ISHNE Heart Failure World-Wide Internet Symposium

Conflicting aspects of the assessment of Heart Rate Variability in Patients with Cardiac Diseases

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Abstract— Conflicting aspects of the clinical application of the heart rhythm variability (HRV) analysis in cardiovascular patients were critically analyzed. It was found that, in cardiovascular patients, the HRV pattern depended on not only mediators of autonomic nervous system but the electrophysiological state of myocardium and cardiac conduction as well. To make the HRV analysis more informative, the integral estimation method was substantiated, which allowed us to carry out the HRV analysis based on the main objective parameter of the rhythm pacing system, i.e., the heart beats, for both sinus and ectopic rhythms. The specific heart rhythm functions, namely *scatter* and *concentration,* were discovered. The *scatter* function was tested using the standard deviation of distribution of the PR-intervals *(SDNN, SDNN-i,* and *SDANN-i).* The *rMSSD* indexes were physiologically treated as the sinus node capacity for the rhythm *concentration.* The diagnostic and prognostic importance of the integral method is discussed, which may be used as a supplementary method when interpreting the results of the HRV analysis in cardiovascular patients.

The heart rhythm variability (HRV) analysis is one of the important component of the examination of patients [1,2]. However, the increasing number of patients to be examined cause the accumulation of the results of the HRV analysis, which are difficult to interpret from a traditional viewpoint. Having analyzed relevant papers over a 20-year period, the experts of the Mayo Clinic explained the absence of a direct correlation between the HRV parameters and the state of the autonomic nervous system in cardiovascular patients by a complex nature of endo- and exogenous factors responsible for the heart rhythm pattern [3].

Accumulation of conflicting data is common in medicine and does not reject the current paradigm. However, it is necessary to combine traditional and new concepts, because the inadequate assessment of the patient's health status and, hence, unjustified clinical conclusions may be a result of outstanding questions that remain to be answered. This may further cause a loss of clinicians' interest in practical implementation of the HRV, which is of primary importance in developing physiological basics of HRV estimation.

The aim of this paper was to analyze conflicting aspects of the HRV analysis application in cardiac patients and to elaborate the possible approaches for correction.

METHODS

We critically analyzed 17 papers [4-15] on the HRV estimation in healthy subjects and cardiovascular patients. In these papers, the HRV was studied using both the time domain and frequency domain in short (5-10 min) or circadian (24-hour Holter monitoring - HM) samples.

RESULTS AND DISCUSSION

Dissimilar heart rhythm responses to modulation of different parts of the autonomic nervous system are described in [4]. Differently directed responses of the low-frequency component *(LF)* of the HRV spectrum were observed during different types of sympathetic activation: a decrease in the *LF* during physical activity and injection of isoproterenol and an increase in the *LF* during tilt-test (causing an increase in sympathetic activity by means of neural regulation) and injection of epinephrine. In this case, no increase in the level of endogenous epinephrine (activating the humoral link of sympathetic regulation) was observed during tilt. According to [5], no correlations were found between the HRV parameters and plasma levels of epinephrine, norepinephrine, and dopamine in patients with acute myocardial infarction. The same results were obtained by other researchers [6-8].

The HRV may depend on the factors, which are considered less when interpreting the obtained results. The parasympathetic nervous system exerts primary control over the heart rhythm regulation in the norm. With no autonomic effects (e.g. a complete pharmacologic vagosympathetic block), the heart rate (HR) (the so-called true heart rate) of a healthy adult is 100 bpm and more [8]. Thus, the increased HR in patients from different nosological or age [9] groups may evidence both increased sympathetic activity and a complete autonomic heart block [1] that is not the same thing.

The formation of the HRV pattern significantly depends not only on the autonomic tone but the state of myocardium and cardiac conduction as well, which is of particular importance for cardiologic patients with heart failure. The heart rhythm pattern typical of a sinoatrial block may be a clear example of the effect of the sinoatrial node status on the formation of the HRV pattern. This pattern is characterized by the HR acceleration before of a pause. If this pause, as heterotopic arrhythmia, is excluded from the HRV analysis, then prior-to-pause acceleration of the sinus rhythm may be analyzed. Hence, tachycardia shall be taken as a period of increased sympathetic effects on the heart rhythm. However, in case of arrhythmia, the HR acceleration is caused by the increasing sinoatrial block, though the impulse activation in the sinus node is uniform. The extent to which the state of the cardiac conduction may affect the changes in the HRV parameters is still unclear.

The changes in the HRV parameters after ablation, depending on localization of accessory pathways, are analyzed in [10]. It was found that the HRV parameters were significantly higher in patients with slow pathways. Similar results were described in several other papers, in which the HRV changes were explained by localization of intracardiac pathways or the effect of the ablation on the myocardium [11, 12]. This proves that changes in the HRV parameters depend on the electrophysiological properties of myocardium and the pathways located below of the sinus node.

The fact that the HRV analysis is commonly used to estimate the sinus rhythm is an obstacle to the application of this analysis. Such an approach makes it impossible for clinicians to estimate the heart rhythm in patients with predominant heterotopic pacemaker. These patients, as a rule, have a chronic disease with pronounced heart rhythm disorders (atrial fibrillation, complete atrioventricular heart block, etc.), whose treatment is impossible without maximum consideration of factors influencing the severity of a disease, therapeutic effectiveness, and prognosis.

Notably, mathematical analysis of non-sinus rhythm has been successfully used by clinicians. Even in 1961, Braunstein and Frank performed an analysis of autocorrelation of the ventricular response in patients with atrial fibrillation, thus showing the efficiency of the HRV analysis of other than sinus rhythm [13]. The clinical efficiency of the estimation of other than sinus rhythm in cardiologic patients was shown in [14]. The analysis of other than sinus rhythm allows for the estimation of the level of autonomic effects. The analysis of the ventricular contraction variability, as a response to medicamental vagosympathetic block, showed that changes in the temporary HRV parameters in patients with stable atrial fibrillation were similar to those in healthy subjects of the control group [15]. The efficiency of the HRV assessment by the results of the HM was shown for estimating digitalization level, prognosis for, and risk of life-threatening arrhythmias in patients with atrial fibrillation.

Computerized algorithms of the HRV analysis are widely used in clinics for the analysis of the HM recordings. In addition to common methods interpretation of the assessment of HRV, the integral estimation method of HRV interpretation we propose to use for patients with myocardial diseases and/or ectopic heart rhythm during the HM. Theoretically, the method is based on several assumptions. The main objective parameter of system functioning is a resulting effect, which ensures the maximum useful body function. In this case, this is a heartbeat providing body hemodynamics and vital activity, irrespective of physiological and/or pathophysiological heart rhythm regulation mechanisms. Blood or urine concentration of mediator substances and the state and activity of cellular structures and enzymes are only the possible realization of the heartbeats. The same catecholamine concentration in blood may result in an output different in strength and direction, depending on receptor sensitivity, functional state of myocardium, cardiac conduction, etc. On the other hand, the HRV expressed as simple parameters (mean, scatter, and amplitude) is the realized stimulus, which formation depends on many potential stimuli.

Thus, when interpreting of the time-domain analysis of HRV in patients with heart diseases or (especially in the case of the HM without a distinct separation into stationary and nonstationary processes in circadian cycle of free activity), it is necessary to estimate the heart rhythm variability with resulting hemodynamics and interpret the HRV parameters not only in terms of possible extracardiac autonomic effects but with respect to specific heart rhythm functions providing cardiovascular homeostasis. This is especially true when the effect of the myocardium state and cardiac conduction on the sinus rhythm is unclear and the main pacemaker may be of a heterotopic nature.

According to this approach, we recognize two main heart rhythm functions, namely *scatter* and *concentration.* The scatter function is tested by *SDNN, SDNN-i, SDANN-i,* i.e. In short sinus-rhythm samples, parasympathetic regulation is tested by the scatter function in case of stationary process, as well as traditional HRV interpretation. However, in patients with nonsinus rhythm (atrial flutter, severe heart failure and etc) these parameters reflect not only autonomic tone but specify the possible adaptive limits of the heart rhythm variability in common.

In the physiological sense, the *rMSSD,* and triangular index may be treated as the sinus node capacity for heart rhythm concentration, which depends on the transition of the control function from the basic pacemaker to different parts of the sinoatrial node with a different level of synchronization of excitability and automatism. With a rapid HR coupled with enhanced sympathetic effects, *rMSSD* parameter decreases, i.e., the rhythm *concentration* is enhanced, and contrary to growing bradycardia with vagal tone enhancement, the heart rhythm concentration decreases. In patients with dominating other than sinus rhythm, the heart rhythm concentration parameter shows no autonomic effects but shows the heart rhythm reserves for maintaining the adequate hemodynamics. In patients with ectopic bradyarrhythmia, an abrupt decrease in the concentration function (asthenia) with high values of the *rMSSD (*more than 350 ms) can use one of the heart rhythm concentration is an indication for implanting an artificial pacemaker.

CONCLUSIONS

(1) The autonomic extracardiac effects, along with the electrophysiological state of myocardium and cardiac conduction, play an important role in the formation of the HRV pattern in cardiovascular patients.

(2) Compared to other methods of the HRV analysis, the integral method based on selecting specific pacing functions *(scatter* and *concentration),* irrespective of the heart rhythm source and stability of the process, may be used as an accessory method for estimating the results of Holter monitoring in patients with myocardial disease, heart failure and impaired cardiac conduction.

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