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Prospects for assessment of heart rate turbulence as a predictor of fatal arrhythmias in patients after acute myocardial infarction

Перспективы оценки турбулентности сердечного ритма как
предиктора фатальных аритмий у пациентов после острого
инфаркта миокарда

Abstract

Over the past 20 years, cardiovascular mortality has decreased in developed countries, as there were taken the preventive measures to reduce the prevalence of the coronary heart disease (CHD). Despite these encouraging results, cardiovascular disease is the leading cause of death of approximately 17 million people per year worldwide. One of the new, non-invasive, advanced methods of prognosis of sudden death in patients with CHD with ventricular arrhythmias after myocardial infarction may be an assessment of heart rate turbulence. The heart rhythm turbulence (HRT) is a change in heart rate that is developed in response to emerging ventricular arrhythmias and manifested in short-term fluctuations of the heart rate.

Keywords: ischemic heart disease, ventricular premature beats, a turbulence of heart rhythm, sudden cardiac death, acute myocardial infarction.

Резюме

За последние 20 лет сердечно-сосудистая смертность в развитых странах снизилась, так как были приняты превентивные меры по снижению распространенности ишемической болезни сердца (ИБС). Несмотря на эти обнадеживающие результаты, сердечно-сосудистые заболевания являются ведущей причиной смерти приблизительно 17 миллионов человек в год во всем мире. Одним из новых, неинвазивных передовых методов прогноза внезапной смерти у пациентов с ИБС с желудочковой экстрасистолой после перенесенного инфаркта миокарда может быть оценка турбулентности сердечного ритма. Турбулентность сердечного ритма – это изменение сердечного ритма, которое развивается в ответ на возникающие желудочковые экстрасистолы и проявляется в кратковременных колебаниях сердечного ритма.

Ключевые слова: ишемическая болезнь сердца, желудочковая экстрасистолия, турбулентность сердечного ритма, внезапная кардиальная смерть, острый инфаркт миокарда.

Over the past 20 years, cardiovascular mortality has decreased in developed countries, as there were taken the preventive measures to reduce the prevalence of the coronary heart disease (CHD). Despite these encouraging results, cardiovascular disease is the leading cause of death of approximately 17 million people per year worldwide [1, 2].

In CHD patients with acute myocardial infarction, the ventricular arrhythmias may be an important prognostic factor. The spectrum of ventricular arrhythmias can range from asymptomatic individual premature ventricular contractions to those, which create serious symptoms of fatal arrhythmias. In addition, in CHD patients with time there can be found multiple forms of ventricular arrhythmias [3].

The prognostic value of premature ventricular contraction (PVC) currently remains poorly studied. Thus, according to a recently published meta-analysis, in patients without structural heart disease in the presence of frequent premature ventricular contraction, an increase of the risk of cardiovascular complications was observed [4]. The role of frequent premature ventricular contraction as a predictor of poor prognosis had been demonstrated in a population of patients with myocardial infarction [5].

The most important instrumental predictor in determining the nature of the activities on primary prevention of sudden cardiac death is a fraction of the left ventricular. However, the current risk assessment of fatal outcome, on the basis of use of a left ventricular ejection fraction, is the subject to criticism. It is shown that the risk of sudden cardiac death in patients with CHD and the only criterion, the left ventricular ejection fraction $<30\%$ makes 2.5% per year [6].

In such a way, practicing physicians, who observe patients with ventricular arrhythmias, are still interested in such an important issue as the choice of the necessary diagnostic tests for the purpose of risk stratification of patients' death. The prediction of adverse outcomes in patients with acute myocardial infarction remains a serious and unresolved to the full degree problem, which pushes researchers to look for the new technologies [3, 7]. One of the new, non-invasive, advanced methods of prognosis of sudden death in patients with CHD with ventricular arrhythmias after myocardial infarction may be an assessment of heart rate turbulence.

The heart rhythm turbulence (HRT) is a change in heart rate that is developed in response to emerging ventricular arrhythmias and manifested in short-term fluctuations of the heart rate, which follow the PVC. After the premature ventricular contraction, there occurs the cycle of a short initial acceleration, followed by deceleration of the heart rate. The heart rhythm turbulence is a physiological, biphasic response of a sinoatrial node to the premature ventricular contraction [8].

The basic mechanism of the HRT is a baroreflex compensation of intracardiac hemodynamic changes. The premature ventricular contraction causes a brief disturbance of blood pressure, with good functional activity of the autonomic nervous system, this fleeting change is registered immediately with an instantaneous response in the form of HRT. If the autonomic control system is impaired, this reaction is either weakened or entirely missing. In such a way, the emergence of HRT can be represented by the following sequence: premature ventricular contraction provokes a compensatory pause, thereby reducing the blood pressure, which first causes, through the

baroreflex, a compensatory increase in heart rate and increase in blood pressure, and then leads to a reflex decrease in heart rate [9].

The basis for emergence of the term “heart rate turbulence” was the works of a group of scientists under the direction of G. Schmidt, which had been held in 1999. Researchers, while studying the predictors of risk of death of patients with acute myocardial infarction, have developed a technique for measuring the HRT [10]. The analysis of heart rate turbulence can be made on the basis of the Holter recording, and can also be studied in the laboratory after the internal pacing (induced heart rate turbulence) [11].

The heart rate turbulence may be quantified by using two numeric parameters, namely the Turbulence Onset and the Turbulence Slope. In accordance with the international standard the HRT is evaluated upon two parameters: Turbulence Onset (TO) – (%) and Turbulence Slope (TS) – (mc/RRi). Turbulence Onset reflects the period of tachycardia, and Turbulence Slope – the period of bradycardia. Physiological normal values of these parameters according to G. Schmidt correspond to $TO < 0\%$ and $TS > 2.5 \text{ mc/RRi}$ [10].

In clinical studies, in order to standardize the HRT meanings, 3 categories are allocated: to the category 0 are referred the patients with normal average values of TO and TS, to the category 1 – in case when one of the average values of TO or TS has abnormal deviation, and to the category 2 – when both predictors of HRT have the abnormal values. In the presence of abnormal values of TO, there occurs the reduction of fast response of heart rate to the premature ventricular contraction, in the presence of abnormal values of TS – the reduction of delayed response. Both of these disorders and each of them individually indicate the malignant nature of ventricular tachyarrhythmias in a given patient and are the predictors of sudden death [12].

The statement that the rate turbulence may be a marker of “malignancy” of premature ventricular contractions and predictor of fatal arrhythmias in patients with myocardial infarction, is based on five retrospective and five prospective researches, which in total joined more than 10 000 patients [13]. Originally, the methodology of HRT was developed on a small number of patients with CHD from the MPIP (Multicenter Post-Infarction Project) and EMIAT (European Myocardial Infarct Amiodarone Trial) researches [10]. However, in the subsequent studies, there were large enough cohorts of patients with acute myocardial infarction.

In the ATRAMI (Autonomic Tone and Reflexes After Myocardial Infarction) research, which originally was planned to assess the predictive power of baroreflex sensitivity, A. Ghuran et al. studied the predictive value of HRT in risk stratification of fatal cardiac arrest [14].

In 2005, the predictive power of HRT has also been tested in the CAST (Cardiac Arrhythmia Suppression Trail) research, AP Hallstrom et al. had concluded that the rate of TS is a strong predictor of the risk of death in patients with myocardial infarction, irrespective of the left ventricular ejection fraction. The determination of HRT can be a cost-effective additional method to determine who should receive a cardioverter defibrillator implantation [15].

The FINGER (FINland and GERmany) research was specifically designed to investigate the issue of expediency of the Holter monitoring and definition of HRT in the risk prediction of the sudden cardiac death among the survivors of acute myocardial infarction. The group of researchers, headed

by T.H. Makikallio had showed that the reduction of TS index is a powerful predictor of death in patients with acute myocardial infarction with preserved fraction of the left ventricle [16].

In the prospective ISAR-HRT research (Innovative Stratification of Arrhythmic Risk by HRT) there was studied the prognostic role of HRT, in patients with myocardial infarction. The results showed that the HRT loses the predictive power in elderly postinfarct patients who are over 80 years. The researchers have suggested that this likely occurs due to the physiological age baroreflex decline [17].

Determination of the optimal time of HRT evaluation after acute myocardial infarction was the purpose of the REFINE research (Risk Estimation Following Infarction, Noninvasive Evaluation). The group of D.V. Exner et al. had found that a relatively simple test protocol of patients, which included the evaluation of left ventricular ejection fraction and HRT 8 weeks after the myocardial infarction, easily determined patients who were destined to bear the fatal arrhythmias [18].

In the largest prospective the ISAR-RISK research (Innovative Stratification of Risk Prediction in Post-Infarction Patients with Preserved Left Ventricular Function) that united 2.343 patients, who were hospitalized with acute myocardial infarction, the Holter monitoring was performed at average in 8 days after the diagnosis of myocardial infarction had been made. Cardiovascular mortality in the presence of abnormal HRT in patients with preserved left ventricular ejection fraction was comparable with the group of patients with reduced ejection fraction <30% [19].

The CARISMA research (Cardiac Arrhythmias and Risk Stratification in Patients with Low Ejection Fraction after Acute Myocardial Infarction) was conducted to determine which tests can predict serious arrhythmic events after acute myocardial infarction in patients with reduced left ventricular ejection fraction (<0.40%). It has been shown that in the prediction of primary endpoint the value of TS index less than 2.5 ms/RRi has a sensitivity of 53% and specificity of 74% [20].

In this latter days there have been actively explored the possibilities of HRT in prediction of adverse outcomes in patients with heart failure [21], dilated cardiomyopathy [22], mitral valve prolapse [23], metabolic syndrome [24] and other clinical situations [25–28]. However, we must be aware of some limitations when using HRT. Firstly, the evaluation of HRT requires the presence of sinus rhythm in the patient. Secondly, the evaluation of HRT also supposes the presence of PVC, that's why according to the researches, the patients without PVC were excluded from analysis (EMIAT, ATRAMI) [10, 14].

The technology of HRT loses some of its predictive value with age in elderly patients (ag >75 years) [29]. The similar observations were made in the ISAR-HRT research [30]. The heart rate turbulence is a significant predictor of the sudden death in people aged only ≥65 years [31].

It is known that in patients, who receive β -blockers, the use of indexes of heart rate variability as a predictor of death in post-infarction period is limited. At examination of 591 patients in the placebo group EMIAT, 271 of them received β -blockers, and 320 did not receive them [32]. Nevertheless, the pathologically changed TO and TS showed a high predictive value in patients treated with β -blockers. The frequency of the heart rate, the myocardial infarction and low ejection fraction, which were independent predic-

tors, lose their significance, if the patient began to take β -blockers. The fact of absence of the significant effect of β -blockers on the HRT parameters was later acknowledged in the clinical studies [33]. Therefore, it is not necessary to cancel β -blockers for the evaluation of the HRT, which has undoubted practical value for patients with CHD and the risk of ventricular arrhythmias. In this regard, the HRT has a clear advantage in comparison with other predictors of fatal arrhythmias.

Thus, in all studies the HRT in patients with myocardial infarction, was a strong and independent predictor of adverse events, including cardiac and sudden death. Measurement of the heart rate turbulence, being simple and easily reproducible method, can be routinely used at daily the Holter monitoring ECG. In the future it is necessary to conduct researches, based on the evaluation of heart rate turbulence in order to determine the effectiveness of the prevention of fatal arrhythmias in patients with myocardial infarction.

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