Dynamics of the States of Heart Rate Regulation during 24-h Monitoring

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Abstract—An attempt was made to classify the heart rate (HR) regulation states observed during 24-h monitoring of HR variability parameters in patients with essential hypertension and coronary heart disease. A continuous chain of nonoverlapping 5-min intervals was studied, and the heart interval mode, the spectral powers in the ranges of respiratory and first-order slow waves, their ratio, and the total spectral power were determined for each interval. Combinations of HR characteristics obtained for 5-min intervals were classified using nonparametric clustering methods. The standard clustering always revealed a limited number (8–13) of classes of HR regulation states. For every patient, the classes of states were numbered and their chronological sequence was studied with a mathematical apparatus for analyzing Markov chains. A set of state-to-state transitions significantly differing in frequency from random transitions was revealed for every patient.

The aim of this work was to attempt to classify the changes in states of the heart rate (HR) regulation during 24-h monitoring in patients with arterial hypertension and coronary heart disease. A HR regulation state was understood as the complex of HR parameters in a preset period of time (5 min) since it is known that the statistical and spectral characteristics of a heart interval time series make it possible to monitor quantitative indices of the tone of the sympathetic and parasympathetic nervous systems, which form the current state of HR regulation [1–11]. The question is whether the sequence of functional states (in terms of the complex of the autonomic regulation characteristics during the 5-min interval) is a nonrepeating continuum of events or there are interleaving “discrete” classes of states. Elucidation of this question might be of importance for constructing models for short-term prediction of states.

METHODS

We tested 30 patients with stage 1 or 2 (according to the Society of Cardiology of the Russian Federation, 2001) hypertension verified by conventional examination. Of them, three patients had coronary heart disease in the form of class II stable angina of effort. The group consisted of 20 men and 10 women. The mean age was 64.6 ± 10.1 years. The mean systolic pressure was 132.3 ± 11.2 mmHg; the mean diastolic pressure, 82.4 ± 9.3 mmHg; and the mean HR, 66.9 ± 9.98 bpm. The patients were treated with hypotenons drugs of the main types. In all patients, cardiointervals were continuously monitored for 24 h using a Cardio Tens-01 instrument (Meditech, Hungary), which allows continuous recording of RR intervals over 24 h and temporal and spectral analyses of the HR for a predetermined time interval. A continuous chain of consecutive nonoverlapping 5-min RR interval segments was analyzed for a 24-h period. Patients with a minimal number of artifacts (no more than five to ten episodes during the observation) and without rhythm disorders were selected. Segments with artifacts were excluded from the analysis. The following parameters were determined for each 5-min interval: the RR interval mode (MoRR, ms), the total spectral power (TP, ms²), the low-frequency component (LF, ms²), the high-frequency component (HF, ms²), and the LF/HF ratio; the technique and the ranges were as recommended in [1]. The number of 5-min intervals analyzed for a patient varied from 239 to 286. Since the above HR parameters reflect the influence of several control systems [1–11], the term functional state of HR regulation in a given segment of time may be used. For example, Fig. 1 shows the chronological sequence of the synchronous HR parameters in a 65-min segment (13 5-min intervals) in patient Kh. The letters a, b, c, and d at the top of vertical lines 7, 8, 9, and 10 designate different functional states of HR regulation. To classify the states changing over 24 h, we used pattern recognition (clustering) methods, including a combination of the hypersphere and potential function methods [12]. Our clustering procedure is nonparametric; i.e., it does not set preliminary requirements for the character of the statistical data distribution and it has the property of convergence to the minimal number of classes with a reference-free classification and with predetermined compactness criteria. Statistical testing of the adequacy of classification was carried out with discriminant analysis, which showed that the percentage of points in the overlap of two classes did not exceed the predetermined threshold (5%). After each group of parameters was
assigned to one of the classes, a class sequence was formed in the chronological order. A metaphor of the sequence obtained is the alternation of letters in a meaningful text. The mathematical apparatus for Markov chain analysis was used to study the regularities of transition from one letter (class) to another [13]. A program of Markov chain analysis with calculation of the $\chi^2$ statistics was used to determine the significance of differences in transition frequencies between the observed and random sequences. Since every patient had no more than ten artifacts, no more than 0.5% of class-to-class transitions were distorted, suggesting virtually no influence on the net result.

**RESULTS AND DISCUSSION**

Standardized reference-free classification revealed 8–13 classes of states for each patient (mean, 10.2 ± 1.2 classes) over 24 h. The classes had specific features of quantitative relationships between the indices of the tone of the sympathetic and parasympathetic systems, ultraslow controlling influences, and the net result of regulation (MoRR). A few classes of HR regulation states had parallels in a limited number (seven) of the types of human functional states identifiable in a day with a more comprehensive set of electrophysiological and autonomic indices [14]. In this work, we analyzed the specific features of class interchange in the sequence rather than the structure of each class of HR regulation states.

Figure 2 shows the 24-h dynamics of classes (clusters) of states for patient Kh. (239 intervals with states assigned to ten classes). The abscissa represents the ordinal number of a state (a 5-min interval) in the chronological sequence observed during the monitoring; the ordinate shows the number of the class (cluster) to which the corresponding state was assigned. In total, 239 states, each characterized by the five parameters (MoRR, HF, LF, LF/HF, and TP), formed ten classes. The largest were classes 2 and 9, reflecting the most frequent states in the daytime and nighttime, respectively. Departures from these basic states to states of the other classes were observed in considerably shorter time intervals. In total, the number of dominant states (each occurring 50–100 times) in individual patients varied from two to four in the group. For a metaphor of the situation discussed, each class of states can be compared with a letter of the alphabet (as the sequence of the states $a$, $b$, $c$, and $d$ in Fig. 1). The mathematical apparatus of analyzing Markov chains is widely used for symbol sequences [13]. The program of Markov chain analysis allowed us to estimate the absolute and relative