

CLINICAL RESEARCH

Features of Heart Rate Variability and Early Postinfarction Remodeling Process in Patients with Recurrent Myocardial Infarction

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Abstract

The purpose of this study was to evaluate the heart rate variability (HRV) level and the features of early post-infarction left ventricular remodeling (PIR) in patients with recurrent myocardial infarction (MI), which developed within six months post the initial Q-wave MI (Q-MI).

Material and Methods: The study surveyed 105 male patients between 29 and 69 years of age (mean age 52.08±8.5), who underwent a Q-MI and who, for various reasons, have not undergone coronary angiography. All patients underwent echocardiography and the LVM, EDV, ESV and their indexed values, as well as the ejection fraction were determined, including Holter ECG monitoring. In the interim, analysis included the indicators recommended by the standards of measurement, physiological interpretation and clinical use of heart rate variability, such as SDNN, SDANN and RMSSD. The reduction of the total reduction of HRV was taken as $SDNN \leq 100ms$, and the marked reduction in HRV - $SDNN \leq 50ms$.

Results: All the patients were divided into two groups: Group I consisted of patients who, within six months after the initial Q-wave MI, developed fatal or nonfatal reinfarction; Group II included those patients with a favorable course of the disease. The patients in both groups belonged to a somewhat similar age category. By localization of MI, occurrence of AH, as well as the incidence of LV aneurysm, both groups were comparable. However, the Group I patients in acute Q-MI showed significantly more preserved signs of residual myocardial ischemia, which was manifested as early post-infarction angina. The average values of SDNN in patients in Group I were noted to be significantly lower than that in the Group II patients. The same ratio was observed in both groups and also the indicator of SDANN, whereas the mean RMSSD values of the patients of both groups were not significantly different. The percentage of patients with reduced HRV in Group I was 1.8 times higher than that in Group II, including those patients with a marked reduction in HRV, which were 25% and 5.1% in Groups I and II, respectively. The patients in Group I compared with Group II patients had significantly higher values for LVM, EDV, ESV, as well as their indexed values for LVMI, iEDV, and iESV. The average values of EF in Group I were significantly lower than those in Group II.

Conclusion: In patients with recurrent MI, which had developed within six months from the time of the initial Q-infarction in the acute phase of the disease, significantly more preserved signs of residual ischemia were revealed. The average EF, SDNN and SDANN values in these patients were significantly lower than in patients having a favorable course of the disease. Patients with recurrent MI differed significantly by showing higher values of the left ventricular mass, left ventricular volume indices, as well as the indexed values determined during the 10-14 day period of the primary IM.

Keywords: recurrent myocardial infarction; heart rate variability; post-infarction left ventricular remodeling.

Introduction

The course of the disease in patients with myocardial infarction (MI) varies in each individual case. MI can occur without or with complications, which do not worsen the long-

term prognosis. At the same time, about half of the patients in the acute and subacute periods have complications leading to deterioration of the disease and even death. Anticipating the development of such complications is not always possible even by experienced specialists. Thus, one of the complications of myocardial infarction is the development of reinfarction, including fatal reinfarction. In light of this fact, predicting the complications caused by MI in order to be able to promptly perform the necessary preventive measures appears to be an urgent need.

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As well recognized, the post-MI decline of heart rate variability (HRV) reliably indicates imminently threatening ventricular tachyarrhythmias (paroxysmal ventricular tachycardia, ventricular fibrillation) and sudden death. However, HRV is not dependent on the decreased left ventricle ejection fraction (LVEF), increased ventricular ectopic activity or the presence of late potentials; it is an independent predictor of the risk of death in patients with acute myocardial infarction. Nevertheless, the combination of reduced HRV with one of the parameters mentioned above, especially with the reduced left ventricular ejection fraction, facilitates a reliable prediction.

The complex set of changes occurring in the heart post acute MI, as described by Pfeffer M. and Braunwald E., involves "post-infarction left ventricular remodeling" (PIR) [1-3]. Remodeling is a process of adaptation of the left ventricle (LV) in an attempt to maintain its contractile function by expanding the heart chambers and myocardial hypertrophy. However, the progression of this process leads to the breakdown of the compensatory mechanisms and the remodeling of the LV acquires maladjustment features revealing the phenomena of increasing dilation, changing the geometry of the LV, eccentric myocardial hypertrophy and thereby the development of chronic heart failure. Patients with severe PIR are at high risk for cardiovascular events, including sudden death due to arrhythmias.

The purpose of this study was to evaluate the HRV level and the features of early PIR in patients with recurrent MI, which developed within six months post the initial Q-wave MI (Q-MI).

Material and Methods

The study surveyed 105 male patients between 29 and 69 years of age (mean age 52.08±8.5), who underwent a Q-MI and who, for various reasons, have not undergone coronary angiography. The diagnosis of acute MI was established based on the complaints, history, electrocardiographic data, as well as laboratory studies in accordance with the WHO-prescribed criteria (1978).

The exclusion criteria included the presence of violations of the sinuauricular or atrioventricular conduction, lack of sustained sinus rhythm (supraventricular tachyarrhythmia, nodal rhythm, frequent premature beats - with allodromy or number of extrasystoles exceeding 20% of total ventricular complexes), previous MI, non-Q MI, hyperthermia, as well as the presence of diseases that induce significant changes in the HRV, such as diabetes mellitus, hypothyroidism or hyperthyroidism, alcoholism, severe respiratory, kidney or liver failure, cancer, etc.

The initial evaluation of the study protocol was conducted 10-14 days post infarction due to the standard therapy, including the agents (antiplatelets, β -blockers, ACE inhibitors or ARA II, statins and, if necessary, nitrates) in adjusted doses. All patients underwent echocardiography and the left ventricular mass (LVM), end-diastolic volume (EDV), end-systolic volume (ESV) and their indexed values, as well as the ejection fraction (EF) were determined, including Holter

ECG monitoring (HMECG) using the «CardioSens+» system (HAI-MEDICA, Ukraine). For a more objective evaluation of the HRV features, monitoring was conducted under condition of free movement of the patients. All HRV parameters are calculated on 'normal-to-normal' (NN) inter-beat intervals (or NN intervals) caused by normal heart contractions paced by sinus node depolarization.

In the interim, analysis included the indicators recommended by the standards of measurement, physiological interpretation and clinical use of heart rate variability, such as: standard deviation of all R-R intervals over the entire 24-hour period (SDNN), standard deviation of the mean RR-intervals counted for each successive five-minute time intervals for the entire ECG recording and serves to assess the variability of low-frequency component (SDANN), and square root of the mean squared differences of successive NN intervals, characterizing the high-frequency components of variability (RMSSD).

Interpretation of HRV was performed according to the recommendations of the working group of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996). The reduction of the total reduction of HRV was taken as $SDNN \leq 100ms$, and the marked reduction in HRV - $SDNN \leq 50ms$.

Echocardiography was performed using the "Sanoline Versa Pro" (Siemens, Germany) according to the standard procedure in the M- and the B-mode using the recommendations of the American society of echocardiography (2004). Measurements were taken in three consecutive cardiac cycles and the average data were obtained.

End-diastolic (EDV) and end-systolic (ESV) left ventricular volumes were determined by the "area-length" proposed by N. Dodge et al. (1996) using the formula:

$$VA/L = 0.85 \times S^2/L,$$

where S - planimetric area measured LV, L - longitudinal dimension of the left ventricle, respectively, in systole and diastole, resulting in B-mode of the four-chamber position.

Estimated total LV contractility was held in his ejection fraction: $EF = (EDV - ESV) / EDV \times 100\%$.

LV myocardial mass (LVM) is defined by R. Devereux et al. [4,5]:

$$LVM = 1.04 \times [(EDD + IVSD + PWLVD)^3 - EDDL^3] - 13.6g,$$

where EDD, IVSD, and PWLVD - respectively the transverse dimension of the left ventricle, interventricular septum thickness and left ventricular posterior wall thickness in diastole obtained from the M-mode access parasternal long axis.

For EDV, ESV and LVM also calculated their indexed (to the body surface area) values $iEDO = EDV / BSA$, $iESV = ESV / BSA$, $LVMi = LVM / BSA$.

To calculate the area of the body we used the formula:

$$BSA = 0.007184 \times weight \times 0.423 \times Height \times 0.725.$$

The endpoints were considered as indicators of the development of fatal or nonfatal reinfarction (FRIM, NFRIM). When there were lethal outcomes, information regarding the circumstances of death was obtained from the medical records.

Results were statistically processed using the software package Statistica 6.0 for Windows and the Excel package of

Microsoft Excel 2007. The mean (M) and standard deviation (SD) were calculated. Student's unpaired and paired t-tests were used to compare two groups for data with normal distribution. Group comparisons with respect to categorical variables are performed using chi-square tests. A value of $P < 0.05$ was considered statistically significant.

Results and Discussion

The purpose of this study was to evaluate the HRV features of and the symptoms of early PIR for the early identification of the possible predictors of acute myocardial ischemia, including those leading to fatal outcomes within six months after suffering a primary Q-MI.

All the patients were divided into two groups: Group I (n=19) consisted of patients who, within six months after the initial Q-wave MI, developed FRIM or NFRPIM; Group II (n=86) included those patients with a favorable course of the disease.

As evident from Table 1, the patients in both groups belonged to a somewhat similar age category (53.7 ± 6.8 vs 51.9 ± 8.9 ; $p = 0.38$). By localization of MI, occurrence of AH, as well as the incidence of LV aneurysm, both groups were comparable ($p < 0.05$). However, Group I patients in acute Q-MI showed significantly more preserved signs of residual myocardial ischemia, which was manifested as early post-infarction angina (EPIA) (57.9% vs 33.7% ; $\chi^2 = 3.86$, $p < 0.05$).

Table 1.

Clinical characteristics of patients

| Parameters | Group I (n = 19) | Group II (n=86) | χ^2 | <i>p</i> | All subjects (n=105) |
|-----------------|------------------|-----------------|----------|----------|----------------------|
| Age (yr) | 53.7 ± 6.8 | 51.9 ± 8.9 | | 0.38 | 52.3 ± 8.6 |
| MI localization | | | | | |
| anterior | 13 (68.4%) | 50 (58.1%) | 0.69 | 0.40 | 63 (60%) |
| posterior | 6 (31.6%) | 36 (41.9%) | | | 42 (40%) |
| AH | 18 (94.7%) | 70 (81.4%) | 2.04 | 0.15 | 78 (74.3%) |
| Aneurysm | 7 (36.8%) | 23 (26.7%) | 0.78 | 0.37 | 30 (28.6%) |
| EPIA | 11 (57.9%) | 29 (33.7%) | 3.86 | 0.049 | 40 (38%) |
| PDVA | 9 (47%) | 25 (29%) | 2.38 | 0.12 | 34 (32.4%) |
| FC HF (Killip) | | | | | |
| 1-2 | 14 (73.7%) | 80 (93.1%) | 6.21 | 0.012 | 94 (89.5%) |
| 3-4 | 5 (26.3%) | 6 (6.9%) | | | 11 (10.5%) |
| Thrombolysis | 2 (10.5%) | 10 (11.6%) | 0.02 | 0.89 | 12 (11.4%) |

On analysis of the results of the HMECG 47% of the cases Group I of patients were noted to have the PDVA. In Group II, the frequency of occurrence of the PDVA was 29%, although the differences between the groups did not reveal a reliable character ($\chi^2 = 2.38$; $p = 0.12$).

Traditionally, the HRV is used for risk stratification post MI and is assessed by a 24-hour ECG recording. Therefore, to be able to reliably predict HRV, measurements should be taken not prior to one week after the myocardial infarction, because in the early days prognostic assessment is not possible due to the alternating changes in the autonomic activity. Following

this principle, our study was performed in the 10-14 day period post MI after relative stabilization of the patient. According to the recommendations of the working group of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996), one clear indicator of a moderate decline is the drop in the HRV SDNN < 100 ms, and a reliable sign of significant decrease is the SDNN < 50 ms. On analyzing the overall HRV, the average values of SDNN in patients in Group I were noted to be significantly lower than that in the Group II patients (74.84 ± 34.28 vs 104.48 ± 30.1 ; $p = 0.0002$) (Table 2). The same ratio was observed in both groups and also the indicator of SDANN (65.29 ± 32.96 vs 92.9 ± 27.43 ; $p = 0.0004$), whereas the mean RMSSD values of the patients of both groups were not significantly different (18.68 ± 9.33 vs 24.26 ± 14.62 ; $p = 0.12$). The percentage of patients with reduced HRV in Group I (84.2%) was 1.8 times higher than that in Group II (45.3%) ($\chi^2 = 9.42$; $p = 0.002$), including those patients with a marked reduction in HRV which were 25% and 5.1% in Groups I and II, respectively ($\chi^2 = 4.61$; $p = 0.03$). These results once again confirm the position that the reduction in the HRV is a significant predictor of overall mortality and serious arrhythmic events in patients post MI [6-8].

Table 2.

HRV in the comparison groups

| Parameters | Group I (n=19) | Group II (n=86) | <i>p</i> |
|------------|---------------------|--------------------|----------|
| mRR, ms | 875.52 ± 162.79 | 893.8 ± 118.03 | 0.57 |
| SDNN, ms | 74.84 ± 34.28 | 104.48 ± 30.1 | 0.0002 |
| SDANN, ms | 65.29 ± 32.96 | 92.9 ± 27.43 | 0.0004 |
| RMSSD, ms | 18.68 ± 9.33 | 24.26 ± 14.62 | 0.12 |

As mentioned above, the "new balance" occurs after the MI based on subsequent dilatation and hypertrophy of the left ventricle, which support adequate myocardial function.

Several distinct stages in the LV changes have been identified in acute MI:

1. In the first hours a necrotic "dead" zone is formed;
2. Within a period of several hours to several days, an expansion zone is observed with the LV wall thinning, akinesia and paradoxical motions (in the formation of acute aneurysm) in the damaged zone;

3. From several days to several months onwards, LV remodeling is seen to occur. On dilating, the LV cavity becomes spherical in shape instead of remaining ellipsoid; this is accompanied by myocardial hypertrophy, violated systolic and diastolic function and reduced contractility.

There are two forms of LV dilatation post MI - early and late. Early dilation of the LV occurs in the first 72 hours of AMI, where its size is directly dependent upon the size of the infarction and the extent of the coronary artery occlusion infarct. Between the necrotic fibers, the myocytes develop connective tissue, which improves the elasticity and prevents its walls from stretching. Late dilatation occurs over a long period after the infarction, wherein stretching occurs in the infarct zone of the myocardium.

On analyzing the nature of the early PIR, it was found that patients in Group I compared with Group II patients had significantly higher values for LVM (290.9 ± 52.02 vs 253.4 ± 6.3 ; $p=0.03$), EDV (175.72 ± 52.9 vs 148.55 ± 50.78 ; $p=0.04$), ESV (103.34 ± 3.2 vs 75.78 ± 42.9 ; $p=0.01$), as well as their indexed values for LVMI (151.38 ± 23.17 vs 129.2 ± 32.05 ; $p=0.006$), iEDV (91.86 ± 29.25 vs 75.56 ± 23.01 ; $p=0.01$), and iESV (54.21 ± 23.7 vs 38.5 ± 20.14 ; $p=0.004$). The average values of EF in Group I were significantly lower than those in Group II (42.2 ± 9.8 vs 50.68 ± 11.45 ; $p=0.004$) (Table 3).

Table 3.

Echo parameters in the comparison groups

| Parameters | Group I (n=19) | Group II (n=86) | P |
|-------------------------|-------------------|--------------------|-------|
| LVM, g | 290.9±52.02 | 253.4±68.3 | 0.03 |
| LVMI, g/m ² | 151.38±23.17 | 129.2±32.05 | 0.006 |
| EDV, ml | 175.72±52.9 | 148.55±50.7 | 0.04 |
| ESV, ml | 103.34±43.2 | 75.78±42.9 | 0.01 |
| iEDV, ml/m ² | 91.86±29.24 | 75.56±23.0 | 0.01 |
| iESV, ml/m ² | 54.22±23.71 | 38.46±20.14 | 0.004 |
| EF, % | 42.2±9.8 | 50.68±11.45 | 0.004 |

As seen from Table 3, patients with recurrent MI differed from patients with a favorable course of the disease revealing significantly greater LV volume indicator, degree of hypertrophy, as well as lesser myocardial contractility, which influenced the clinical course of the disease in the acute phase of the disease. In Group I, the patients show significantly more similarity in the FC 3-4 of the HF (5 (26.3%) vs 6 (6.9%); $\chi^2 = 6.2$, $p=0.012$) (Table 1).

Conclusions

In patients with recurrent MI, which had developed within six months from the time of the initial Q-infarction in the acute phase of the disease, significantly more preserved signs of residual ischemia were revealed.

The average EF, SDNN and SDANN values in these patients were significantly lower than in patients having a favorable course of the disease.

Patients with recurrent MI differed significantly by showing higher values of the left ventricular mass, left ventricular volume indices, as well as the indexed values determined during the 10-14 day period of the primary IM.

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