Analysis of Nonlinear Characteristics of Heart Rate for Predicting Sudden Cardiac Death

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Abstract. The paper examines the indicators of the complexity of the dynamic series of heart rhythm. The possibility of their use for early detection of signs of sudden cardiac death is considered. Two approaches to solving this problem are applied. The first is based on the calculation of entropy indices on the functions of empirical mode decomposition of 2-minute fragments of the heart rate signal. The second approach analyzes longer 10-minute fragments. It is based on the computation of a multiscale variation function obtained by mathematical analysis of multiscale Poincaré graphs. Based on the ECG of PhysioNet data, the dynamics of these indicators was analyzed during a certain time (14 minutes - the first set, 70 minutes - the second set) preceding the critical situation. This made it possible to experimentally assess the possibility of predicting an extremely dangerous condition at sites of different distances from the moment of sudden cardiac death. The findings are important for patient monitoring and early warning of sudden cardiac arrest.

Keywords: Sudden cardiac death, Heart rate variability, Nonlinear analysis, Entropy, Multiscale permutations, Classification.

1 Introduction

Sudden cardiac death (SCD) is an unexpected death caused by heart disease, and from 50 to 75% of deaths are associated with cardiovascular diseases, most often with coronary heart disease (CHD) [1]. The problem of preventing SCD remains one of the most important in cardiology.

The main mechanism of SCD is the appearance of a dangerous arrhythmia - ventricular fibrillation (VF) [2]. The presence of at least two factors: myocardial arrhythmia and its ischemia trigger VF, which leads to a sharp violation of hemodynamics. Survival rates after the onset of VF are reduced by about 10% every minute. In a clinic, only the use of resuscitation measures can save a person's life. But the chance of salvation is only 20% [3].

Currently, various methods based on the analysis of ECG signals and heart rate variability (HRV) are proposed for the prediction of SCD. The following main groups of methods can be distinguished [3-6]: (1) - classical linear methods using various

indicators in the time and frequency domains; (2) - methods of frequency-time analysis (wavelet transformation); (3) - nonlinear methods that assess the complexity and randomness of the heart rhythm; (4) methods based on deep learning (neural network methods). As shown in the reviews [3, 4, 7], a higher ability to detect SCD early is demonstrated by methods that assess the degree of complexity of the dynamic series of heart rate. In particular, they include Sample entropy (SampEn), permutation entropy (PE), approximate entropy (ApEn), as well as a number of parameters based on the analysis of Multiscale Poincare (MSP) plots [8, 9]. It is noted that the predictive ability of entropy characteristics on short signal fragments (1-2 minutes) is quite limited [10], and the analysis of Poincaré plots requires fairly large amounts of data. Taking into account these recommendations, two approaches to forecasting SCD have been developed and studied in this paper.

The first is based on the analysis of two improved entropy characteristics of HRV calculated from short 2-minute ECG fragments. They combine ensemble empirical mode decomposition (EEMD) with nonlinear complexity metrics. The second involves analyzing 10-minute segments of the ECG signal and calculates several signs of HRV complexity (nonlinearity), including a Multiscale variation feature. This makes it possible to identify structural changes in HRV in longer time periods. In accordance with the methods used, the short-term and long-term forecast of the SCD is considered. All studies were carried out on samples of experimental data obtained from two ECG databases of the PhysioNet portal [11, 12].

2 Preparation of Experimental Data

Two data samples were formed to conduct the study: the first sample of SCD signals from the MIT BIH Sudden Cardiac Death Holter Database (SCD) [11], containing 20 patients with confirmed episodes of SCD; a second sample of normal sinus rhythm from the MIT BIH Normal Sinus Rhythm (NSR) database [12], including 18 recordings from individuals without significant rhythm disturbances. Further, the data were processed in accordance with the tasks to be solved.

In the task of short-term prediction of SCD by entropy characteristics, a 14-minute segment immediately preceding the moment of SCD onset was allocated from the continuous ECG recording. This 14-minute interval was evenly divided into seven consecutive 2-minute intervals (i.e., 1st interval: 14 - 12 minutes before the SCD, 2nd interval: 12 - 10 minutes, etc.). For the Normal Rhythm Recordings (NSR), random 14-minute fragments were similarly taken, which were also divided into seven 2-minute intervals.

In the problem of long-term forecasting of SCD based on multiscale Poincaré graphs, ECG recordings lasting 70 minutes before the occurrence of SCD were selected. These fragments were divided into seven 10-minute fragments, each of which was considered as a segment for predicting the SCD. For a normal rhythm, 10-minute fragments were also chosen, but the timing of the fragments was arbitrary.

Thus, for each of the tasks, 40 SCD signals (2 channels for each of the 20 patients) and 36 normal rhythm signals (2 channels for each of the 18 NSR recordings) were

obtained. To ensure consistent data samples, all signals were resampled to a single frequency of 360 Hz.

Figure 1 shows a fragment of the ECG signal for recording No30 (two leads) 2 minutes before the onset of SCD. The ordinate axis shows the ECG amplitude in mV, and the abscissa axis shows the time in seconds. The figure clearly shows the transition from the background state to the SCD.

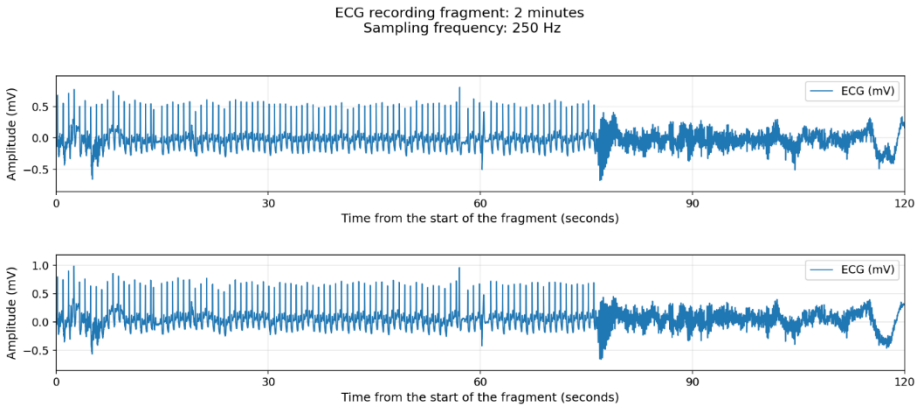

Fig. 1. A fragment of an ECG signal in two leads containing the onset of SCD, entry №30 from the MIT BIH SCD database

Pre-processing included the following steps: (1) resampling of the ECG signals to a single frequency of 360 Hz, since the records from the MIT BIH NSR and MIT BIH SCD databases had different sample rates (128 Hz and 250 Hz, respectively); (2) contour drift correction using a high-pass filter (order 4, 0.5 Hz cutoff frequency) to eliminate low-frequency artifacts associated with respiratory distortions and patient movements; (3) detection of QRS complexes and measurement of RR intervals; the Pan-Tompkins algorithm was used; (4) correction of RR intervals using a median filter that ensures the elimination of artifacts and smoothing the effect of extrasystolic beats; the values were adjusted with a deviation of more than 20% from the mean.

This processing procedure was applied to both SCD records and records of the NSR class.

3 Forecasting SCD by Entropy Characteristics

In the method of short-term forecasting of SCD, ensemble empirical mode decomposition (EEMD) was applied to 2-minute HRV signals [13]. Conventional empirical mode decomposition of EMDs is the decomposition of the signal into internal mode functions, which allows the best identification of local hidden features of the signal. The EEMD method is a development of EMD and is aimed at reducing the effect of mode mixing by adding white noise implementations to the original signal and averaging the decomposition results. The i-th component of white noise $n_i(t)$ with a speci-

fied dispersion is added to the original *x(t)* signal. After that, the sum ($x(t)+n_i(t)$) is decomposed by the EMD method. The procedure is repeated for a given number of ensembles, and the resulting mode functions are defined as the average of the corresponding components across all noise implementations. The algorithm for calculating EEMD is given in [13, 4].

As a result of EEMD application, each 2-minute interval of the HRV signal was represented as a sum of internal mode functions and a residual component. Further analysis was carried out for the first four mode functions, since they concentrate the main signal power and, therefore, the main information about the processes of heart rate regulation.

To quantify the complexity and nonlinearity of the obtained mod functions, the following entropy indices were used: fuzzy entropy (FuEn) [14] and improved entropy of multiscale permutations (IMPE) [11]. Fuzzy entropy was used to estimate the regularity of time series and was calculated based on the analysis of proximity measures between nesting vectors of dimension m at a given tolerance threshold r. The ownership function is defined as an exponential function, which ensures the continuity and stability of the score obtained. The entropy of FuEn is found as the logarithm of the ratio of the mean values of the membership function in the transition from dimension m to m+1. In this work, the values m=2, r=0.15×SD were used, where SD is the standard deviation of the data sample.

The second entropy index IMPE, in contrast to traditional entropy indicators (SampEn, PE), made it possible to quantify the dynamics of HRV on several time scales. This is important for identifying both local and extended changes in the structure of rhythm. To calculate entropy, the initial time series was subjected to a multiscale transformation procedure, which includes averaging successive samples on a given scale. For each scale, sequences of permutation patterns of a given dimension and delay were formed, after which the probability distribution of the occurrence of each pattern was calculated. Calculations were carried out for the dimension of the embedding m = 3 and the scale factor s = 2. The IMPE index was calculated as for the normalized Shannon entropy, and the use of the improved version made it possible to increase the stability of the resulting estimate [11].

As a result, for each two-minute interval, an 8-dimensional feature vector was obtained, including four values of fuzzy entropy FuEn and permutation entropy IMPE, calculated for the first four mode functions. Samples of the obtained vectors were formed separately for SCD class and NSR class signals.

The classification of fragments into SCD and NSR was carried out by the k-nearest neighbors (k-NN) method for the sequence of values of the k parameter from 1 to 5. For each of the seven time intervals, training and test samples were formed in a ratio of 75% to 25% and the Accuracy (%) Sensitivity (%) and Specificity (%) indicators were evaluated. Table 1 shows the classification performance for seven consecutive 2-minute intervals calculated at k = 1.

The best k-NN classification quality indicators were obtained for the first two-minute interval preceding the SCD at k = 1. In this case, the classification accuracy was 94.74%, sensitivity was 90%, and specificity was 100%. For subsequent intervals, as they moved away from the SCD, a decrease in the values of these indicators

was observed for all specified k. The average classification accuracy for all time intervals was 78.95%, which indicates the reliability of the proposed method for short-term forecasting of the SCD.

Table 1. Classification performance indicators (k=1) for seven consecutive 2-minute intervals preceding SCD

Beginning of the 2-minute fragment before the SCD	Accuracy, %	Sensitivity, %	Specificity, %
2 min.	94.74	90	100
4 min.	78.95	70	88.89
6 min.	84.21	80	88.89
8 min.	63.16	50	77.78
10 min.	78.95	80	77.78
12 min.	78.95	70	88.89
14 min.	63.16	70	55.56

4 Forecasting SCD Using Multiscale Variation

For the method of long-term forecasting of the SCR based on 10-minute fragments of the HRV, a description was chosen that includes the following parameters: the Multiscale variation feature, the Standard Deviation of the RR-Interval (SDRR) and the Shannon entropy.

Multiscale variation (MSP method) is a development of the method of constructing and analyzing Poincaré graphs [8]. Interest in it is due to the fact that physiological systems generate oscillations over a wide range of scales. These fluctuations can be considered as markers of the complexity of biological dynamics, which change over time, especially when pathological processes appear. As shown in [3, 8], in heart failure, there is a decrease in multiscale complex rhythm variability, which is an important diagnostic factor. The method used in this paper includes three steps: (1) construction of a set of coarse-grained time series obtained using non-overlapping moving average low-frequency filters; (2) displaying them on multiscale Poincaré graphs; (3) calculation of the feature of multiscale variation S_v [3].

A Poincaré plot for a time series is most often elliptical or comet-shaped, indicating positive correlations between successive heart rate intervals. The parameter $SD1$ used to characterize MSP is the length of the transverse axis of the ellipse (the standard deviation along the line perpendicular to the line of identity). This parameter reflects the short-term variability of HRV and is determined as:

$$SD1_s = \sqrt{variance\left(\frac{Z_s(i) - Z_s(i-1)}{\sqrt{2}}\right)}, 2 \le i \le \frac{N}{s},$$

where $Z_s(i)$ is a coarse-grained time series of scale s; variance(.) is the variance of the measured value; $SD1_s$ is the value of $SD1$ on the s-th scale; s is a scale factor equal to the width of the moving average window.

A multiscale variation of an MSP is calculated as:

$$S_v = \frac{1}{I}\sum_{s=1}^{I}(SD1_{s+1} - SD1_s),$$

where *I* correspond to the number of scale factors used.

In this paper, it was decided to use *I*=9, i.e. the total variability of HRV was estimated at eight enlarged scales. The SDRR and Shannon entropy parameters were calculated in a standard way. They complemented the multiscale HRV analysis with an estimate of time series variability at scales *s*=1.

For the obtained set of features, the Fisher Linear Discriminant Analysis (LDA) method classified two states: normal state (NSR class) and critical state (SCD class). The ability of the algorithm to predict the SCD was assessed by the overall classification accuracy indicator A (Accuracy), calculated as the proportion of correct answers of the SCD/NSR classifier.

The LDA method calculates the optimal weight vector **W** in the space of initial features when maximizing the Fisher criterion *J*, calculated in the form:

$$J(\mathbf{W}) = \frac{(m_1 - m_2)^2}{s_1^2 + s_2^2},$$

where m_1, m_2 are projections on **W** vectors of the average values of the two classes of objects; s_1^2, s_2^2 is the selective spread of projections within each class.

Criterion *J* was used to construct the separating hyperplane, as well as to assess the informative value of the features considered above. The higher the value of criterion *J*, the more significant the feature for object recognition. Table 2 shows the numerical values of criterion *J* obtained separately for each characteristic.

Table 2. Fisher's *J* test values for each feature (SCD/NSR)

Beginning of 10-minute fragment before SCD	Shannon Entropy	*SDRR*	*MSP*
10 min.	**0.82**	**0.63**	0.8
20 min.	0.71	**0.15**	**0.17**
30 min.	**0.08**	0.15	0.83
40 min.	0.06	0.3	0.95
50 min.	0.07	0.39	0.77
60 min.	0.33	0.41	**1.33**
70 min.	0.27	0.3	0.66
J_{avg}	0.33	0.33	**0.79**
J_{max}	0.82	0.63	**1.33**
J_{min}	0.08	0.15	0.17

The table shows that the highest average value of the Fisher criterion Javg is observed for the MSP trait (Javg=0.79), and the highest values of the maximum value of the Jmax criterion were shown by the MSP (Jmax=1.33) and Shannon entropy (Jmax=0.82). This indicates a greater discriminative ability of the MSP trait, which evaluates the multi-scale variation of the HRV signal.

Next, the classification of 10-minute signal fragments was carried out, the accuracy of A was estimated, the values of which are shown in Table 3. The experiments were carried out on fragments of the heart rate signal before and after filtering with a median filter. The main description included three features: SDRR, Shannon entropy, and a multiscale variation of MSP.

Table 3. Classification Accuracy A Values (SCD/NSR)

Beginning of 10-minute fragment before SCD	Before filtration, *A*, %	After filtration, *A*, %
10 min.	**95.0**	**97.5**
20 min.	**72.5**	80.0
30 min.	85.0	85.0
40 min.	77.5	**77.5**
50 min.	87.5	90.0
60 min.	87.5	85.0
70 min.	82.5	87.5
A_{avg}	84.0	**86.0**
A_{max}	95.0	**97.5**
A_{min}	72.5	77.5

As follows from the comparison of the data in Table 3, filtering slightly increased the accuracy of the classification, namely, with (A_{max}=95.0%; A_{avg} = 84.0%) – without filtration up to (A_{max} = 97.5%; A_{avg} = 86.0%) – after filtration. It should be noted that the fragments of the heart rhythm closest to the time of the occurrence of SCD (10 minutes before SCD) are recognized with the highest accuracy of 97.5%. 50-70 minutes before the SCD, the accuracy of predicting the critical condition also remains at a fairly high level (A=90.0%; 85.0%; 87.5%).

5 Discussion of the Results of the Experiments

The results of short-term prediction of SCD from 2-minute fragments of the ECG signal confirm the hypothesis that the entropy characteristics (FuEn, IMPE) contain useful information about the nonlinearity of HRV, which makes it possible to predict the development of sudden cardiac death. The use of ensemble empirical mode decomposition made it possible to adaptively isolate signal components corresponding to different time scales of cardiac regulation, which increased the informative value of subsequent entropy analysis. The average accuracy of classification in the interval of 14 minutes before the critical event was 78.95%, which is an indicator of the reliability of the method. The high specificity values given in Table 1 indicate a low probability of false positive decisions, which is important for resuscitation measures immediately before SCD. This approach can be useful in the event of a sudden onset of a pre-critical condition, when minutes decide everything - urgent defibrillation is required.

Long-term prediction of 10-minute signal fragments using the multiscale variation function was quite successful, providing an average classification accuracy of 86.0% over the interval of 70 minutes to the SCD. This indicates the importance of assessing multiscale changes in heart rhythm for the early detection of signs of possible sudden cardiac arrest. Analysis of the data in Table 3 shows the stability of the estimates of accuracy A, which remains at a fairly high level even in the early forecast areas. 70 minutes before the critical event, the accuracy of the forecast is 87.5%. In such cases, depending on the situation, therapeutic measures can be taken to help restore the normal contractile function of the heart in the early stages. Early prognosis of SCD remains the most important task of cardiac monitor monitoring.

6 Conclusion

The article presents the results of the development and experimental study of methods for short-term (14 minutes) and long-term (70 minutes) prediction of SCD based on the analysis of nonlinear and multiscale changes in heart rate. The first method uses fuzzy entropy (FuEn) and enhanced entropy of multiscale permutations (IMPE) computed for the first four mode functions obtained by the ensemble empirical mode decomposition (EEMD) method of the HRV signal. The second method, along with estimating Shannon variance and entropy, analyzes the multiscale variation (MSP) function obtained as a result of constructing multiscale Poincaré plots. The experimental studies carried out made it possible to assess the effectiveness of solving the problem of early detection of SCD. It was found that the average accuracy of classification of the two conditions (normal and sudden cardiac death) is: 79% and 86% for short-term and long-term prognosis, respectively. With the highest accuracy, at the level of 95%, the fragments closest to the time of SCD occurrence are recognized. The data obtained confirm the effectiveness of the developed methods of early warning of the development of SCD.

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