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The Dynamics of 0.1 Hz Oscillations Synchronization in Cardiovascular System during the Treatment of Acute Myocardial Infarction Patients

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Abstract
Aim: The aim was the studying of synchronization between 0.1 Hz oscillations in heart rate (HR) and plethysmographic peripheral microcirculation (PM) in acute myocardial infarction (AMI) patients and in healthy subjects. *Material and Method:* 12 healthy volunteers aged 26±5 years and 125 patients with AMI aged 65±9 years were involved in the study. Simultaneous registration of electrocardiogram and photoplethysmogram were performed during 10 min. In AMI patients the signals were recorded twice: the first record was done during 3-5 days after AMI, the second record was done during the third week after AMI. Phase differences between HR and PM oscillations were used to measure the degree of synchronization (S). Data are submitted as medians with inter-quartile ranges (25%, 75%). *Results:* S was 65.8% (50.5%; 79.5%) in healthy subjects whereas in AMI patients at the first week after AMI S was 16.3% (9.4%; 24.6%) ($p<0.001$). In records made at the third week after AMI index S was 18.4% (11.2%; 28.2%). Two groups of AMI patients were identified on the basis of individual S dynamics. In 100 AMI patients no dynamics of S was observed during the observation period and in 25 AMI patients the increase of S was observed. The group of AMI patients with increase of S had greater HR values during the first week after AMI. *Conclusion:* The index S of synchronization of 0.1 Hz oscillations in HR and PM appears to be a sensitive indicator of autonomic control dynamic disturbances in AMI patients.

Keywords: Synchronization; 0.1 Hz oscillations; Heart rate variability; Microcirculation; Acute myocardial infarction.

Introduction

At present time much attention is paid to studying non-linear characteristics of heart rate variability (HRV) [1-3]. Non-linear characteristics are used in clinical practice for describing the autonomic control of cardiovascular system (CVS) together with classical linear methods [1-5].

Several main oscillations are revealed in human CVS [6]. These processes can be synchronized with each other [7-10]. Synchronization means adjustment of frequencies and phases of main oscillations in different parts of CVS during their dynamic interaction. Detection of synchronization indicates the presence of adequate interaction between functional components of CVS during adaptation to external and internal changes.

The oscillations with a basic frequency close to 0.1 Hz are observed in heart rate (HR) and peripheral microcirculation (PM) [11-15]. These oscillations are believed to characterize the properties of central link of autonomic CVS control [16-21]. It is necessary to note that PM control is predominantly performed by means of the autonomic control of hydrodynamic resistance [22].

The aim of this study was studying of synchronization between 0.1 Hz oscillations in HR and PM in acute myocardial infarction (AMI) patients and healthy subjects. The problem was posed to apply synchronization of 0.1 Hz oscillations for clinical assessment of CVS autonomic control in AMI patients against the background of medical treatment.

Material and Method

Study Setting and Patient Selection

Two groups of subjects were involved in this study: 12 male healthy volunteers aged from 20 to 34 years (26±5 years) and 125 AMI patients (72 men and 53 women) aged from 30 to 83 years (65±9 years) treated in the clinic of the Saratov Research Institute of Cardiology. All the subjects gave written informed consent to participate in the study. They had the right to withdraw from the study at any time.

Complete clinical examination was performed to all AMI patients. Q-myocardial infarction was revealed in 79 patients, non-Q-myocardial infarction was revealed in 46 patients. Patients were administered beta-blockers, angiotensin-converting enzyme inhibitors according to their clinical indications [23].

For the further analysis we did not divide AMI patients according to myocardial contractile function damage, because it has been shown that such dependence became uncertain in case of AMI development in spite of strong HRV dependence on the severity of heart failure [24-28]. We also did not accentuate on age peculiarities of these patients because age differences were almost absent under AMI [27].

Simultaneous registration of electrocardiogram (ECG), photoplethysmogram (PPG) measured on the middle finger of the subject's hand and respiration was performed in the horizontal position of patient's body (Fig. 1). The duration of all records was 10 minutes. All signals were sampled at 250 Hz and digitized at 14 bits. The signals were recorded between 13 and 15 hours under spontaneous breathing. The record of respiration was used to control evenness of breathing. We excluded from the analysis the series with forced inspiration and delays in breathing. For further analysis only ECG and PPG records without artifacts, extrasystoles and considerable trends were left.

In AMI patients the signals (ECG, PPG and respiration) were recorded twice. The first record was done during 3-5 days after AMI; the second record was done during the third week after AMI. All records were performed from 1 to 4 p.m.

Statistical Analysis

The Shapiro-Wilk test was applied to check whether the HRV spectral data are approximately normally distributed. Since these data occur to be non-normal, their further analysis was carried out using non-parametric statistical methods. To compare the variables we used the Mann-Whitney test. Continuous variables are reported as medians with inter-quartile ranges (25%, 75%). Categorical data are presented as frequencies and percentages. The obtained estimations were considered statistically significance if $p < 0.05$. Statistica 6.1 was used for statistical analysis.

Spectral characteristics of HRV were calculated using parametric method of spectrum estimation based on autoregression model construction. High-frequency (HF) range, 0.15-0.4 Hz,

and low-frequency (LF) range, 0.04-0.15 Hz, of HRV were analyzed [29]. Within these ranges, frequency power of spectrum was estimated (Fig. 2). Moreover, the total frequency power (TP) and the level of mean value of RR-intervals were evaluated.

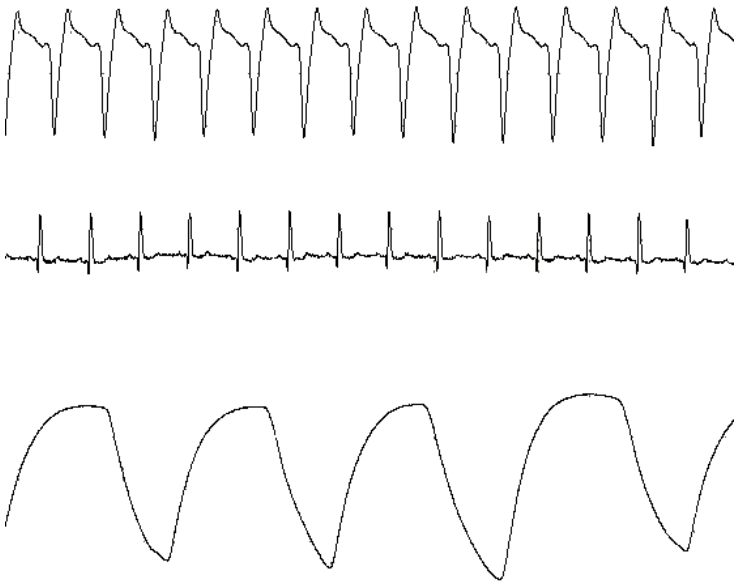

Figure 1. Fragments of simultaneous ECG, PPG and respiration signals for one of the subjects. Recording speed is 10 mm per minute

To estimate synchronization between 0.1 Hz oscillations in HR and PM we used the method proposed by us recently [30]. At first, we extracted LF components of RR-intervals and PPG using bandpass filtration (0.05-0.15 Hz). Then we determined the phases of these components and calculated their difference φ. At last, we detected all epochs of synchronization as the regions where φ fluctuates in time around a constant value, calculate their total duration S, and express it in percent of the duration of the entire record. Index S defines the relative time of synchronization between the considered 0.1 Hz oscillations. Note that amplitude of fluctuations in φ and average speed of φ variation should be small to be captured in S. On the contrary, the duration of a region with approximately constant φ should be sufficiently large to be captured in S. The speed of φ variation and duration of plateaus in φ with almost constant φ values are the parameters of our algorithm for automated detection of phase synchronization epochs. Choosing these parameters we were guided by the following concept: the automated procedure should identify the epochs of synchronization similarly to the usually used visual detection of synchronization and ensure a statistical significance of the results [30]. We found out that these conditions are satisfied if change in φ is less than 0.4π per 10 seconds and the duration of plateaus in φ exceeds 16 seconds.

We tested the proposed measure S by calculating it for the same subject several times per day and within several days. The obtained results show that S takes very close values for the data recorded within one or next day.

Results

The data analysis revealed reliable distinctions in index S of synchronization between 0.1 Hz oscillations for healthy subjects and AMI patients (Table 1). Distinctions in S values against the stage of AMI were also revealed.

Table 1. Spectral characteristics of HRV and index S of 0.1 Hz oscillations synchronization in healthy subjects and AMI patients

Parameter	Healthy subjects (n=12)	AMI patients at the first week (n=125)	AMI patients at the third week (n=125)
S, %	65.8 (50.5; 79.5)	16.3 (9.4; 24.6)*	18.4 (11.2; 28.2)*
TP, ms^2	2030 (1218; 2606)	586 (397; 1007)*	779 (334; 1052)*
LF, ms^2	587 (450; 752)	127 (51; 313)*	116 (65; 243)*
HF, ms^2	898 (381; 1732)	181 (79; 438)*	214 (81; 676)*
HR, sec^{-1}	81 (74; 89)	68 (60; 75)*	66 (59; 74)*

Notes: *- significant difference from the group of healthy subjects ($p<0.001$)

Two groups of AMI patients were identified on the basis of individual index S dynamics. The first group was composed of AMI patients (n = 100) with no dynamics of index S during the period of observation (from the first week to the third week after AMI). We named this group as (S_0) patients. The second group was composed of patients (n = 25) with increase of S during the observation period. This group was named as (S+) patients.

It is necessary to note that (S+) patients had greater HR values during the first week after AMI (Table 2). At the same time, the both groups of (S_0) patients and (S+) patients are comparable by their basic clinical characteristics (Table 3), absolute values and dynamics of HRV spectral characteristics (LF, HF, TP) through the first three weeks after AMI, and index S at the first week after AMI (Table 2).

Table 2. Spectral characteristics of HRV and index S of 0.1 Hz oscillations synchronization in (S+) and (S_0) groups of AMI patients

Parameter	(S+) patients (n=25)		(S_0) patients (n=100)	
	The first week	The third week	The first week	The third week
S, %	18.0 (9.4; 24.3)	40.7 (36.1; 46.2)*	15.7 (10.0; 24.8)	15.9 (9.9; 20.1) ††
TP, ms^2	836 (392; 944)	834 (436; 968)	716 (444; 1012)	646 (310; 1056)
LF, ms^2	121 (52; 177)	110 (51; 180)	98 (66; 158)	104 (76; 114)
HF, ms^2	101 (56; 224)	102 (53; 174)	90 (51; 195)	98 (43; 236)
HR, sec^{-1}	69 (61; 76)	65 (61; 70)	61 (56; 72)††	63 (58; 70)

Notes:
*- significant difference in comparison with the first week after AMI ($p < 0.05$)
†† - significant difference in comparison with the similar parameters in (S+) group of AMI patients ($p < 0.05$)

Table 3. Clinical characteristics of (S+) and (S_0) groups of AMI patients

Parameter	(S+) patients (n=25)	(S_0) patients (n=100)
Age, years	65 (54; 71)	65 (57; 70)
Arterial hypertension, number of subjects	12	10
Signs of extensive AMI, number of subjects	5	2
Acute heart failure (Killip 3-40, number of subjects)	1	0
Bundle-branch block, number of subjects	7	3
Pathologic Q-wave presence on ECG, number of subjects	12	6
Ejection fraction, %	50 (42; 57)	57 (49; 66)

The healthy subjects had higher values of power both in LF and HF ranges of HRV spectrum as well higher values of TP than AMI patients. At the same time, healthy subjects had higher mean values of HR than AMI patients. Reliable dynamics of HRV spectral characteristics was not revealed in AMI patients during the observation period (Table 1).

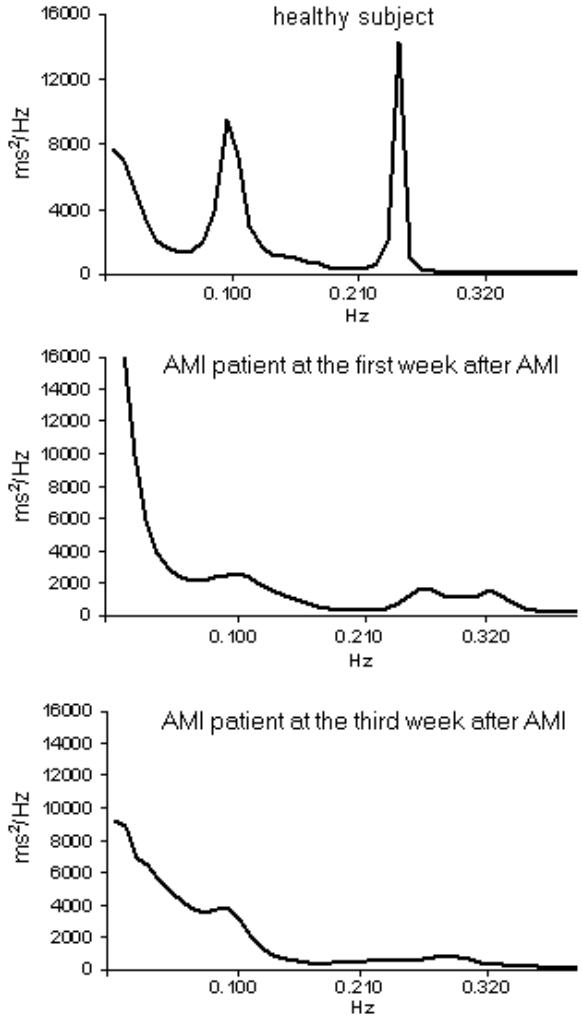

Figure 2. Patterns of HRV spectrum attributed to healthy subjects and AMI patients during the first three weeks after AMI

Discussion

In healthy subjects 0.1 Hz oscillations in HR and PM are well-synchronized between themselves. Therefore, index S takes high values (Table 1). Detection of synchronization at the frequency of 0.1 Hz may be considered as the evidence of adequate autonomic control over functional components of CVS during adaptation to different external and internal conditions [7].

The dependence of synchronization parameters on age, sex, Q-myocardial infarction, and extensiveness of myocardium damage was not revealed. This result agrees well with other studies [24-28].

We observed a sharp decrease of synchronization quality (decrease of index S) in AMI patients both during the first and the third week after AMI in comparison with healthy subjects. We assume that disturbances of autonomic control over functional components of CVS were displayed in such a way during AMI. Patients after AMI showed on average insignificant increase of S at the third week as compared to the onset of AMI. This fact may reflect repairing of functional couplings between CVS components, i.e. HR and PM, as the result of therapeutic and rehabilitation interventions. Nevertheless, 0.1 Hz oscillations synchronization in patients during the first three weeks after AMI was reliably lower in comparison with healthy subjects ($p < 0.001$) (Table 1).

Distinctions revealed in HRV spectral characteristics of healthy subjects and AMI patients are in a good agreement with the results of other researchers [27,28]. Autonomic control of CVS became damaged under AMI. It leads to the decrease of both the total HRV level [31] and the power of 0.1 Hz spectral component of HRV [26]. Thus, the HRV evaluations supplement the results of clinical examination such as ejection fraction, stress tests results and some other [24,31].

Observation of AMI patients over the first three weeks after AMI revealed the absence of HRV spectral characteristics dynamics against a background of the insignificant increase on average of index S among AMI patients. Thus, estimation of synchronization of 0.1 Hz oscillations in HR and PM appears to be a more sensitive method for evaluation of autonomic disturbances dynamics under AMI as compared with HRV spectral analysis.

It is necessary to note that all AMI patients were administered complex therapy. Therefore, low values of average HR observed in AMI patients (Table 1) may be determined by beta-blockers intake. Dose titration of beta-blockers was continued until HR values of about 50-60 beat per minute were achieved.

The analysis of individual dynamic of 0.1 Hz oscillations synchronization in AMI patients during the first three weeks after AMI showed the increase of synchronization quality in some patients (20% subjects) under complex treatment background. These AMI patients differed by reliably higher initial HR values in comparison with the other AMI patients (100 patients of (S_0) group).

In treatment of AMI patients such drugs were used which had a significant influence on the autonomic control of CVS. Repairing of autonomic control of CVS components damaged initially followed by an increase of degree of synchronization between 0.1 Hz oscillations may be the result of drugs action. However, in majority of AMI patients, drug therapy was not accompanied by any change in quality of 0.1 Hz oscillations synchronization, i.e. the treatment including beta-blockers did not result in repairing of adequate autonomic control of functional components of CVS. We believe that further investigations in this area will allow us to develop criteria for choice of treatment and its efficiency evaluation in AMI patients basing on calculation of index S of 0.1 Hz oscillations synchronization in CVS.

Conclusions

Synchronization of 0.1 Hz oscillations in HR and PM allows one to evaluate the quality of interrelations between functional components of CVS, whereas spectral characteristics of HRV provide autonomic control assessment only in respect to influence on the HR.

The obtained results show that index S of 0.1 Hz synchronization appears to be the indicator of autonomic control dynamic disturbances in AMI patients, which may be used for the assessment of therapeutic and rehabilitation interventions efficiency at the acute stage of myocardial infarction.

Ethical Issues

The study was approved by the Ethics Committee of the Saratov Research Institute of Cardiology in Saratov, Russia, and informed consent was obtained from all participants.

Conflict of Interest

The authors declare that they have no conflict of interest.

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