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Artificial intelligence for heart rate variability analyzing with arrhythmias

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Abstract

Introduction. Existing standards of Heart Rate Variability (HRV) technology limit its use to sinus rhythm. A small number of extrasystoles is allowed, if the device used has special procedures for the detection and replacement of ectopic complexes. However, it is important to expand the indicated limits of the applicability of the HRV technology. This specially regards the cases when the HRV technology looks promising in the diagnostics, as, for example, in atrial fibrillation and atrial flutter.

Materials and Methods. All ECG measurements were performed on XAI-MEDICA® equipment and software. Processing of the obtained RR Series was carried out using the software Kubios® HRV Standard. All recommended HRV characteristics for Time-Domain, Frequency-Domain and Nonlinear were calculated.

The purpose of the work. The article presents an artificial intelligence (AI) procedure for detecting episodes of arrhythmias and reconstruction of core patient's rhythm, and demonstrates the efficacy of its use for the HRV analysis in patients with varying degrees of arrhythmias.

The results of the study. It was shown efficiency of developed artificial intelligence procedure for HRV analyzing of patients with different level of arrhythmias. These were demonstrated for Time-Domain, Frequency-Domain and Nonlinear methods. The direct inclusion into review of Arrhythmia Episodes and the use of the initial RR Series leads to a significant distortion of the results of the HRV analysis for the whole set of methods and for all considered options for arrhythmia.

Conclusion. High efficacy of operation of the procedure AI core rhythm extraction from initial RR Series for patients with arrhythmia was reported in all cases.

Key words: Hearth rate variability; Arrhythmias; Artificial intelligence.

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Introduction

The study of heart rate variability (HRV) is based on measuring (time) intervals between R-peaks (of RR-intervals) of an electrocardiogram (ECG) and plotting a rhythmogram on their basis with its subsequent analysis by various mathematical methods that are classified as Time-Domain, Frequency-Domain and Nonlinear [1, 2]. Existing standards of HRV technology limit its use to sinus rhythm [1]. A small (up to 3 per minute) number of extrasystoles are allowed, if the device used has special procedures for the detection and replacement of ectopic complexes [2]. However, it is important to expand the indicated limits of the applicability of the HRV technology. This specially regards the cases when the HRV technology looks promising in the diagnostics, as, for example, in atrial fibrillation and atrial flutter (AF) [2]. An atrial flutter is the most common arrhythmia, the development of which is associated with arrhythmogenic cardiomyopathy, disorders of the pumping function of the heart, the occurrence and/or progression of heart failure, stroke and other complications. At the same time, the mortality rate with atrial flutter is 2 times higher than with sinus rhythm. Thus, the purpose of this work is presentation and demonstration of the capabilities of an effective procedure based on artificial intelligence (AI) for detecting arrhythmia episodes and reconstruction of core patient's rhythm with following application of standard methods for HRV analysis. The newest presentation of artificial intelligence (AI)-enabled electrocardiograph (ECG) using a convolutional neural network to detect the electrocardiographic signature of atrial fibrillation present during normal sinus rhythm using standard 10-second, 12-lead ECGs was given in The Lancet [3].

Materials and Methods

All ECG measurements were performed on XAI-MEDICA® equipment using CardioLabCS® and CardioSensCS® software. The ECG signal was detected with a sampling rate of 1 kHz. Processing of the obtained RR Series was carried out using the software Kubios® HRV Standard (ver.3.x) by «Kubios Oy». All recommended HRV characteristics for Time-Domain, Frequency-Domain and Nonlinear were calculated. However, the article presents the most characteristic ones: Stress Index (SI) for Time-Domain;

Total Power (TP) for Frequency-Domain; Sample Entropy (SampEn) for Nonlinear.

Since 1950, when Alan Turing defined artificial intelligence (AI) as computer ability to achieve human-level performance in cognitive tasks [4], researchers have explored the potential applications of AI in every field of medicine [5, 6, 7]. Recently artificial intelligence techniques have sent vast waves across healthcare, even fuelling an active discussion of whether AI doctors will eventually replace human physicians in the future [8]. Specifically, in the diagnosis stage, a substantial proportion of the AI literature analyses data from diagnosis imaging (57%), genetic testing (22%), electrodiagnosis (18%) and others (3%) [8]. Despite the increasingly rich AI literature in healthcare, the research mainly concentrates around a few disease types: cancer (48%), nervous system disease (32%), cardiovascular disease (19%) and others (11%) [8]. The first three diseases are leading causes of death therefore, early diagnoses are crucial to prevent the deterioration of patients' health status and early diagnoses can be potentially achieved through improving the analysis procedures on imaging, genetic, evoked potentials (EP) or electronic medical records (EMR), which is the strength of the AI system [8].

Medical AI applications mainly fall into two major categories [8]: the first one includes machine learning (ML) techniques that analyze structured data such as imaging, genetic and EP data for attempt to cluster patients traits, or infer the probability of the disease outcomes [9]; the second category includes natural language processing (NLP) methods that extract information from unstructured data such as clinical notes/medical journals to supplement and enrich structured medical data. The NLP procedures target at turning texts to machine-readable structured data, which can then be analyzed by ML techniques [10]. Depending on whether to incorporate the outcomes, ML algorithms can be divided into two major categories: unsupervised learning and supervised learning. Unsupervised learning is well known for feature extraction, while supervised learning is suitable for predictive modeling via building some relationships between the patient traits (as input) and the outcome of interest (as output) [8].

There are two major unsupervised learning methods: principal component analysis and clustering. Clustering groups subjects with similar attributes together into clusters, without using the outcome information. On the other hand, supervised learning considers the subjects outcomes together with their traits, and goes through a certain training process to determine the best outputs associated with the inputs that are closest to the outcomes on average. The outcome can be the probability of getting a particular clinical event, the expected value of a disease level or the expected survival time. Clearly, compared with unsupervised learning, supervised learning provides more clinically relevant results; hence AI applications in healthcare most often use supervised learning. Relevant techniques include linear regression, logistic regression, naive Bayes, decision tree, nearest neighbour, random forest, discriminant analysis, support vector machine (SVM) and neural network [11]. Compare the popularity of the various supervised learning techniques in medical applications clearly shows that SVM (42%) and neural network (31%) are the most popular ones (others – 27%) [8].

The main usage of SVM is classification the subjects into two groups, – in our case: group 1 is arrhythmias episodes, group 2 – core patient RR's. There is the outcome Y_i is a classifier: $Y_i = -1$ or 1 represents whether the i-th subject is in group 1 or 2, respectively. The basic assumption is that the all RR's can be separated into two groups through a decision boundary defined on the traits X_{ij}, which can be written as:

$$a_i = \sum_{j=1}^{p} x_{ij} c_j + b,$$

where c_j is the weight putting on the j-th trait to manifest its relative importance on affecting the outcome among the others. The decision rule then follows that if $a_i > 0$, the i-th subject is classified to group 1, that is, labeling $Y_i = -1$; if $a_i < 0$, the subject is classified to group 2, that is, labeling $Y_i = 1$. The class memberships are indeterminate for the points with $a_i = 0$ [8].

The goal of training is c_j optimization that the resulting classifications agree with the outcomes as much as possible. That is, with the smallest misclassification error, the error of classifying a RR-interval into the wrong group. The best weights must allow (1) the sign of ai to be the same as Y_i so the classification is correct; and (2) $|a_i|$ to be far away from 0 so the ambiguity of the classification is minimized [8]. These can be achieved by selecting c_j that minimize a quadratic loss function [12]. Furthermore, assuming that the new RR-interval come from the same record, the resulting c_j can be applied to classify these new RRs based on their traits. An important property of SVM is that the determination of the model parameters is a convex optimization problem so the solution is always global optimum.

This SVM algorithm and program for detecting arrhythmia episodes and reconstruction of core patient's rhythm was developed at the Medical Faculty of V. N. Karazin Kharkiv National University as a result of original research by the authors and with the advisory support of the scientists of the Medical Faculty of the «Sapienza» University of Rome. The first presentation of the arrhythmia detection algorithm was performed at the Scientific Conference «eHealth» Computer Medicine'2005 in Kharkiv. Further improvement of the artificial intelligence program for detecting arrhythmia episodes and reconstruction of core patient's rhythm was carried out both by complicating of global optimization procedure and improving the training method. The data for artificial intelligence training, as well as the examples of HRV analysis presented in the article were taken from the extensive ECG measurement databases of university clinics of the V.N. Karazin Kharkiv National University and the «Sapienza» University of Rome.

Results and Discussion

1. Single Arrhythmia Episodes

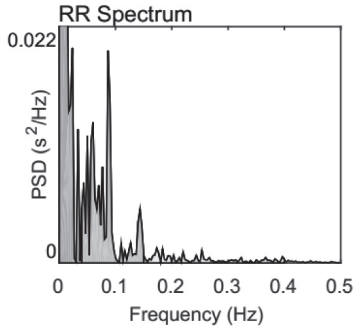
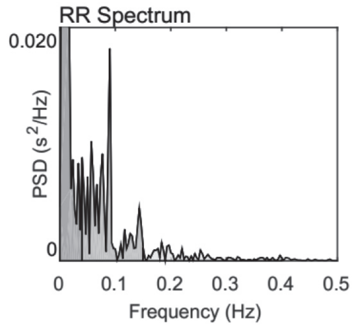
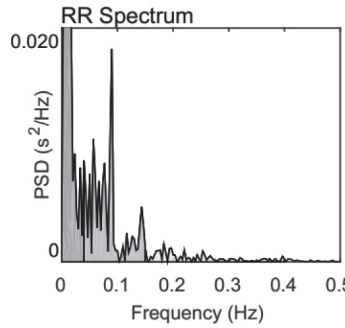
Here, cases of Single Arrhythmia Episode up to 20 s long are considered, with a total recording time of at least 6 minutes. The first two cases are the easiest to analyze, since Single Arrhythmia Episode are located directly at the beginning (Tab. 1) and at the end of the records (Tab. 2). For these cases, it is easy to isolate 5 min long recording sites free from single arrhythmia episodes. This allows to make a direct comparison of 5 min long records free from arrhythmia episodes with the results of operation of the artificial intelligence core rhythm extraction from the initial RR Series, as well as to assess the effect of Single Arrhythmia Episodes on the results of HRV analysis.

This approach allows achieving results of HRV analysis, obtained by isolating a 5 min interval free from Single Arrhythmia Episode and the AI core rhythm extraction from the initial RR Series practically coincide for all elements of the analysis: Time-Domain, Frequency-Domain and Nonlinear. At the same time, the inclusion of Single Arrhythmia Episodes into consideration substantially distorts the pattern of the HRV analysis in all cases.

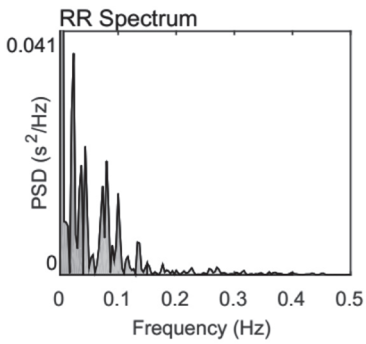
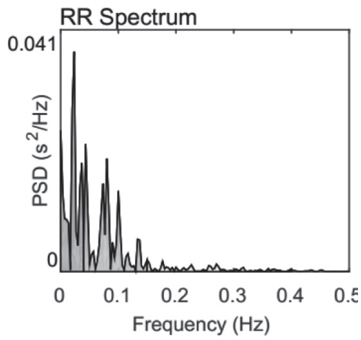
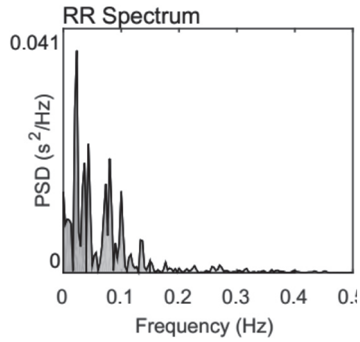
The most difficult case for the HRV analysis is when a Single Arrhythmia Episode is located in the middle of the recording interval (Tab. 3). In this case, it is impossible to isolate a 5 min interval for the analysis, and only short records with duration of about 2 minutes 30 s before and after a Single Arrhythmia Episode can be compared with the results of operation of artificial intelligence core rhythm extraction from initial RR Series.

In this case, we can see that the artificial intelligence core rhythm extraction from the initial RR Series copes well with the

Tab. 1. Single Arrhythmia Episode at the beginning of the record.

Initial RR Series with an arrhythmia episode at the beginning of the record	5-min RR Series directly after an arrhythmia episode at the beginning of the record	AI core rhythm extraction from initial RR Series
		
Stress Index = 5,2 Total Power = 2037 ms^2 Sample Entropy = 0,371	Stress Index = 16,6 Total Power = 1397 ms^2 Sample Entropy = 1,134	Stress Index = 16,2 Total Power = 1363 ms^2 Sample Entropy = 1,136

Tab. 2. Single Arrhythmia Episode at the end of the record.

Initial RR Series with an arrhythmia episode at the end of the record	5-min RR Series directly before an arrhythmia episode at the beginning of the record	AI core rhythm extraction from initial RR Series
		
Stress Index = 5,2 Total Power = 2036 ms^2 Sample Entropy = 0,348	Stress Index = 10,3 Total Power = 1183 ms^2 Sample Entropy = 0,764	Stress Index = 10,2 Total Power = 1148 ms^2 Sample Entropy = 0,760

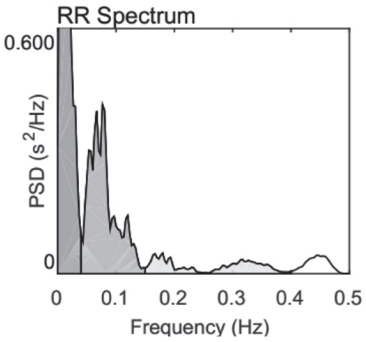
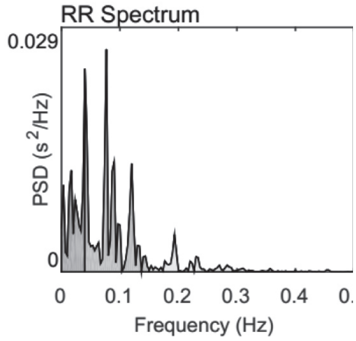
task set, and the data of HRV analysis are comparable to those observed before and after the Single Arrhythmia Episode. At the same time, the inclusion of Single Arrhythmia Episode in the HRV analysis catastrophically distorts the results of the HRV analysis, for example, increases the Total Power by a factor of 500!

2. Multiply Arrhythmia Episodes

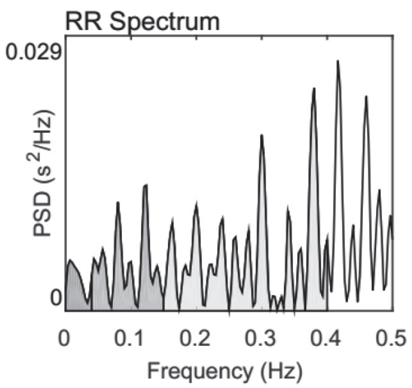
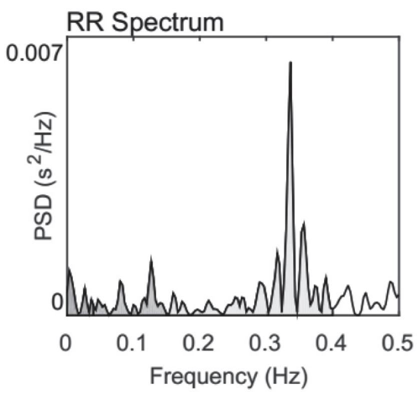
This option is represented by records of patient B. (83 years old) provided by Dr. Nicola Marchitto. Records are made at the time of admission (Tab. 4) and discharge (Tab. 5) to the clinic. Arrhythmia is characterized by recurring every 30–40 s isolated supraventricular ectopic beat or pair of beats. In this case, it is impossible to isolate the parts of the records of the length sufficient for the analysis, free from arrhythmias, and to compare them with the operation of the artificial intelligence core rhythm extraction from initial RR Series. However, it is possible to match the records of the same patient and evaluate their evolution in the analysis of the initial RR Series and those after artificial intelligence core rhythm extraction.

Although such records allow direct HRV analysis [2], in practice the results are highly distorted and do not correspond to the objective condition of the patient, as well as his age and gender. The HRV spectrum is also significantly distorted. At the same time, the analysis of HRV indicators after artificial intelligence core rhythm extraction from the initial RR Series shows their compliance with age and gender indicators, as well as highlights the positive dynamics resulting from the patient's stay in the clinic.

Tab. 3. Single Arrhythmia Episode at the middle of the record.

Initial RR Series with an arrhythmia episode at the middle of the record	2,5-min RR Series before/after an arrhythmia episode at the middle of the record	AI core rhythm extraction from initial RR Series
	**Continuously 5-min RR Series is absent**	
Stress Index = 5,5 Total Power = 52090 ms^2 Sample Entropy = 0,379	**2,5 min before an arrhythmia episode** Stress Index = 20,1 Total Power = 1641 ms^2 Sample Entropy = 0,995 **2,5 min after an arrhythmia episode** Stress Index = 16,4 Total Power = 970 ms^2 Sample Entropy = 1,076	Stress Index = 16,7 Total Power = 974 ms^2 Sample Entropy = 1,131

Tab. 4. Multiple Arrhythmia Episodes at the admission to clinic (patient B.).

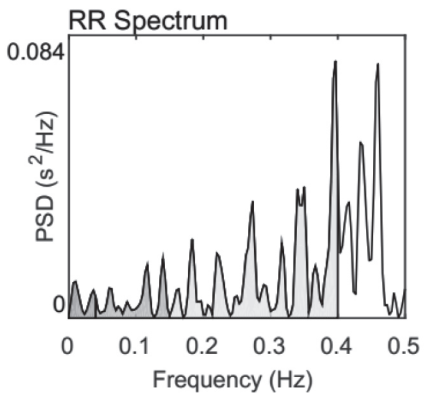
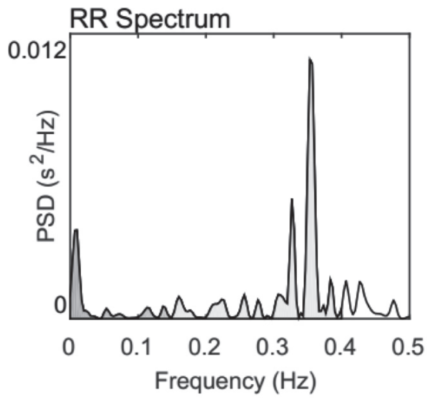
Initial RR Series with multiple arrhythmia episodes (record B.1, 10 arrhythmia episodes)	AI core rhythm extraction from initial RR Series
	
Stress Index = 7,1 Total Power = 2106 ms^2 Sample Entropy = 0,858	Stress Index = 20,5 Total Power = 199 ms^2 Sample Entropy = 1,892

3. Heavy Arrhythmia

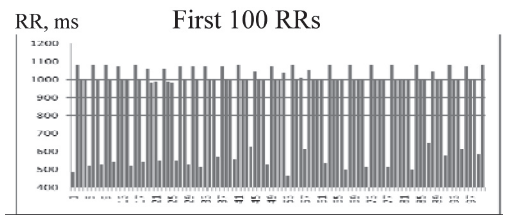
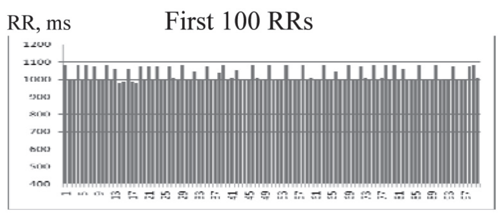
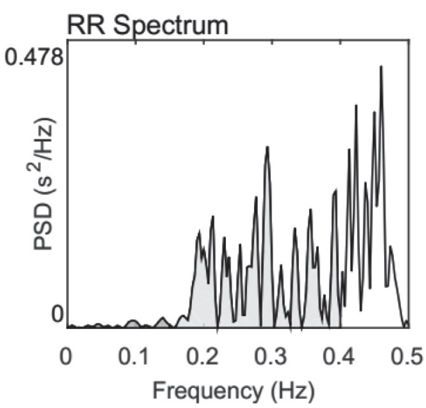
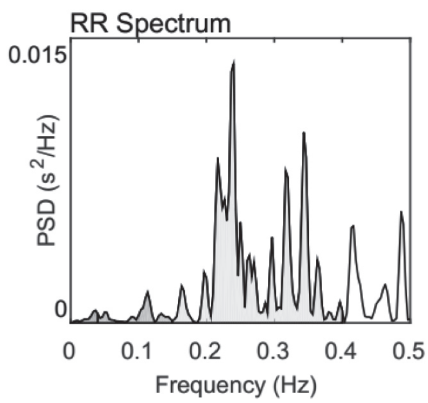
This option is represented by a record of patient C. (78 years old). Arrhythmia is characterized by recurring every 3–4 seconds isolated supraventricular ectopic beat or pair of beats. 121 arrhythmia episodes are observed in just 6 minutes of the record!

In this case, direct analysis of HRV cannot be performed, as it does not meet the standards [1] or advanced requirements [2]. We see that the analysis results are significantly distorted, for example, with an abnormally high Total Power value or the highest possible values in the spectrum outside the high frequencies range. At the same time, the artificial intelligence core rhythm extraction from

Tab. 5. Multiple Arrhythmia Episodes at the discharge from clinic (patient B.).

<table>
<tr><th>Initial RR Series with multiple arrhythmia episodes
(record B.2, 12 arrhythmia episodes)</th><th>AI core rhythm extraction from initial RR Series</th></tr>
<tr><td>
</td><td>
</td></tr>
<tr><td>Stress Index = 6,4
Total Power = 4056 ms^2
Sample Entropy = 0,514</td><td>Stress Index = 18,3
Total Power = 326 ms^2
Sample Entropy = 1,285</td></tr>
</table>

Tab. 6. Heavy Arrhythmia (patient C.).

<table>
<tr><td>
</td><td>
</td></tr>
<tr><td>
</td><td>
</td></tr>
<tr><td>Stress Index = 6,2
Total Power = 21480 ms^2
Sample Entropy = 0,517</td><td>Stress Index = 17,6
Total Power = 762 ms^2
Sample Entropy = 0,707</td></tr>
</table>

initial RR Series does an excellent result and shows the values that are adequate to the objective condition of the patient, age and gender characteristics, in the HRV analysis.

Conclusions

The article presents an artificial intelligence procedure for detecting episodes of arrhythmias and reconstruction of core patient's rhythm, and also demonstrates the efficacy of its use for the HRV analysis in patients with varying degrees of arrhythmias: Single Arrhythmia Episodes, Multiple Arrhythmia Episodes and Heavy Arrhythmia. The HRV analysis used Time-Domain, Frequency-Domain and Nonlinear methods. High efficacy of operation of the procedure artificial intelligence core rhythm extraction from initial RR Series for patients with arrhythmia was reported in all cases.

This allows:

- in the case of Single Arrhythmia Episodes, to get a match for all elements of the analysis (Time-Domain, Frequency-Domain and Nonlinear) upon isolation of a 5 min interval free from Single Arrhythmia Episodes and artificial intelligence core interval rhythm extraction from initial RR Series (Tab. 1–3);
- in the case of Multiple Arrhythmia Episodes, taking as an example the records of the same patient, made at the time of admission to the clinic (Tab. 4) and discharge from the clinic (Tab. 5), to obtain the results corresponding to the patient's objective condition, age and gender indicators, and also to highlight the positive dynamics resulting from the patient's stay in the clinic;
- in the case of Heavy Arrhythmia, to obtain the results of HRV analysis adequate to the objective condition of the patient, age and gender characteristics (Tab. 6);
- in all cases, the direct inclusion into review of Arrhythmia Episodes and the use of the initial RR Series leads to a significant distortion of the results of the HRV analysis for the whole set of methods (Time-Domain, Frequency-Domain and Nonlinear) and for all considered options for arrhythmia (Tab. 1–6).

The studies were carried out in compliance with international bioethical standards and the provisions of the Helsinki Declaration (as amended in 2013). The authors of the article, A. Martynenko, G. Raimondi, N. Marchitto, S. Ostropolets, confirm that they have no conflict of interest.

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Штучний інтелект для аналізу варіабельності серцевого ритму з аритмією

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Резюме

Вступ. Існуючі стандарти технології варіабельності серцевого ритму (ВСР) обмежують її використання синусовим ритмом. Допускається невелика кількість екстрасистол, якщо у використовуваному приладі є спеціальні процедури детекції та заміни екстрасистолічних комплексів. Однак, є важливим розширення зазначених меж застосування технології ВСР. Особливо якщо технологія ВСР виглядає перспективною в діагностиці як, наприклад, при фібриляція і тріпотінні передсердь.

Мета роботи. Метою роботи є представлення процедури штучного інтелекту для детектування епізодів аритмій і реконструкції вільної від аритмій варіабельності серцевого ритму пацієнта, а також демонстрація ефективності її використання для аналізу ВСР у пацієнтів з різним ступенем прояви аритмій.

Матеріали та методи. Всі вимірювання ЕКГ проводилися на обладнанні та із застосуванням програмного забезпечення «ХАІ Медика». Аналіз ВСР виконувався за допомогою програми Kubios® HRV Standard (ver.3.x) by «Kubios Oy». Обчислювалися всі рекомендовані характеристики ВСР для часової і частотної областей, а також нелінійний аналіз ВСР.

Результати. Була показана ефективність розробленої процедури штучного інтелекту для аналізу ВСР у пацієнтів з різними рівнями аритмій. Ефективність аналізу ВСР після реконструкції з використанням штучного інтелекту, продемонстрована для всього набору методів: в часовій і частотній областях, а також для нелінійного аналізу. Безпосереднє включення в розгляд епізодів аритмій і використання вихідних ритмограмм призводить до суттєвого спотворення результатів аналізу ВСР для всього набору методів і для всіх розглянутих варіантів аритмії.

Висновки. У всіх розглянутих випадках записів пацієнтів з аритміями відзначається висока ефективність роботи процедури штучного інтелекту для детектування епізодів і реконструкції ВСР вільного від аритмій.

Ключові слова: варіабельність серцевого ритму; аритмії; штучний інтелект.

Искусственный интеллект для анализа вариабельности сердечного ритма с аритмией

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Резюме

Введение. Существующие стандарты технологии вариабельности сердечного ритма (ВСР) ограничивают ее использование синусовым ритмом. Допускается небольшое число экстрасистол, если в используемом приборе имеются специальные процедуры детекции и замены экстрасистолических комплексов. Однако, представляется важным расширение указанных границ применимости технологии ВСР. Особенно если технология ВСР выглядит перспективной в диагностике как, например, при фибрилляции и трепетании предсердий.

Цель работы. Целью работы является представление процедуры искусственного интеллекта для детектирования эпизодов аритмий и реконструкции свободного от аритмий ВСР пациента, а также демонстрация эффективности ее использования для анализа ВСР у пациентов с различной степенью проявления аритмий.

Материалы и методы. Все измерения ЭКГ производились на оборудовании и с применением программного обеспечения «ХАИ Медика». Анализ ВСР выполнялся с помощью программы Kubios® HRV Standard (ver.3.x) by «Kubios Oy». Вычислялись все рекомендованные характеристики ВСР для временной и частотной областей, а также нелинейный анализ ВСР.

Результаты. Была показана эффективность разработанной процедуры искусственного интеллекта для анализа ВСР у пациентов с разными уровнями аритмий. Эффективность анализа ВСР после реконструкции с применением искусственного интеллекта продемонстрирована для всего набора методов: во временной и частотной областях, а также для нелинейного анализа. Непосредственное включение в рассмотрение эпизодов аритмий и использование исходных ритмограмм приводит к существенному искажению результатов анализа ВСР для всего набора методов и для всех рассмотренных вариантов аритмии.

Выводы. Во всех рассмотренных случаях записей пациентов с аритмиями отмечается высокая эффективность работы процедуры искусственного интеллекта для детектирования эпизодов и реконструкции ВСР свободного от аритмий.

Ключевые слова: вариабельность сердечного ритма; аритмии; искусственный интеллект.