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Original Research Article

Analysis of heart rate variability as a predictor of mortality in cardiovascular patients of intensive care unit

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ABSTRACT

Objective: Dynamic changes of heart rate variability (HRV) reflect autonomic dysfunction in cardiac disease. Some studies suggest the role of HRV in predicting intensive care unit (ICU) mortality. The main object of this study was analyzing the HRV to design an algorithm to predict mortality risk.

Methods: We evaluated 80 cardiovascular ICU patients (45 males and 45 females), ranging from 45 to 70 years. Common time and frequency domain analysis, non-linear Poincaré plot and recurrence quantification analysis (RQA) were used to study the HRV in two episodes. The episodes include 8–4 h before death, and 4 h before death to death. Independent sample *t*-test was used as statistical analysis.

Results: Statistical analysis indicates that frequency domain and Poincaré parameters such as LF/HF and SD2/SD1 show changes in transition to death episode ($p < 0.05$). Moreover, L_{mean}, v_{max} and RT measures showed meaningful changes ($p < 0.01$) in closer segments to the death.

Conclusions: Analysis of physiological variables shows that there are significant differences in RQA measures in episodes close to death. These changes can be interpreted as more stability and determinism behavior of HRV in episodes close to death. RQA parameters can be used together with HRV parameters for description and prediction of mortality risk in ICU patients.

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Abbreviations: HRV, heart rate variability; ICU, intensive care unit; RQA, recurrence quantification analysis; RP, recurrence plots; REC, recurrence rate; ENTR, entropy; TT, trapping time; RT, recurrence trend.

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1. Introduction

Illness defined as a state of altered physiological function, which leads to reduction in the quality or quantity of life in patients whereas disease is an illness that has a sole and definable pathogenesis [1]. The main challenge of critical care is that the treated disorders are mostly illnesses rather than diseases. The physicians treat the specific signs and symptoms in patients, but there are lacks of information about how these signs combine as manifestations of a particular biological process. The behavior of critical illness is more complex because it arises through the interactions of the causative stimuli with multiple remedial and physiological responses.

Healthy state exhibits chaotic behaviors in physiological variables, such as heart rate. Loss of such variability means loss of complexity that accompanies critical illness [2,3]. It can be postulate that physiological systems consist of various components and small changes have significant effects on the behavior of the system [4]. Intensive care may extend the dying process in patients who do not show the possibility of retrieving an acceptable quality of life.

Experimental studies showed that large amounts of death in ICUs are receded by the prohibition or requisition of treatments. While a variety of the clinical parameters are associated with the decision to limit the treatments [5–12]. The frequencies of the prohibition or requisition of treatments and the degree of involvement of relatives in decision making are influenced by the cultural context [13,14].

Over the past decades, several studies focused on the data collected in the ICUs, especially in the field of data mining [15]. However, some reasons include lack of experts and busy physicians may lead to the elimination of important details while automated prediction methods could analyze the raw data and extract fundamental information for physicians to make a better decision [16]. Moreover, the data collected in the ICUs can be implemented to discover the relation of different types of illness, diagnosis, therapeutic and mortality risk factors.

However, it is hard to develop a clinically applicable prediction algorithm as there are several issues involved with data collection and various analysis methods. In recent years, numerous studies and methods attempted to predict the mortality risk of admitted patients in ICU [17–21]. However, these predictions are not accurate enough and still there is not any reliable tool to predict the dynamics leads to death in ICU patients.

Some research used machine learning algorithms, such as artificial neural networks and decision trees as a prediction algorithm in different critical care settings [22–28]. However, the evaluation of their performance is still under discussion. Mentioned methods include statistical analysis, machine learning algorithms and artificial neural networks require clinical inputs such as sodium, glucose, albumin, bilirubin, urine output, respiratory rates, etc. However, the issues in recordings of each input can lead to less accuracy in prediction algorithm. To the best of our knowledge, few studies considered the dynamics of HRV in death patients admitted in ICU.

In recent years, several techniques are used to describe the behaviors of complex systems such as autonomic nerve system. Heart rate variability analysis is a well-known method to measure the autonomic regulation of cardiac activity, which is mediated by the parasympathetic and sympathetic nerves, reflects the capacity for the parasympathetic inhibition of autonomic arousal and the coupling between the autonomic nervous system and the sinoatrial node. Increased HRV reflects a healthy autonomic nervous system [29–31] while decreased HRV is a marker of autonomic inflexibility [32,33] that may precede more systemic problems. There is mounted evidence that a strong association exists between low measures of HRV and severity of illness [33,29].

The support vector machine (SVM) is a relatively new classification or prediction method developed by Cortes and Vapnik in the 1990s as a result of the collaboration between the statistical and the machine learning research community. SVM tries to classify cases by finding a separating boundary called hyperplane. The main advantage of the SVM is that it can, with relative ease, overcome 'the high dimensionality problem'. Moreover, SVM has demonstrated high performance in solving classification problems in bioinformatics [34].

Beside time and frequency analyses used for evaluation of HRV, nonlinear techniques enable us to describe the behaviors of complex systems such as ANS and HRV. Recurrence plots (RP) allow visualization of phase space trajectories using two-dimensional graph. It can be used to detect transitions between different states or to find interrelations between several systems. The structures created in RP represent the basis for RQA. Recurrence analysis, which is selected method in this study, is used in special cases such as evaluation of HRV before the onset of ventricular tachycardia or prediction of epileptic seizures [35].

In this paper, we analyzed the HRV of ICU patients by means of time and frequency domain, non-linear Poincaré plot analysis and RQA measures to find whether any significant changes can be seen in death episode.

This manuscript is organized as follows: Section 2 describes the database and feature extraction methods. Section 3 illustrates obtained results. Sections 4 and 5 represent the discussion and conclusions, respectively.

2. Materials and methods

Heart rate variability (HRV) analysis is affected by sinus pause and non-sinus beats. Sinus pause is a medical condition wherein the sinoatrial node of the heart transiently ceases to generate the electrical impulses that normally stimulate the myocardial tissues to contract and thus the heart to beat. It is defined as lasting from 2.0 s to several minutes. Since the heart contains multiple pacemakers, this interruption of the cardiac cycle generally lasts only a few seconds before another part of the heart, such as the atrio-ventricular junction or the ventricles, begins pacing and restores the heart action. This condition can be detected on an electrocardiogram (ECG) as a brief period of irregular length with no electrical activity before either the sinoatrial node resumes normal pacing, or another pacemaker begins pacing. If a pacemaker other than the sinoatrial node is pacing the heart, this condition is known