Towards a Decision Support System for Disorders of the Cardiovascular System
Diagnosing and Evaluation of the Treatment Efficiency

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Abstract: The study describes a preliminary stage of the decision support system development for cardiovascular system disorders. As the clinical model of the disorders, the arterial hypertension was used. The study consisted of two steps: diagnosing of the arterial hypertension and an evaluation of the treatment efficiency during the neuro-electrostimulation application. For the diagnosing part, a clinical study was conducted involving heart rate variability signals recording while performing tilt-test functional load. Performance of different machine learning techniques and feature selection strategies in task of binary classification (healthy volunteers and patients suffering from arterial hypertension) were compared. The genetic programming feature selection and quadratic discriminant analysis classifier reached the highest classification accuracy. Best feature combinations were used to evaluate a treatment efficiency. The results indicate the potential of the proposed decision support system.

1 INTRODUCTION

When human organism is normal, the cardiovascular system function as coherent whole. One can highlight etiological factors among variety of reasons causing disorders of the cardiovascular system normal functioning. These factors mainly affect the vascular wall, changing its structure and causing disorder of the vascular tone. The vascular tone is essential for organism adaptation to the constantly changing environment(Mohr et al., 2011).

Disorders of the cardiovascular system can be subtle for a rather long time. However, abruptly they can lead to the acute impairments. According to the World Health Organization data, the heart failure and insult remain the leading causes of death in the world (Mendis et al., 2011). Therefore, the task of the early pre-clinical express diagnosing is relevant. Among the challenges in the diagnosing of the cardiovascular system disorders are the situational changes, like stress.

Thus it is apropriate to develop a objective decision support system. In present work arterial hypertension is used as a clinical model for cardiovascular system disorders. The following tasks are considered: application of the machine learning techniques for diagnosing of the arterial hypertension and evaluation of the neuro-electrostimulation treatment efficiency.

2 CLINICAL MODEL OF THE STUDY

As noted in World Health Organization (WHO, 2013) arterial hypertension is among the most frequent cardio-vascular pathologies and occurs in around 15-20% of the elderly population. The hypertension is considered to be among the most prominent factors of the heart failure, insult and coronary failure. Therefore arterial hypertension is suitable clinical model of the cardiovascular disorder.

The nature of the arterial hypertension is multifactorial. The hypertension arises as the disorder of the vascular wall tone. The vascular tone's most important feature is the arterial pressure. This is, in turn controlled by the regulatory mechanisms within the autonomic nervous system (ANS) (Kseneva et al., 2016).

The heart rate variability (HRV) is one of the indirect means of the ANS monitoring. The heart

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rate varies from beat to beat. This is caused by the constant adaptation processes, which are launched by the ANS to keep balance of the cardiovascular system. The HRV reflects the functioning of the cardiovascular system and regulatory mechanisms of the organism, as well as the ratio between sympathetic and parasympathetic departments of the ANS. Changes of the HRV features can be preemptive indicators of the health disorders (Ahmad et al., 2009).

It is worthy to stress out evaluation of the HRV features during the functional loads. This has a range of advantages as it allows minimizing the personal differences and estimating the direction of the changes. As an example of the functional load one can consider the tilt-test(Ducla-Soares et al., 2007). The tilt-test is an experimental way to test organism reaction on the crossover from the horizontal position to the vertical one (head up). Usually the rotating table is used for this load. Among the benefits of the rotating table application is increased sensitivity, improved reproducibility of conditions and results, safety and possibility to control the angle of the rotation as well as its speed. Finally it reduces the noise of the biomedical signals registration, as it prevents active body movement (Turk et al., 2010).

The organism reaction to the tilt-test is well studied for both, healthy persons and in case of the some pathologies. As studied are the systems that are activated as the response of the cardiovascular system. Therefore one can compare changes of the HRV during the tilt-test with the well-known physiological reactions of the cardiovascular system.

3 CLINICAL STUDY DESCRIPTION

The pilot clinical study was approved by the local Ethics Committee in Ural State Medical University, Yekaterinburg, Russian Federation (protocol № 8 from 15 October 2015). 68 people have participated in the study: 28 healthy people and 40 patients. All the patients were diagnosed with the II/III degree of arterial hypertension. All participants were volunteers, listened to the detailed explanation of the study stages and had signed the written participation consent. The clinical study itself took place at the Sverdlovsk Clinical Hospital of Mental Diseases for Military Veterans (Yekaterinburg, Russian Federation).

The following exclusion criteria were considered for the patients: liver, respiratory or kidney failure, diabetes of I type, diffusion collagen disease, heart failure of III-IV class (by the NYHA classification), acute impairment of cerebral circulation (6 month prior to the study), unstable angina or myocardial infarction (6 month prior to the study), permanent atrial fibrillation. Women during pregnancy and lactation period were also not included in the participation group.

Patients suffering from arterial were taking standard pharmacological therapy –angiotensin-converting-enzyme inhibitor, calcium channel blockers, and diuretics in the medium therapeutic doses. As an addition to the pharmacological therapy the methods of the physiotherapy can apply which are directed to the normalization of the autonomic regulation and improvement of the cardiovascular system functioning. The SYMPATHOCOR-01 neuro-electrostimulator (registration certificate № FCR 2007/00757) is one of such devices. The neuro-electrostimulator can control the vascular tone by means of the sympathetic nervous system correction (Petrenko et al., 2017).

During the study the electrocardiography (ECG) signals were recorded by the electroencephalograph-analyzer “Encephalan-131-03” (“Medicom-MTD”, Taganrog, Russian Federation) in the first limb lead (Kleiger et al. 2005). Afterwards the ECG signal recording the “Encephalan-131-03” software automatically derives the HRV signals.

The clinical data was recorded in three functional states involving the rotating table Lojer (Vammalan Konepaja DY, Finland). During the first state the participants were calmly lying on the exanimating table (**state F**). At the second state the tilt-test was performed – the head end of the table is lifted up to 70º from the horizontal position (**state O**). At the final state the participant returns to the horizontal position (**state K**). The duration of the signal record in each state was 300 seconds. The whole study was supervised by a physician.

4 METHODS OF DATA PROCESSING

4.1 Heart Rate Variability Features

That list of 64 HRV features in this study consisted of time-domain and frequency-domain features established by the European Society of Cardiology (Malik, 1996; Tarvainen et al., 2014) as well as relevant non-linear features (Sivanantham and

Shenbaga Devi, 2014). In our study, in addition to commonly used features, the wavelet transform features were used (Egorova et al., 2014). The detailed list of the features was described in our previous works on this topic (Vladimir Kublanov et al., 2017).

Even though getting as much features from the signal is vital, one should also consider proper feature selection to avoid using redundant data (Thangavel and Pethalakshmi, 2009). In this work HRV features in three functional states were used for the diagnosing of the arterial hypertension. In particular the classification task was solved by means of different machine learning techniques.

4.2 Machine Learning Techniques

The aim of the study was to evaluate variety of machine learning techniques which are based on the different core principles. In particular, the considered machine learning techniques included:

- Linear and Quadratic Discriminant Analysis (LDA and QDA) – are based on the finding the separating hyperplane, either linear or quadratic(Cacoullos, 2014);
- k-Nearest Neighbors (k-NN) – analyzing the similarity between the closet objects in the training subset (Peterson, 2009);
- Decision Trees (DT) – representation of the classification rule as an hierarchical sequence of Boolean blocks «if…then…» (Rokach and Maimon, 2008)
- Naïve Bayes classifier (NB) – taking into account posterior probabilities of the dataset, with additional assumptions of the independency of the features (Ng and Jordan, 2002).

As different machine learning techniques are involved one have to use similar metric to compare classification efficacy. For this, the leave-one-out cross-validation (LOOCV) metric was used. LOOCV implies using one of the observations in the dataset as the test set, while the remaining data is used as the training set. This procedure is repeated for all the observations in the dataset. Application of LOOCV procedure tends to minimize overfitting as the efficacy is estimated on the external data, previously not shown to the classifier (Zhang and Yang, 2015).

4.3 Feature Selection Strategies

The principal component analysis (PCA) procedure is commonly used to reveal internal structure of the data by converting original features into set of principal components – linearly uncorrelated features combinations. This is a dimension reduction technique, as it allows to project original features dataset into a smaller number of principal components. The first principal component is selected in a way that it has the highest possible variance of the dataset (Jolliffe, 2002).

The exhaustive search is guaranteed to find the most optimal solution, in our case combination of features with the highest classification accuracy. However there is obvious limitation – time to evaluate all the possible combinations. As example the number of 5-combinations in 64 features set extends 7 million. At the same time number of 5-combinations in 128 features set (features of two different states used simultaneously) is over 250 million. In order to reduce the search space it was suggested to consider only such combinations that are formed by features with low correlation coefficient (less than 0.25). It is acceptable restriction for HRV features, as part of them are duplicates in the mathematic aspects as well as in the biological interpretation (V. S. Kublanov et al., 2017).

The greedy search algorithm core principle is to take on each iteration the most optimal decision (Ruiz and Stützle, 2007). In our study at the first step, classification efficiency of all features is evaluated separately. The feature with the highest classification accuracy is selected. On the second step, combinations of the selected feature with the remaining ones are evaluated. The combination with the highest classification accuracy is selected. The algorithm is repeated until all features are picked on the classification accuracy decreases.

As alternative to the exhaustive search the genetic programming (GP) can be used. This heuristic approach - involves application of the Darwin's evolutionary strategies for improvement of the task's solution (Koza, 1992). In this work the binary encoding was picked. The ratio between main genetic operations (copy, crossover, mutation) was 1:2:7. The initial population was 100 randomly picked 3-combinations of the non-correlated features. Maximal number of generations – 20. Overall the evolution was repeated for 50 times (V. Kublanov et al., 2017).

5 RESULTS

5.1 Arterial Hypertension Diagnosing

In the study the classification accuracy of two groups – healthy and patients suffering from arterial hypertension was evaluated for each of the machine learning technique. Table 1 presents maximal classification accuracy, reached by each of the classifiers for different feature selection strategies. It is worthy to point out, that different datasets were considered: features of the single functional state (F, O or K), features in two functional states (F-O, F-K, O-K) and features in three functional states (F-O-K).

Table 1: Maximal Classification Accuracy, %.

Feature Selection	*LDA*	*QDA*	*3-NN*	*4-NN*	*5-NN*	*DT*	*NB*
All features	73.5	66.2	76.5	**79.4**	**79.4**	76.5	70.6
PCA	**86.8**	83.8	83.8	82.4	**86.8**	77.9	76.5
Non-correlated space	89.7	91.2	91.2	89.7	91.2	**95.6**	92.6
Greedy algorithm	94.1	**95.6**	91.2	91.2	92.6	94.1	94.1
Genetic programming	95.6	**98.5**	91.2	91.2	92.6	97.0	97.1

In case when all features were used the maximal accuracy was achieved by NN classifiers when F-O features were used. It is worthy to point out, that all highest results were obtained in those cases, when features of state O were included. However, the highest classification accuracy is capped at 79,4 in this case. Therefore it is appropriate to optimize inclusion of the features.

When PCA was used the classification accuracy was evaluated using combinations of first 10 principal components. The explained variance was not less than 0.80. Similarly, high classification accuracy was reached, when features of state O were involved. The highest results were obtained by the LDA classifier, using 9 first principles components of features O-K; by the 5-NN classifier, using first 8 components of state O.

The semi-optimal search on the non-correlated space was limited due to number of combinations. Therefore, only combinations including up to 5 features were considered. Again, the highest classification accuracy was associated with the state O (around 90 %). When features of states F and K were used separately, the results were comparable to those of PCA. Overall, the DT classifier with the following combination F *EnInterp*, O *HFn f*, K *fVLFmax*, K *SDLF*, reached the highest classification accuracy. Here *EnInterp* is the Shannon Entropy of interpolated time-series, *HFn f* – normalized spectral power of High Frequency band, evaluated by means of the Fast-Fourier transform, *VLFmax* – maximum of the Very Low Frequency spectral power, *SDLF* – standard deviation of the Low Frequency time-series derived by the wavelet transform. Even though, the accuracy improved the question was open – are these the best possible results or they can be improved by adding additional features?

As can be noted from the results in table 1, application of the greedy algorithm allows improving results of the LDA, QDA and NB, due to increase of the used features. For example, the QDA classification accuracy improved up to the 95.6% when using 6 features of the F-O. However, this approach does not guarantee the optimal solution, as results of the DT classifiers have become slightly worse. Because of that, the genetic programming paradigm was used.

Data in last row in table 1 show that application of the genetic programming allowed to improve classification accuracy for all machine learning techniques but nearest neighbors. The highest accuracy – 98.5% – was reached by the QDA classifier. Actually, four combinations reached such accuracy. They are presented in table 2. These combinations were selected for evaluation of the treatment process efficiency.

Table 2: Best Features Combinations for Arterial Hypertension Diagnosing.

Combination id	*Features*
QDA-1	F SI F EnInterp O kurtosis O ZCR O LF/HF f O RF O f(LFmax) O f(VLFmax) O LFn wt K HR K f(LFmax) K VLFmax K EnHF K EnVLF
QDA-2	F SI F EnInterp O HR O kurtosis O LF/HF f O RF O f(VLFmax) O LFn wt O EnVLF K f(LFmax) K VLFmax K HF wt K EnHF K EnVLF
QDA-3	F SI F EnInterp O kurtosis O ZCR O LF/HF f O RF O f(LFmax) O f(VLFmax) O LFn wt O EnVLF K f(LFmax) K VLFmax K EnHF K EnVLF
QDA-4	F SI F EnInterp O kurtosis O ZCR O LF/HF f O RF O f(LFmax) O f(VLFmax) O LFn wt O EnVLF K HR K f(LFmax) K VLFmax K EnHF K EnVLF

In table 2, *SI*, is the Stress Index; *ZCR* is the zero-crossing rate (in relation to the mean of the R-R time series); *LF/HF* – ratio of the Low and High Frequency spectral bands; *f*(*LFmax*) and *f*(V*LFmax*) are the frequencies, corresponding to the maximums of the Low and Very Low Frequency spectral power respectively; *LFn* normalized spectral power of High Frequency band; *HR* is Heart Rate, *EnHF* and *EnVLF* are the entropies of the High and Very Low Frequency time-series derived by the wavelet transform; RF is the respiration frequency (frequency, corresponding to the maximum of the High Frequency spectral power). The *f* affix denotes features evaluated by means of the Fast-Fourier transform; *wt* affix denotes features evaluated by means of the wavelet transform.

5.2 Evaluation of the Treatment Efficiency

In order to evaluate efficiency of the treatment process HRV features of eight patients were analyzed. Data of these patients was not previously used for the evaluations in chapter 5.1. The HRV signals were registered in accordance with the description, presented in chapter 3. Biomedical signals were registered several times: the initial registration; after a single procedure of the SYMPATHOCOR-01 device neuro-electrostimulation; after five procedures of the SYMPATHOCOR-01 device neuro-electrostimulation. The neuro-electrostimulation procedures were performed in accordance with the dynamic correction of the sympathetic nervous system methodology (Petrenko et al., 2015).

First of all, it is worthy to point out that all eight patients were classified by the combinations QDA-(1-4) as ones, suffering from arterial hypertension. This was in line with the physician diagnosing. After that dynamics of the distance, until the separating hyperplane, was analyzed. The estimates were compared with data of the arterial pressure changes.

In order to evaluate arterial pressure not less than two measurements on each arm was done. Interval between each measurement was not less than 2 minutes. If there was difference more than 5 mmHg than additional, measurement took place. The lowest measurement was taken as the final one (Mancia et al., 2013).

Table 3 presents correlation coefficients of the systolic and diastolic arterial pressure (Ads and ADd), with the distance, until the separating hyperplane, evaluated using features combinations QDA-(1-4).

Table 3: Correlation of the HRV Features Prediction with the Arterial Pressure Dynamic.

	QDA-1	QDA -2	QDA -3	QDA -4
ADs	0,714	0,700	0,708	0,707
ADd	0,798	0,779	0,795	0,795

Presented in table 3 data has high degree of significance (p-value <0,0001). The obtained results highlights agreement between HRV features and arterial pressure. The actual dynamic of the evaluations shows a tendency toward the healthy people. This was in line with physician comments and subjective feeling of the patients.

6 DISCUSSION

Development of the decision support system is the emerging area. There are works that use anthropometric data to classify arterial hypertension. However, despite having relatively high accuracy there are some limitations. As we think the most significant is limited possibility to quantify dynamics of the physiological changes during the treatment (Pytel et al., 2015).

Systems, which are based only on the data of arterial pressure, also have limitations. The single measurement of the arterial pressure does not always correctly reflect current functional state. Features of the arterial pressure can be distorted by the stress situations (including the white coat hypertension) or circadian rhythms.

Heart rate variability features are less susceptible to such changes, as they are, essentially averaged over a relatively long time interval. In addition, application of the functional load allows to '*direct*' functional changes. Lastly the proposed procedure allows preventing stress situations, as it is in fact, 15 minutes of lying.

Within the study, it was multiple times noted that features of the state O (tilt-test), have the higher classification possibilities. This fact confirms feasibility of such functional load application.

In present works, pilot results of the neuro-electrostimulation device SYMPATHOCOR-01 application were obtained. The device can be used as the physiotherapeutic method for treatment of the arterial hypertension. However, in order to accurately evaluate applicability of the device one has to conduct full-scale clinical double-blind studies. This is not within the tasks of present study.

The limitation of the present study can be relatively small clinical data sample. However, preliminary results of the study on data, not used for the classifiers training, demonstrate potential of the proposed system. In future studies, our research group is interested in conductance of the additional studies on a bigger data sample. Moreover it is possible to improve results by means of bagging, boosting and stacking as it was shown in .

7 CONCLUSIONS

The present work described initial steps of the decision support system development for cardiovascular system disorders. The arterial hypertension was used as the clinical model.

At first, the diagnosing accuracy was evaluated. For that heart rate variability signal were registered during the tilt-test functional load. The heart rate variability is one of the indirect means to assess functioning of the autonomic nervous system, which, in turn, is essential in the pathogenesis of the arterial hypertension

Possibilities of different machine learning techniques were analyzed, in particular linear and quadratic discriminant analysis, k-nearest neighbors, decision trees and Naïve Bayes classifier. Various feature selection techniques were tested: principal component analysis, semi-optimal search on non-correlated features space, greedy algorithm and genetic programming. It was noted that the genetic programming feature selection and quadratic discriminant analysis classifier reached the highest classification accuracy.

Best feature combinations were used to evaluate treatment efficiency during the neuro-electrostimulation by the SYMPATHOCOR-01 device. The results highlight significant agreement of the heart rate variability with the arterial pressure data.

The accumulated during the present study groundwork will become a basis for a decision support system for disorders of the cardiovascular system.

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