# The effects of intracoronary autologous mononuclear bone marrow cell transplantation on cardiac arrhythmia and heart rate variability

Ewa Trzos[1], Maria Krzemińska-Pakuła[1], Tomasz Rechciński[1], Michał Plewka[1], Jarosław Kasprzak[1], Jan Z. Peruga[1], Anna Korycka[2], Agnieszka Wierzbowska[2], Małgorzata Kurpesa[1]

[1] 2nd Department of Cardiology, Medical University, Lodz, Poland

[2] Department of Hematology, Medical University, Lodz, Poland

**Abstract**

**Background:** The results of stem cell therapy after myocardial infarction (MI) have been conflicting. The effects of this therapy on ventricular arrhythmias and autonomic control of heart rate have not yet been established.

**Aim:** To assess the effects of bone marrow cell (BMC) transplantation on the occurrence of arrhythmias and heart rate variability (HRV) parameters in short-term observation after ST-elevation myocardial infarction (STEMI).

**Methods:** Sixty patients with STEMI who underwent primary PCI, were randomly assigned to two groups: Group 1 – 36 patients selected for active treatment (autologous BMC, intracoronary injection mean 7 days after STEMI), and Group 2 – 24 control patients not treated with BMC transplantation. In all patients the infarct-related artery was the left anterior descending, and the left ventricular ejection fraction was < 40%. Two Holter sessions were performed: at baseline (HM1), on average 6 days after MI, and another one (HM2), 1 month after BMC implantation. From these recordings the frequency of non-sustained ventricular tachycardia (nsVT) episodes and the parameters of HRV were calculated.

**Results:** Both groups were comparable with regard to demographic data, the presence of risk factors and electrocardiographic parameters. In HM2 examination the frequency of nsVT tended to be higher in Group 1 (25 vs. 12.5%, NS). The HRV analysis showed lower HF and significant SDNN increase in the BMC group. In controls all the HRV parameters increased. The increase in HF was significantly lower in the BMC group than in controls (22.4 vs. 89.2 $ms^2$, $p < 0.011$).

**Conclusions:** 1. During the first month after the intracoronary injection of BMC, non-significant increase of nsVT was observed. 2. The lack of significant increase in HF power after BMC infusion may be a sign of depressed parasympathetic tone.

**Key words:** stem cell therapy, myocardial infarction, arrhythmic safety

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## Introduction

Despite prompt and successful mechanical revascularisation, a negative remodelling of the left ventricle (LV) after myocardial infarction (MI) can occur [1]. Its consequences include heart failure which causes significant impairment of the quality of life and increased mortality. Therefore, new effective therapeutic methods which could improve clinical outcome in this population are being sought. In 1994 Soonapaa et al. demonstrated that fetal cardiomyocytes introduced into the heart of an adult syngeneic mouse showed full integration with the myocardium of the recipient mouse [2]. The results of this study gave hope for regeneration of cardiac muscle damaged by ischaemia. The main factors determining development of this new therapeutic method include cells' plasticity, easy availability, and simple procedure of administration. Although few randomised studies have been published so far, the results of many of them (TOPCARE-AMI, MAGIC, REPAIR-AMI) are very promising [3-5]. On the other hand, there are available data (studies BOOTS, ASTAMI) which call the benefits of stem cell therapy into question [6, 7]. It has been hypothesised that therapy with the use of stem cells leads only to the acceleration of the natural recovery mechanisms of the myocardium.

**Address for correspondence:**

Ewa Trzos MD, PhD, II Katedra i Klinika Kardiologii, Uniwersytet Medyczny, ul. Kniaziewicza 1/5, 91-347 Łódź, tel.: +48 42 251 60 15, fax: +48 42 251 60 15, e-mail: ewa_trzos@op.pl

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The primary hypothesis that bone marrow derived stem cells can differentiate into cardiac myocytes was not confirmed in humans. On the basis of the current knowledge it has been assumed that the therapeutic effects depend on the number of directly administered cells, their retention in the cardiac muscle and on their ability to colonise the myocardium [8]. The main issue might be differentiation of the administered cells into cardiac myocytes or cells forming heart vessels or paraendocrine influence [9]. Reports on beneficial effects of mononuclear bone marrow cells (BMC) transplanted into the infarct-related artery are particularly promising [10, 11]. These studies confirmed that this route of administration of mononuclear cells is safe and is not associated with increased risk of negative events, including arrhythmias.

The 24-hour heart rate variability (HRV) analysis is useful in assessing arrhytmic risk. Decreased parameters of HRV are independent predictors of arrhythmia occurrence in patients after MI [12, 13]. Improvement of LV perfusion and contractility positively influences HRV parameters. A question arises does therapy with bone marrow derived cells influence parameters of HRV?

The aim of the study was to assess safety (measured as occurrence and frequency of arrhythmias) of intracoronary administration of mononuclear BMC into the infarct-related artery and to evaluate short-term effects on HRV parameters.

## Methods

### Study population

The study population was recruited from patients admitted to the Second Chair and Department of Cardiology of the Medical University in Łódź with the diagnosis of acute coronary syndrome with ST-segment elevation treated with primary percutaneous coronary intervention (PCI) with stent implantation. The time from onset of symptoms of MI to PCI varied from 90 min to 7 h. Electrocardiographic criteria of reperfusion (decrease of the ST-segment elevations by more than 50%) assessed 90 min after recanalisation of the infarct artery-related were present in 72% of patients.

There were the following inclusion criteria: 1. Left anterior descending artery (LAD) as an infarct-related artery; 2. Lack of significant stenosis (> 50%) in other coronary arteries; 3. LV ejection fraction (LVEF) < 40% assessed during the first 48 hours of hospitalisation.

The exclusion criteria were the following: haemodynamic instability in the early postinfarction period, active infection, neoplastic disease and chronic systemic disorder.

All the patients signed informed consent to participate in the study which was approved by the Ethical Committee.

### Intracoronary administration of bone marrow derived cells

Patients were randomised in a blinded fashion into one of the following groups: the active treatment group (n = 36) with the intracoronary administration of mononuclear bone marrow derived cells into the infarct-related artery, or the control group (n = 24). In patients from the active treatment group mononuclear stem cells were administered intracoronary from 3 to 11 days (mean 7 days) after MI. The isolation of mononuclear cells was performed in sterile conditions in the laminar column Safe Flow (Bioair, USA). The methodology has previously been described in detail [14].

### ECG Holter monitoring

In patients from both studied groups 24-hour ECG Holter monitoring was performed before randomisation (mean on the 6$^{th}$ day after MI). The follow-up studies were performed between the 5$^{th}$ and 7$^{th}$ week after treatment according to the randomisation. The analysis of the 24-hour ECG monitoring was performed using the Cardio Scan system. The following parameters were analysed: mean, maximal and minimal heart rate, the presence of ventricular extrasystolic beats and episodes of non--sustained ventricular tachycardia (nsVT), defined as more than three consecutive beats lasting less than 30 s with spontaneous termination.

The HRV was assessed according to the guidelines of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology [15]. The analysis was performed after excluding artefacts and arrhythmias. Time-domain analysis was performed from the whole 24-hour Holter recording and included: standard deviation of normal to normal intervals (SDNN), root mean square of successive differences (rMSSD) and the triangular index (total number of all RR intervals divided by the peak height of the histogram of all RR intervals measured on a discrete scale with bins of 1/128 s). The frequency-domain analysis was performed with the fast Fourier transform method, and the following parameters were assessed: total power (TP), low- (LF: 0.04-015 Hz) and high-frequency (HF: above 0.15 Hz) spectral power of the RR intervals variability and LF/HF ratio. The power spectrum for both frequencies was expressed in ms$^2$. Each hour of the Holter recording was divided into 5-minute intervals. In order to measure analysed parameters of the spectral analysis of HRV from each hour, a 5-minute period from the first 4 intervals with the lowest percentage of exclusions was chosen. The presented values of LF and HF are means of the results of analysed ECG intervals.

### Statistical analysis

Continuous variables are expressed as means ± standard deviation (SD). Categorical variables are presented as numbers (%).

For comparisons between the active treatment group and the control group two-sided t-test for independent samples was used (when the distribution of the continuous

variables in both groups was normal), two-sided Mann-Whitney test for independent samples (when the continuous variable in at least one group was not normally distributed) and two-sided $\chi^2$ test or $\chi^2$ with Yates' correction for categorical variables.

The results of the first and the second ECG Holter monitoring were compared using the two-sided t-test for paired samples (when there was normal distribution of a variable defined as the difference between two measurements), two-sided Kruskal-Wallis test for paired samples (when a variable defined as the difference between two measurements was not normally distributed), or two-sided McNemar test (for categorical variables). Normal distribution was tested with the Kolmogorov-Smirnov test. The p value < 0.05 was considered statistically significant.

## Results

Sixty patients aged 34-72 years (44 male, 16 female) fulfilling the inclusion and exclusion criteria, entered the study. In 36 patients mononuclear bone marrow derived cells were administered into the infarct-related artery. The remaining 24 patients formed the control group. Baseline characteristics including demographic and clinical data are presented in Table I. There were no significant differences between the studied groups according to sex, age and selected clinical parameters (markers of myocardial damage, creatinine concentration, LVEF, results of the PCI – TIMI 2 or TIMI 3). Moreover, the percentage of patients receiving beta-blockers, statins, angiotensin-converting enzyme inhibitors was similar in both groups.

**Table I.** Baseline characteristics of the active treatment group and the control group

| | Active treatment group n = 36 | Control group n = 24 | p |
|---|---|---|---|
| Age [years], mean ± SD | 56 ± 9.1 | 58.7 ± 7.6 | 0.245 |
| Sex [male/female], n (%) | 26 (72)/10 (28) | 18 (75)/6 (25) | 0.952 |
| Troponin I [μg/l], mean ± SD | 25.7 ± 20.9 | 19.0 ± 14.2 | 0.177 |
| CK-MB [mg/dl] | 211.2 ± 265.7 | 180.1 ± 153.1 | 0.492 |
| Creatinine [mg/dl] | 0.9 ± 0.2 | 0.9 ± 0.2 | 0.105 |
| LVEF [%] | 34.2 ± 5.9 | 33.6 ± 5.8 | 0.694 |
| Diabetes, n (%) | 6 (16.6) | 5 (20.3) | 0.165 |
| Hypertension, n (%) | 8 (22.2) | 6 (25) | 0.075 |
| TIMI start 0/1, n (%) | 33 (92)/3 (8) | 20 (83)/4 (17) | 0.566 |
| TIMI end 2/3, n (%) | 0/36 (100) | 2 (8)/22 (92) | 0.304 |
| Collateral circulation, n (%) | 5 (14) | 3 (13) | 0.816 |
| Pharmacotherapy | | | |
| Beta-blockers, n (%) | 29 (80.5) | 20 (83.3) | 0.67 |
| ACEI, n (%) | 27 (75) | 19 (79.1) | 0.85 |
| Statins, n (%) | 33 (91.6) | 22 (91.6) | 0.46 |

*Abbreviations: CK-MB – myocardial fraction of creatine kinase isoenzyme, LVEF – left ventricular ejection fraction, TIMI start/end – coronary flow in the infarct-related artery before and after PCI*

**Table II.** Comparison of the results of baseline Holter monitoring in the active treatment group and the control group

| | Active treatment group | Control group | p |
|---|---|---|---|
| Heart rate | | | |
| maximal | 102.1 ± 8.7 | 109.9 ± 9.2 | < 0.05 |
| minimal | 51.7 ± 8.4 | 54. 0 ± 7.9 | 0.292 |
| mean | 71.2 ± 8.7 | 70.0 ± 9.2 | 0.618 |
| Number of ExV/24 h | 747.3 ± 13.1 | 560.3 ± 16.5 | < 0.01 |
| Number of patients with nsVT, n (%) | 5 (14) | 4 (17) | 0.386 |
| SDNN [ms] | 89.5 ± 28.8 | 80 ± 22.7 | 0.178 |
| LF [ms$^2$] | 369.2 ± 28.8 | 256.5 ± 22.7 | 0.167 |
| HF [ms$^2$] | 127.1 ± 343.2 | 106.6 ± 237.4 | 0.477 |
| LF/HF | 3.3 ± 121.8 | 2.7 ± 84.9 | 0.155 |

*Abbreviations: nsVT – non-sustained ventricular tachycardia, HRV parameters: SDNN – standard deviation, LF – spectrum power low frequency, HF – spectrum power high frequency, ExV – ventricular extrasystolic beats, data are presented as means ± SD*

The baseline parameters of the electrocardiographic assessment in the studied groups are presented in Table II. Both mean and minimal heart rate were similar in the studied groups. Maximal heart rate was significantly lower and ventricular extrasystolic beats – significantly more frequent in the active treatment group. The mean values of the HRV parameters were similar in both groups.

Five to 7 weeks after intracoronary autotransplantation of mononuclear bone marrow derived cells the second ECG monitoring was performed (Table III). In the active treatment group, when compared to the control group, significantly fewer ventricular extrasystolic beats were recorded. However, there were more episodes of nsVT in the active treatment group, although the difference did not reach statistical significance level. The second analysis of the parameters of HRV revealed that in patients who received bone marrow derived stem cells, significantly lower values of the HF spectrum were noted.

The next step was the comparison of the results of the first and the second ECG Holter monitoring separately for the active treatment group and the control group (Tables IV and V). In both groups a significant decrease of the minimal heart rate was observed. Comparison of the HRV parameters revealed a significant increase in the SDNN value in the active treatment group (Table IV), whereas in the control group there was a significant increase of both time and frequency parameters (Table V).

In order to perform more precise analysis of the influence of the implemented treatment, the differences between electrocardiographic parameters obtained during first and second ECG Holter monitoring in both groups were assessed. Although in both groups during the follow-up period a significant increase in the spectrum power of HF was observed, in the active treatment group the increase of HF value by 22.4 ms was significantly lower than in the control group (Table VI). Individual HF values are presented in Figure 1.

## Discussion

Studies on bone marrow derived stem cells in the regeneration of the injured myocardium are performed in a high-risk population – patients with LV dysfunction after MI. This group of patients has a priori high risk of serious ventricular arrhythmias and the implementation of therapy with stem cells needs monitoring and assessment of safety of the used method. Regional improvement of myocardial contractility is considered as an important measure in many randomised clinical studies evaluating this therapy [5, 16], but only a few studies (among others TOPCARE-AMI and MAGIC) showed significant improvement of LVEF when compared to the control group [3, 4]. The majority of studies published so far confirmed the safety of therapy using bone marrow derived stem cells in patients with heart failure after MI. However, there are studies indicating the opposite [17, 18]. Also Villa et al. observed episodes of VT during the first month after intracoronary administration of bone marrow derived stem cells. In one patient in the long-term follow-up episodes of symptomatic sustained VT were recorded [19].

These results justify the need of further attempts in order to assess the influence of treatment with stem cells on the risk of arrhythmia occurrence. Ventricular arrhythmias are the classic markers, which have been used in risk assessment since the 1980s, when it was demonstrated that the presence of ≥ 10 ventricular beats per hour in the ECG Holter monitoring is associated with

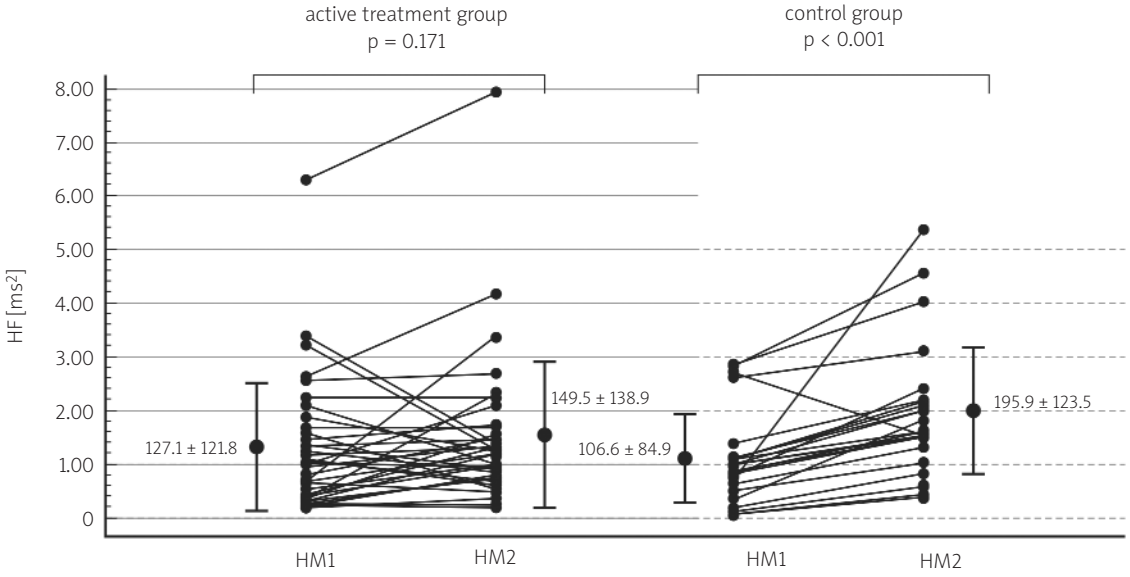


**Figure 1.** Individual values of HF obtained from the baseline (HM1) and follow-up (HM2) Holter monitoring in both studied groups

**Table III.** Comparison of the results of follow-up Holter monitoring in the active treatment group and the control group

| | Active treatment group | Control group | p |
|---|---|---|---|
| Heart rate | | | |
| maximal | 106.1 ± 14.4 | 110.2 ± 13.0 | 0.265 |
| minimal | 49.3 ± 8.0 | 49.6 ± 5.7 | 0.896 |
| mean | 68.8 ± 9.8 | 68.5 ± 6.6 | 0.901 |
| Number of ExV/24 h | 172.4 ± 527.9 | 297.0 ± 647.5 | < 0.002 |
| Number of patients with nsVT, n (%) | 9 (25) | 3 (13) | 0.566 |
| SDNN [ms] | 111.5 ± 29.8 | 108.5 ± 26.4 | 0.695 |
| LF [ms$^2$] | 439.7 ± 379 | 409.8 ± 318.7 | 0.748 |
| HF [ms$^2$] | 149.5 ± 138.9 | 195.9 ± 123.5 | 0.019 |
| LF/HF | 3.3 ± 1.7 | 2.3 ± 1.6 | 0.026 |

*Abbreviations: see Table II*

**Table IV.** Comparison of the results of the baseline and follow-up Holter monitoring in the active treatment group (n = 36)

| ECG Holter monitoring | Baseline | Follow-up | Difference | p |
|---|---|---|---|---|
| Heart rate | | | | |
| maximal | 102.1 ± 8.7 | 106.1 ± 14.4 | 3.9 ± 16.8 | 0.171 |
| minimal | 51.7 ± 8.4 | 49.3 ± 8.0 | –2.4 ± 6.9 | 0.047 |
| mean | 71.2 ± 8.7 | 68.8 ± 9.8 | –2.4 ± 8.8 | 0.109 |
| Number of ExV/24 h | 747.3 ± 13.1 | 172.4 ± 527.9 | –574.8 ± 3007.3 | 0.579 |
| Number of patients with nsVT, n (%) | 5 (14) | 3 (13) | –2 | 0.386 |
| SDNN [ms] | 89.5 ± 28.8 | 111.5 ± 29.8 | 22.0 ± 28.2 | < 0.001 |
| LF [ms$^2$] | 369.2 ± 28.8 | 439.7 ± 379 | 70.5 ± 329.2 | 0.069 |
| HF [ms$^2$] | 127.1 ± 343.2 | 149.5 ± 138.9 | 22.4 ± 96.1 | 0.171 |
| LF/HF | 3.3 ± 121.8 | 3.3 ± 1.7 | 0 ± 1.9 | 0.963 |

*Abbreviations: see Table II. If not otherwise indicated, data are presented as means ± SD*

**Table V.** Comparison of the results of the baseline and follow-up Holter monitoring in the control group (n = 24)

| ECG Holter monitoring | Baseline | Follow-up | Difference | p |
|---|---|---|---|---|
| Heart rate | | | | |
| maximal | 109.9 ± 9.2 | 110.2 ± 13 | 0.3 ± 15.5 | |
| minimal | 54.0 ± 7.9 | 49.6 ± 5.7 | –4.4 ± 5.6 | < 0.001 |
| mean | 70 ± 9.2 | 68.5 ± 6.6 | –1.5 ± 7.1 | |
| Number of ExV/24 h | 560.3 ± 16.5 | 297 ± 647.5 | –263.2 ± 1302.2 | 0.339 |
| Number of patients with nsVT, n (%) | 4 (16.7) | 3 (12.5) | | |
| SDNN [ms] | 80.0 ± 22.7 | 108.5 ± 26.4 | 28.6 ± 24.5 | < 0.001 |
| LF [ms$^2$] | 256.5 ± 22.7 | 409.8 ± 318.7 | 153.4 ± 177 | < 0.001 |
| HF [ms$^2$] | 106.6 ± 237.4 | 195.9 ± 123.5 | 89.2 ± 98.4 | < 0.001 |
| LF/HF | 2.7 ± 84.9 | 2.3 ± 1.6 | –0.4 ± 1.1 | 0.065 |

*Abbreviations: see Table II*

increased risk of death in patients after MI [20]. In our study, in the active treatment group 5 to 7 weeks after autotransplantation of bone marrow derived cells the number of ventricular extrasystoles was lower when compared to the control group. However, the number of episodes of nsVT tended to be higher in the active treatment group. In the randomised study BOOST, in which 24-hour ECG monitoring was also used to compare the frequency of ventricular arrhythmias in the active treatment group and the control group, the occurrence of arrhythmias was similar both in short- and long-term follow-up [6]. Also, in patients in whom electrophysiological

**Table VI.** Comparison of changes (Δ) in electrocardiographic parameters between baseline and follow-up Holter monitoring in the active treatment group and the control group

| | Active treatment group n = 36 | Control group n = 24 | p |
|---|---|---|---|
| Δ Number of ExSV/24 h | –574.8 ± 3007.3 (–15638-2960) | –263.2 ± 1302.2 (–4807-2776) | 0.782 |
| Δ SDNN [ms] | 22 ± 28.2 (–54-84) | 28.6 ± 24.5 (–7-103) | 0.355 |
| Δ LF [ms$^2$] | 70.5 ± 329.2 (–622.5-973.4) | 153.4 ± 177.9 (11.9-820.5) | 0.134 |
| Δ HF [ms$^2$] | 22.4 ± 96.1 (–199.9-271.2) | 89.2 ± 98.4 (–117.4-468.2) | 0.011 |
| Δ LF/HF | 0 ± 1.9 (–3-7) | –0.4 ± 1.1 (–2.9-2.1) | 0.345 |

*Abbreviations: ExSV – supraventricular extrasystolic beats; other abbreviations: see Table II*

study was performed in the long-term follow-up no increase in the number of episodes of VT after bone marrow derived stem cell therapy was observed.

The value of 24-hour ECG monitoring with HRV analysis in predicting arrhythmic complications in patients after MI was confirmed in the clinical studies [21, 22]. Therefore, the aim of our study was not only to assess arrhythmic safety of the treatment in this population but also to analyse the influence of this therapy on HRV parameters.

Published data provide evidence that the basic parameters of time-domain analysis, in particular SDNN, identify patients with a risk of nsVT or sudden cardiac death [23, 24]. Considering frequency-domain analysis, there is no consensus which parameter may be the strongest predictor of risk and what is the cut-off value for determining prognosis. The majority of the published studies indicate that VLF, LF and HF components have predictive value [25]. In our study, patients had Holter ECG monitoring at the mean time of 6 weeks after MI when the HRV parameters should be normalising after the initial rapid decrease in the acute phase of MI. Indeed, in the control group there was a significant increase in both time and frequency-domain parameters of HRV. In the active treatment group, the improvement of only SDDN value was observed, and the increase in the power spectrum in this group was significantly lower than in the control group. Huikuri et al. [26] in a study performed 6 months after intracoronary administration of stem cells observed an increase in the SDNN values in both the active treatment group and the controls, but there was no difference in the increment between studied groups. The authors did not assess HRV parameters, but they analysed occurrence of ventricular late potentials and the presence of microvolt T-wave alternans. The occurrence of these markers, indirectly indicating the presence of arrhythmia substrate, did not differ between the studied groups either in short- or long-term follow-up. According to our observations, the change of the HRV parameters in patients who were not treated with autologous bone marrow derived stem cells is in concordance with the complex neurohormonal mechanisms described after MI [12, 27]. On the other hand, a less prominent decrease of parasympathetic activity in patients treated with stem cells, when compared to the control group, may suggest the influence of bone marrow derived cells on processes occurring in patients after MI.

Lack of significant improvement in parasympathetic activity in the active treatment group when compared to the control group can be in part explained by the interesting hypothesis presented by Pak et al. [28]. In their experimental work, the authors noted that administration of mesenchymal stem cells leads to development of new dendrites of the vagus nerve and the inhomogeneity of their distribution, which influences electrophysiological characteristics of the tissue such as automaticity and conduction velocity.

Inducibility of arrhythmias can be influenced by the method of cell administration, number of cells, the time of administration and the target site. The intracoronary route, which is more and more often used, enables more homogeneous BMC distribution in the myocardium, and causes significantly smaller mechanical injury as well as a small inflammatory response. In our study, in patients randomised into the active treatment group, intracoronary autotransplantation of the cells was performed at the mean time of 7 days after MI. The published data indicate that the best results are achieved when transplantation is performed later than 5 days after MI. The authors of the REPAIR-AMI underlined that administration of stem cells earlier than 3 days after infarction can lead to a diminished beneficial effect of the therapy [5], because earlier administration is associated with higher risk of active inflammatory response and necrosis resorption [29]. On the basis of current knowledge, the reason for occurrence of arrhythmias after therapy with stem cells may be the type of cells used, their quality, route of administration and the target site. Another possible cause of arrhythmias may be the negative influence of the transplanted cells

such as insufficient development of intracellular communication sites.

For validation of arrhythmia risk not only is direct analysis of occurrence and frequency of arrhythmias needed, but also risk stratification should be used. Yet, the sensitivity and specificity of HRV in prediction of serious ventricular arrhythmias in patients with ventricular arrhythmias is 49% and 85%, respectively [30]. Therefore, the method of 24-hour HRV analysis should be used more often in the assessment of efficacy and safety of stem cell therapy. To the best of our knowledge the current work is one of the few studies evaluating the effects of bone marrow derived stem cells on the parameters of HRV analysis. A limitation of our study is the small number of studied patients and the lack of sham administration of cells in the control group.

## Conclusions

In patients after myocardial infarction during the first month after administration of autologous bone marrow stem cells no significant increase in the frequency of complex ventricular arrhythmias was observed.

Bone marrow derived stem cell therapy in patients with LV dysfunction after MI seems to less favourably modulate parasympathetic activity during the first weeks after MI compared with standard treatment.

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# Wpływ dowieńcowej autotransplantacji jednojądrzastych komórek szpiku kostnego na częstość występowania arytmii komorowej oraz parametry zmienności rytmu zatokowego u chorych po zawale serca

Ewa Trzos[1], Maria Krzemińska-Pakuła[1], Tomasz Rechciński[1], Michał Plewka[1], Jarosław Kasprzak[1], Jan Z. Peruga[1], Anna Korycka[2], Agnieszka Wierzbowska[2], Małgorzata Kurpesa[1]

[1] II Katedra i Klinika Kardiologii, Uniwersytet Medyczny, Łódź

[2] Klinika Hematologii, Uniwersytet Medyczny, Łódź

## Streszczenie

**Wstęp:** Od ponad 10 lat zainteresowanie budzi terapeutyczne zastosowanie komórek macierzystych, które są zdolne do regeneracji uszkodzonego miokardium. Dotychczasowe wyniki leczenia chorób serca za pomocą terapii komórkami macierzystymi są jednak niejednoznaczne.

**Cel:** Ocena bezpieczeństwa arytmicznego chorych, którym dowieńcowo podano jednojądrzaste komórki szpiku, oraz ocena wpływu tych komórek na parametry zmienności rytmu zatokowego w obserwacji wczesnej.

**Metody:** Sześćdziesięciu chorych losowo przydzielono do dwóch grup: grupa 1. – 36 chorych zakwalifikowanych do leczenia aktywnego (dowieńcowo podano 20 ml zawiesiny zawierającej komórki macierzyste szpiku kostnego), oraz grupa 2., kontrolna – 24 chorych. U wszystkich tętnicą odpowiedzialną za zawał serca (MI) była gałąź przednia zstępująca lewej tętnicy wieńcowej, a frakcja wyrzutowa lewej komory (LVEF) wynosiła < 40%. W obu grupach wykonano wyjściowe 24-godzinne monitorowanie EKG metodą Holtera (MH1) (średnio 5. doba zawału). Badanie powtórzono miesiąc po leczeniu (MH2). Analizie poddano: średnią częstotliwość akcji serca, obecność arytmii komorowych, parametry zmienności rytmu zatokowego (HRV).

**Wyniki:** Badane grupy były porównywalne pod względem danych demograficznych, obecności czynników ryzyka i chorób współistniejących. W grupie 1. w MH2 zarejestrowano nieistotny statystycznie wzrost częstości występowania epizodów nieutrwalonego częstoskurczu komorowego (13,9 *vs* 25%). W grupie badanej stwierdzono istotny wzrost wartości SDNN (odchylenie standardowe czasów trwania wszystkich odstępów RR rytmu zatokowego), w grupie kontrolnej natomiast istotnie wzrosły zarówno parametry czasowe, jak i częstotliwościowe. W celu dokładniejszej oceny wpływu zastosowanego leczenia porównano zakres zmian wskaźników elektrokardiograficznych między MH1 i MH2. Chociaż w obu grupach w okresie obserwacji doszło do zwiększenia mocy widma HF, to w grupie badanej wzrost ten był istotnie, o 22,4 ms, niższy niż w grupie kontrolnej.

**Wnioski:** 1. W okresie pierwszego miesiąca po podaniu dowieńcowym jednojądrzastych komórek szpiku nie obserwowano istotnego wzrostu częstości występowania złożonych form arytmii komorowej. 2. Wzrost aktywności parasympatycznej w grupie kontrolnej w porównaniu z badaną można wiązać z obniżeniem protekcyjnego wpływu układu przywspółczulnego u chorych, którym podano komórki szpiku kostnego.

**Słowa kluczowe:** implantacja komórek macierzystych, zawał serca, bezpieczeństwo arytmiczne terapii

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**Adres do korespondencji:**

dr n. med. Ewa Trzos, II Katedra i Klinika Kardiologii, Uniwersytet Medyczny, ul. Kniaziewicza 1/5, 91-347 Łódź, tel.: +48 42 251 60 15, faks: +48 42 251 60 15, e-mail: ewa_trzos@op.pl

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