nmol/l)</td>
<td>0.09 ± 0.10 0.07 ± 0.05</td>
<td>0.15 ± 0.24 0.13 ± 0.13</td>
<td>nst nst</td>
</tr>
</tbody>
</table>

### Table 4. Differences (Δ) between concentrations of the studied factors before and after exercise; nst – lack of statistical significance

<table>
<thead>
<tr>
<th>Factor</th>
<th>HF patients (Chorzy z niewydolnością serca)</th>
<th>Control group (Grupa kontrolna)</th>
<th>Statistical significance (Istotność statystyczna)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔANP</td>
<td>0.1052 ± 0.291</td>
<td>-0.0007 ± 0.090</td>
<td>nst</td>
</tr>
<tr>
<td>ΔBNP</td>
<td>0.0268 ± 0.670</td>
<td>0.0268 ± 0.145</td>
<td>nst</td>
</tr>
<tr>
<td>ΔET-1</td>
<td>0.0226 ± 0.217</td>
<td>-0.0161 ± 0.045</td>
<td>nst</td>
</tr>
<tr>
<td>ΔNO</td>
<td>-3.0002 ± 14.090</td>
<td>-0.20952 ± 10.001</td>
<td>nst</td>
</tr>
<tr>
<td>ΔvWF</td>
<td>-5.8241 ± 25.030</td>
<td>10.5956 ± 33.135</td>
<td>( p = 0.028 )</td>
</tr>
<tr>
<td>ΔNOR</td>
<td>-0.1060 ± 0.2032</td>
<td>0.7014 ± 1.187</td>
<td>nst</td>
</tr>
<tr>
<td>ΔADR</td>
<td>-0.0198 ± 0.478</td>
<td>-0.0254 ± 0.247</td>
<td>nst</td>
</tr>
</tbody>
</table>
ity of life. The strength of patients’ arms and legs increased, but it did not improve the result of the exercise test. There was also no improvement of heart failure [17]. Despite the fact that most of the authors underline the benefits of physical exercise in patients with HF, all of them stress that more studies are needed to explain the issues that have not been investigated so far and to build a basis for guidelines of using physical exercise as a standard therapy for HF patients.

In the present study the influence of a single bout of physical exercise on changes in the serum concentrations of selected neurohormonal factors (ANP, BNP, ET1, NO, vWF, ADR, and NOR) in patients with HF was examined as well their correlations. Correlations of the concentrations with the results of the exercise test and with the parameters measured in cardiac ultrasound were also studied. It was decided to analyze them regarding the benefits or potential threats of physical exercise in the group of patients with heart failure. In accordance with expectations, both the groups differed significantly in the results of cardiac ultrasound. The HF group had significantly larger left atrium and left ventricular (systolic and diastolic) diameter, larger interventricular septum thickness, larger right ventricular diameter, and significantly larger left ventricular mass compared with the control group. This shows significant heart muscle damage and remodeling in the HF patient group. In the control group, the echocardiographic parameters were normal.

On analysis of the exercise test parameters, many significant differences were found confirming the lower exercise tolerance of the HF group compared with the control group. The HF patients performed less intense exercise (measured in METs and calculated as the DP). The baseline systolic blood pressure (RR bs) was similar in both groups, whereas the difference in baseline heart rate, which was higher in the HF group, was statistically insignificant. Both parameters differed significantly after exercise. In the HF patients, lower systolic blood pressure (RR e) and lower heart rate (HRe) were observed compared with the control group. A smaller increase in heart rate in the HF patients was explained by Cohen-Solal et al. [17] by the action of negative chronotropic drugs, the lower intensity of exercise in the HF group caused by lower motivation, and lower fatigue threshold and also by decreased chronotropic reserve of the heart, which is expressed not only by a higher baseline HR, but also by impaired sympathetic system response to physical exercise. Regarding the significantly lower post-exercise HR in the HF group, where the left ventricular ejection fraction is also significantly lower, it is understandable that those patients have lower maximal systolic blood pressure. The statistically significant difference in the mean double product (DP), a derivative of the RR and HR values, between the two groups can be explained in the same way.

The exercise test is believed to be a safe test, although there are reports of acute myocardial infarction and death during exercise and shortly after its termination. In patients with coronary artery disease, as many as 10 myocardial infarctions, deaths, or both events together can be expected for every 10,000 exercise tests [18]. During the exercise tests and directly after the exercise tests performed for the present study, no adverse effects in either of the patient groups were observed, which confirms the safety of exercise testing and is consistent with widespread opinion [13–15, 19].

In the present study the concentrations of both natriuretic peptides (ANP and BNP) was higher in the HF patients than in the control patients. These observations are consistent with many studies in which the investigators stress the role of the two peptides as markers of heart failure, demonstrating that the concentrations of these peptides are elevated and correlate with advancement of HF [20–23]. A statistically insignificant minor decrease in ANP level was observed in the controls. In the HF group, an increase in ANP concentration was observed, which is consistent with the opinion of other authors who explain the situation by increased secretion of ANP by the overloaded left ventricle during exercise [20]. On the other hand, the lack of statistical significance of this difference between the two groups and similar changes in BNP concentration, which increased in the same way in the two groups after exercise, suggest that one cannot speak of impaired neurohormonal response in the HF patients compared with the control group. This point of view is also confirmed by Ferrari and Anand [20]. The increase in BNP level during exercise in HF patients was also observed by other authors [24].

In the two groups the differences in catecholamine concentrations (NOR and ADR) were not statistically significant.

The baseline NO concentration was slightly lower in the CG than in the HF patient group. The difference was not statistically significant. A decrease in NO concentration after exercise was observed in both groups and it was greater in the HF group. The difference also did not reach statistical significance. It may, however, suggest a worse response of the vascular endothelium to physical exercise in the HF group. It plays a key role in such patients, particularly when confronted with the changes in ET-1 concentration, which was lower in this group than in the CG at baseline (a sta-
Statistically insignificant difference), but increased after exercise, whereas it decreased slightly in the CG. Although the differences did not reach statistical significance, the observed trend suggests potentially impaired endothelial function in the HF patient group, which may provoke major dis-equilibrium between the vasoconstricting action of ET-1 and the vasodilating action of NO during physical exercise and may lead to an excessive increase in blood pressure, as pointed out by Stewart et al. [25]. As shown by Macarthur [26], the release of ET-1 is provoked by, among other factors, the influence of shear stress on endothelial cells. The unfavorable effects of ET-1 in the HF patient group, such as systemic, renal, pulmonary, and coronary vasoconstriction, apoptosis, hypertrophy, and fibrosis of heart muscle and vessels as well as proinflammatory and proarrhythmic action, were described by Teerlink et al. [27]. The impaired equilibrium between the actions of NO and ET-1 in patients with heart failure has been described in several independent studies [28–30]. 

The endothelial dysfunction results in impaired synthesis and release of NO, which may provoke stretching of endothelial cells and release of ET-1 [26] with a subsequent increasing disproportion favoring vasoconstriction. These findings may speak against physical exercise in HF patients; however, it has to be said that they apply to reactions to a single episode of physical activity and that they did not reach statistical significance in the present study. On the other hand, many studies on regular physical exercise performed by HF patients showed an important improvement in vascular endothelial function with an increase in NO synthesis and release, which decreases peripheral vascular resistance and improves tissue blood flow [31–32]. They justify the use of controlled, repeated physical exercise by patients with HF.

Many significant differences in the changes in vWF concentrations in both groups were observed. In the HF patients, a statistically significant decrease in vWF concentration was seen but in the control group a significant increase was observed. Montalescot et al. [33] reported that in patients with acute coronary syndromes, vWF may, in contrast to other inflammatory proteins, be released rapidly and take part in local coagulation processes as a thrombogenic factor. The lack of correlation with the increase in troponin concentration suggests that the increase in vWF concentration is not secondary to myocardial cell damage during acute coronary syndrome and it may be an independent unfavorable prognostic factor. Therefore the statistically significant decrease in its concentration in HF patients as seen in the present study may become a strong argument in favor of physical exercise in those patients. vWF was also investigated by Sabelisa et al. [34], who examined the influence of exercise on its concentration in HF patients who previously limited their physical activity and then in the same group after 26 weeks of training. At baseline, physical exercise provoked a statistically insignificant decrease in vWF concentration, but after 26 weeks of training, a statistically significant increase in its concentration was observed after a single episode of physical exercise. Gibbs et al. also did not see an increase in vWF concentration after physical exercise in HF patients [35]. Earlier studies in healthy persons revealed an important 2–3 fold increase in vWF concentration provoked by a single episode of physical exercise [36]. The decrease in vWF concentration observed in the present study group (while it increased in the CG) was most likely caused by endothelial dysfunction. More conclusions could have been drawn if the concentrations of vWF had been measured not only directly after physical exercise, but also after a “recovery” phase. It is possible that the release of vWF in response to physical exercise is delayed due to chronically increased endothelial enzyme activity and to insufficient triggering stimulus (shearing of the endothelial cells), which is a consequence of impaired vasorelaxation [37, 38]. This phenomenon is also influenced by muscle atrophy in HF patients, concerning mainly type I fibers (oxidative), causing a relative domination of type IIb glycolytic fibers. The type II fibers are accompanied by fewer capillaries, which may explain the lack of a vWF increase [39]. Thus the increased release of vWF as an effect of long-term physical training performed by HF patients seen by Sabelis et al. [34] may suggest a general improvement in endothelial function. After regular physical training, the HF group reacts to physical exercise in the same way as the group of healthy volunteers.

In summary it has be said that in patients with chronic heart failure, the relationship between neurohumoral factors of proven importance in the etiopathogenesis of HF and physical exercise still requires further investigation that will help to optimize the rehabilitation of this group of patients.

The authors concluded that decrease in vWF concentration seen in the group of HF patients seems to be a significant marker of endothelial dysfunction. The lack of statistically significant differences in the concentrations of BNP, NO, ET-1, NOR, and ADR after physical exercise may suggest similar changes in the parameters in the two studied groups. This fact, together with the absence of side effects and adverse effects of exercise, speaks for the relative safety of physical effort and, as shown by other authors, also for many advantages of its systematic use. The small number of stud-
References


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