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Multi-stage classification of congestive heart failure based on short-term heart rate variability

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ABSTRACT

In this study, we propose an automatic system to diagnose congestive heart failure using short-term heart rate variability analysis. The system involves a multi-stage classifier. The features of heart rate variability are computed from time-domain and frequency-domain measures through power spectral density estimations of different transform methods. Nonlinear heart rate variability measures are also calculated by using Poincare plot, symbolic dynamics, detrended fluctuation analysis, and sample entropy. Different combinations of heart rate variability features are selected according to their statistical significance levels and then applied to the classifier. The first two stages of the classifier consist of simple perceptron classifiers that are trained by a genetic algorithm. Five different classifiers, namely k-nearest neighbors, linear discriminant analyses, multilayer perceptron, support vector machines, and radial basis function artificial neuronal network, are tested for the third stage. The proposed system results in a classification performance of an accuracy of 98.8%, specificity of 98.1%, and sensitivity of 100%. We show that our approach provides an effective and computationally efficient tool to automatically diagnose congestive heart failure patients.

1. Introduction

The degradation in the pumping function of a heart is named as heart failure [1,2]. Many organs gradually lose their proper function since they cannot receive enough oxygen and nutrients due to this disorder. Congestive heart failure (CHF) is amongst the main culprits in this series of events [3]. Symptoms of CHF occur depending on its severity. In early stages, patients may not notice this condition. In mild CHF, the symptoms arise when the patient becomes more active than daily routine, but in severe heart failure, the symptoms persist even at rest. In addition, patients face severe symptoms that gradually become worse with age. McMurray and Pfeffer [4] reported that the incidence of CHF is exploded in the adults by approximately 1–2% while the rate is 6–10% in people over 65 years old. Moreover, the incidence of CHF is also closely related to the gender.

Some of typical signs for the diagnosis of CHF are relative among doctors and these signs may be invisible. Although an expert cardiologist can diagnose the CHF easily in practise, daily physicians may be confused in the diagnosis. In addition, some of CHF symptoms are very similar to other medical conditions among elderly patients, which results in a delay in the treatment [5]. After CHF is suspected, further tests are applied to the subjects. These tests involve the echo-cardiogram, heart catheterization, chest X-ray, chest CT scan, cardiac MRI, nuclear heart scans, and ECG [6]. ECG is the prior technique to diagnose a cardiac-related disease. However, its use is limited to detect abnormal beats as a sign of CHF in general [7].

The heart rate variability (HRV) analysis, conventionally based on the inter-beat intervals of two contiguous ECG peaks, has been widely used for both the diagnosis [8–19] and the prognosis [20–23] to discriminate the CHF for a long time. Many classifiers have been investigated in these studies. Among these studies, Asyali [8] studied the long-term HRV data to distinguish CHF patients from healthy subjects. He used two classifiers of linear discriminant analysis and Bayesian classifier with only nine common time-domain and classical FFT-based frequency-domain HRV measures. In another study, Isler and Kuntalp [9] studied the short-term HRV data to discriminate the CHF patients. They applied standard time- and frequency-domain HRV measures by combining Wavelet Entropy to the input of the Nearest Neighbor classifier. They also investigated the effect of a new preprocessing step of the heart rate normalization in another study [10]. Other classifiers have also been used in the literature. Linear kernel based Support Vector Machines (SVM) with standard time-doamin HRV fea-

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tures and frequency-domain features based on the bispectral analysis has been investigated by Yu and Lee [11]. Jovic and Bogunovic [12] have applied conventional time-domain features with nonlinear measures to classifiers of SVM, MLP, C4.5, and Bayesian in ECG beat classification. Pecchia et al. [13] used non-standard features and CART classifier to diagnose CHF. Narin et al. [14] used conventional time-domain features, frequency-domain measures using FFT, several nonlinear parameters, and extra frequency-domain measures based on wavelet packet transform. They investigated the performance of the SVM algorithm with 27 features chosen by the backward elimination method. Altan et al. [15] studied on the diagnosis of CHF patients from normal subjects using the Hilbert-Huang Transform on HRV signal. They used the MLP structure of artificial neural networks. In another study, Acharya et al. [16] used Empirical Mode Decomposition (EMD) on HRV signals to distinguish CHF patients from normal subjects via probabilistic neural networks and SVM. Similarly, Meillo et al. [17] used the CART classifier on HRV signals to determine the patients with CHF. Li et al. [18] used convolutional neural network (CNN) based deep learning classifier with measures calculated by distance distribution matrix method from 300-sample HRV signals. Kumar et al. [19] used Fuzzy and Permutation Entropy measures from 500-sample HRV signals. They applied 20 features to the least sqaures SVM (LS-SVM) classifier.

Most of these studies used one-stage classification procedures. Nonetheless, some studies related to heartbeat classification from ECG signals [24] and epileptiform spike detection from EEG signals [25,26] have used multi-stage structures. A recent study showed that a multi-stage model provides powerful outcomes to predict the life expectancy for CHF patients [20].

In this study, we consider a multi-stage classifier system to maximize the diagnosis accuracy of CHF based on short-term HRV. For this purpose, we used open databases from Physionet, Normal Sinus Rhythm Database (NSR2DB) and Congestive Heart Failure Rhythm Database (CHF2DB). These databases contain 24-h heart rate data from 54 normal subjects and 29 CHF patients. HRV features for only the first 5-min data segments are calculated from time-domain, frequency-domain and nonlinear features. Different combinations of the HRV features are selected by statistical evidence levels of 1%, 2%, 5%, 10%, and 20% and then applied to the proposed classifier structure. The first two stages are simple perceptrons that are trained by genetic algorithm. In these stages, the obvious decisions of healthy and patient are determined. If the diagnosis is not given in these stages, the data is applied to the final stage. Five different classifiers of k- nearest neighbors, linear discriminant analyses, multilayer perceptron, support vector machines, and radial basis function artificial neaural network are involved in the third stage. Then, the classifier performances are computed by the leave-one out cross-validation method through the whole three-stage classifier system.

2. Materials and methods

2.1. Data

In this study, we used two databases of Normal Sinus Rhythm Database (NSR2DB) and Congestive Heart Failure Rhythm Database (CHF2DB), which are free and online available to all researchers on Physionet website [27]. The NSR2DB contains heart beat intervals datasets from 54 normal subjects and the CHF2DB contains intervals datasets from 29 patients with CHF. The original ECG signals are digitized by the sampling rate of 128 Hz. It is obvious that the proper sampling rate is necessary to detect the precise peaks in ECG. Although the offered optimal sampling range is 250–500 Hz or higher, lower sampling rate (equal to or greater than 100 Hz) has been reported for a considerable result [28]. Therefore, we used these databases confidentially in this study.

2.2. Data segmentation

Standard HRV analysis can be conducted using both HRV data of short-term (5 min) and long-term (24 h) [28]. The short-term is preferred if the fast diagnosis is desired. The task force offers using artifact-free data segments. If it is not possible to find an ectopic-free data segment, the ectopic removal process is offered before calculating HRV features [28]. Therefore, throughout all HRV data, 5-min data segments having the minimum number of ectopic beats are traced for each subjects.

2.3. Ectopic removal

The use of only regular heartbeats, which are not affected by the previous or following beats, is offered in HRV analysis. Therefore, these abnormal beats and their neighbors are excluded from the data in general [29]. Although Langley and colleagues offer an algorithm to identify possible ectopic beats [30], it is not necessary in this study since ectopic beats are already annotated. We simply removed these beats from the data.

2.4. Resampling

Although the HRV data has unequally-sampled nature, some well-known feature extraction methods require evenly-sampled data. Therefore, a resampling (interpolation) method must be utilized to the data to make it evenly-sampled one. The task force defines the upper frequency of the HRV data is 0.5 Hz [28]. The interpolation of the HRV data with the rate of 1–10 Hz is offered in the literature [29]. We preferred the resampling rate of 4 Hz in this study.

There are many resampling methods already defined in the literature. Among them, the Cubic Spline method is possibly the most used one [31]. In addition, Clifford and Tarassenko [32] compared interpolation methods by investigating effects on HRV analysis. They offered the Cubic Spline method that gives the minimum interference to frequency-domain HRV measures. Therefore, we applied the Cubic Spline resampling method defined in detail in [33,34] with the sampling rate of 4 Hz to HRV data.

2.5. Detrending

Although HRV data has also some trends that make the data non-stationary, some of feature extraction methods require at least weakly stationary data. A number of methods have been developed to overcome this issue in the literature including choosing shorter analytical epochs, eliminating or filtering slowly-changing trends and using techniques that are robust to non-stationarities such as the Wavelet transform. In this study, we preferred a widely-used robust detrending method, which is called as Smoothness Priors. It has been widely used in applications of the HRV data among other methods [35]. The stationary part of the HRV data can be found as follows:

$$x_{\text{stationary}} = x - H\theta_{\lambda} = \left(I - \left(I + \lambda D_2^T D_2\right)^{-1}\right)x \tag{1}$$

where x is HRV data, D_2 is the second order difference operator, λ is the regulatory parameter ($\lambda = 1000$), and $x_{\text{stationary}}$ is the detrended stationary signal. Tarvainen and collegeaous explained the method in detail and presented its Matlab code in [35].

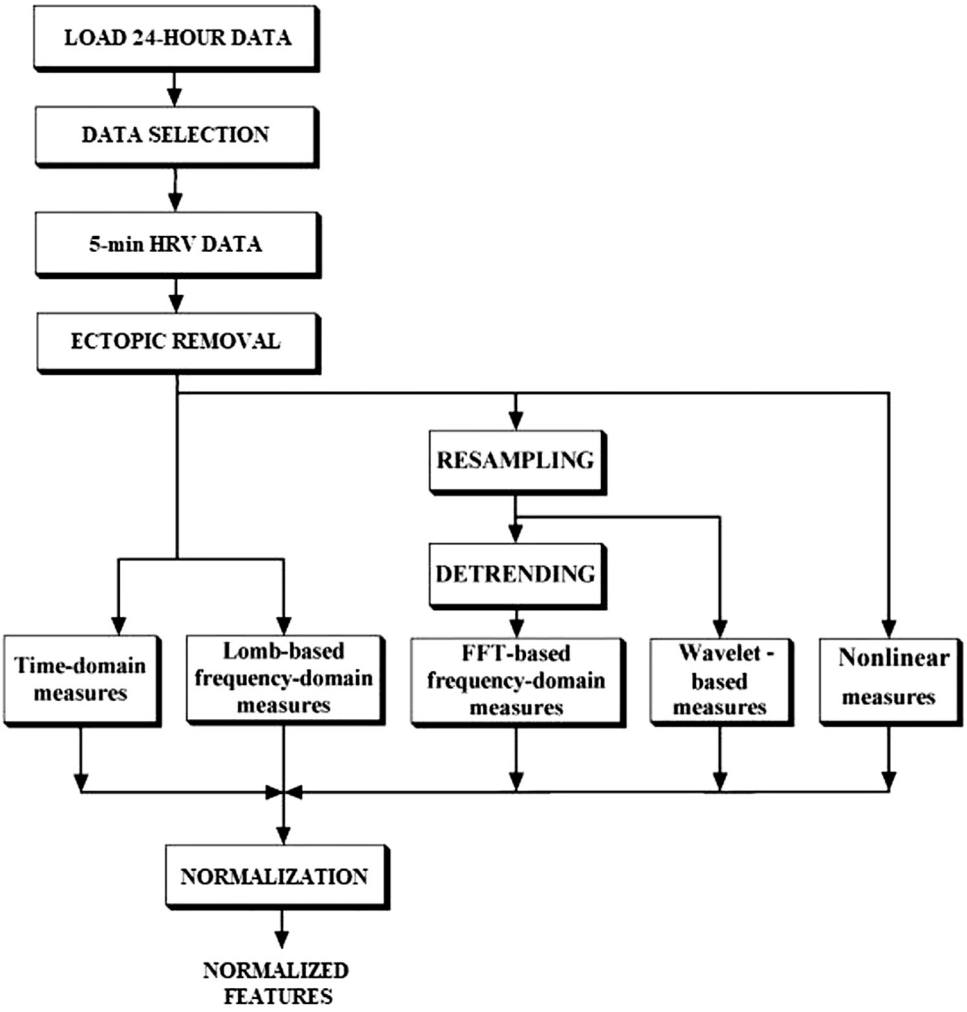

Fig. 1. The block diagram of the feature extraction stages from the 5-min HRV data through time and frequency domain measures and nonlinear measures. Ectopic removal, resampling or detrending processes are applied before the feature selection depending on the feature extraction method.

2.6. Feature extraction

McMurray and Pfeffer [4] have reported the importance of age and gender to differentiate the CHF patients out of normal subjects. Because the gender information for all records is not available in these databases, the gender is excluded from the study but the age information is included as a feature in this study. HRV features can be obtained through time-domain, frequency-domain, and nonlinear measurements [36]. All of the features, which are obtained from the 5-min ectopic-free data segments, are defined briefly in this section. All methods mentioned in this section similar given in [14] are visualized together with the relations to preprocessing methods in the Fig. 1.

2.6.1. The HRV time-domain features

The time-domain features are computed from the heart beat intervals data. These features are Mean (mean of all RR intervals), SDNN (standard deviation of all RR intervals), RMSSD (root means square of differences between adjacent NN intervals), and SDSD (standard deviation of differences between adjacent NN intervals) [9,10,14,36].

2.6.2. The HRV frequency-domain features

These features are obtained from the power spectral density (PSD) estimation from the HRV data. There are some methods to estimate PSD that require some preprocessing steps. In both the Fast Fourier Transform (FFT) and the Wavelet Transform algorithms, the interpolation step is necessary to convert HRV data to an equally sampled data [36,37]. In addition, the FFT also requires the stationary, which requires an extra detrending procedure [32].

The spectrum of the short-term HRV analysis consists of components from three main frequency bands: very-low-frequency (VLF), low-frequency (LF), and high-frequency (HF) bands [28]. Frequency features from the power spectrum are absolute values of power (power very-low-frequency (PVLF), power low-frequency (PLF), and power high-frequency (PHF) components). Normalized versions of PLF and PHF (NLF and NHF, respectively) are also used in the literature, which interpret the relative value of each power component in proportion to the total power except the VLF component. Although a recent study contradicts with the hypothesis on the ratio of the LF to HF components [38], it has been one of conventional HRV measures [39]. That is the reason why the RATIO is also included in this study. We used the total power and these six features as frequency-domain HRV features. We calculated the frequency-domain HRV features by using FFT-based periodogram,

LS-based periodogram, Wavelet energies, Wavelet variances, and Wavelet entropies [32,40–47].

2.6.3. Nonlinear features of HRV

Nonlinear characteristics are inherently involved in the HRV. In order to obtain the HRV nonlinear features, we used Poincare Plot [48–52], Detrended Fluctuation Analysis [53], Symbolic Dynamics [54–64] and Sample Entropy [65].

2.7. Feature normalization

The features may have different ranges. In order to prevent biases on the classification, input feature values should be normalized [9,10]. When the feature normalization is performed, the unit and magnitude differences between features will be eliminated, which is very important for many pattern recognition methods [66]. In this context, we used the Min-Max normalization, where all features are scaled into the interval of [0,1] defined as follows:

$$f_{i,j} = \frac{f_{i,j} - \min f_i}{\max f_i - \min f_i} \tag{2}$$

where $f_{i,j}$ is the Jth trial of the ith feature.

2.8. Feature selection

A classifier may not result in the best performance by using the all features in many cases [66]. Therefore, the feature selection is of great importance to obtain an optimal performance for the classifier. We used the independent t-test to judge which features show the difference between patients and normal subjects [68]. For this aim, we obtained p-values indicating statistical significances through the IBM SPSS Statistics 22 software package. We repeated the process for six different input combinations: all features, selected features using different statistical significance values of 1%, 2%, 5%, 10%, and 20% to determine whether the feature selection has a positive contribution or not in the performance of classifiers.

2.9. Classification algorithms

In this study, we implemented a three-stage classifier system. The perceptron algorithm is constructed in the first two stages because of its simplicity and lower computational complexity. Genetic Algorithm (GA) is used to find the best weight and threshold values of the perceptron to obtain the highest classification accuracies. In the last stage, we used five different classification algorithms including k-Nearest Neighbors (KNN), Linear Discriminant Analysis (LDA), Multi-Layer Perceptron (MLP), Linear Support Vector Machines (SVM), and Radial Basis Functions Artificial Neural Network (RBF). Different combinations of related parameters for each classifier have also been checked over.

2.10. The classifier performance

Data are splitted into the train and the test segments to obtain the classifier performance. In this study, one of samples is utilized for test while other samples are handled for train classifiers. This was iterated until each sample was handled for testing, which is called as the leave-one-out method [33]. True positive (TP), true negative (TN), false positive (FP) and false negative (FN) values are computed. True means correct classification, false means misclassification, positive means patient, and negative means normal subject.

After computing these values, the performance of the classifier is calculated as follows [67]:

$$SEN = \frac{TP}{TP + FN} \tag{3}$$

$$SPE = \frac{TN}{TN + FP} \tag{4}$$

$$ACC = \frac{TP + TN}{TP + FN + FP + TN} \tag{5}$$

where *SEN, SPE* and *ACC* denote sensitivity, specificity, and accuracy, respectively.

3. Results and discussion

In this study, we investigated which feature and classifier combinations can give the maximum discrimination accuracy related to the CHF. NSR2DB (which contains inter-beat series data from 54 normal subjects) and CHF2DB (which contains inter-beat series data from 29 CHF patients) databases obtained from Physionet website are used to design an automatic CHF diagnosis system. We calculate time-domain features (4 features), frequency-domain features (7 features from FFT, 7 features from Lomb-Scargle, 8 energy features from the Wavelet transform, 7 variance features from the Wavelet transform, 8 entropy features from the Wavelet transform), nonlinear features (4 from Poincare plot, 10 from symbolic dynamics, 1 from DFA, 1 from approximate entropy, and 1 from sample entropy).

We applied the independent sample t-test to obtain statistically significant HRV features. Among all HRV measures, we found the numbers of features which show the statistical significance as 22 in the level of 1%, 26 in the level of 2%, 34 in the level of 5%, 39 in the level of 10%, 48 in the level of 20%.

In designing the multi-stage classifier, we investigated the performance of two approaches. The first approach is the Normal-first case as shown in Fig. 2(a). At the first stage of this approach, all the training data is applied to the perceptron to discriminate Normal Subjects from the patients with the sensitivity of 100%. This quarantees all the classifier decisions are true if the classifier's output is "Normal". On the other hand, the classifier decision is suspicious if the classifier's output is "CHF" and the data should be investigated by the next stage. The second stage is designed to discriminate the patients from normal subjects with the sensitivity of 100%. This also quarantees all the classifier decisions are true if the classifier's output is "CHF". On the other hand, the classifier decision is suspicious if the classifier's output is "Normal" and the data should be investigated through the final stage. The classifier algorithm used in the first two stages is perceptron and the classifiers are trained by GA. At the last stage, the data is applied to the inputs of a more complex classifier algorithm. Five different classifier algorithms are tested: KNN ($k = 1, 3, 5, 7, 9, 11, 13$), LDA, MLP (the number of neurons in the hidden layer from 1 to 50), linear SVM (margin from 0.05 to 3.0 of 0.05 increments), and RBF ANN (the distribution parameter from 0.1 to 3.0 of 0.1 increments).

The second approach is simply switched the order of the first two stages from the first approach as shown in Fig. 2(b). This approach is the CHF-first case. All the procedure mentioned above was repeated for this approach.

In sum, the investigation was repeated 2 (Normal-first and CHF-first cases) × 6 (using selected features of 5 different statistical significance levels and using all features) × 148 (7 for KNN, 2 for LDA, 50 for MLP, 60 for SVM, 30 for RBF) × 83 (leave-one-out cross-validation) = 294,816 times and the classifier performances were computed. The performances of the three-stage system were evaluated together and summarized in Table 1, where the NORMAL-first approach is indicated by "-N" and the CHF-first approach is indicated by "-C" in the algorithm column. The values of 1%, 2%, 5%, 10% and 20% are statistical significance levels used to select features and ALL means all features were used without the feature selection. We found that there are eight different combina-

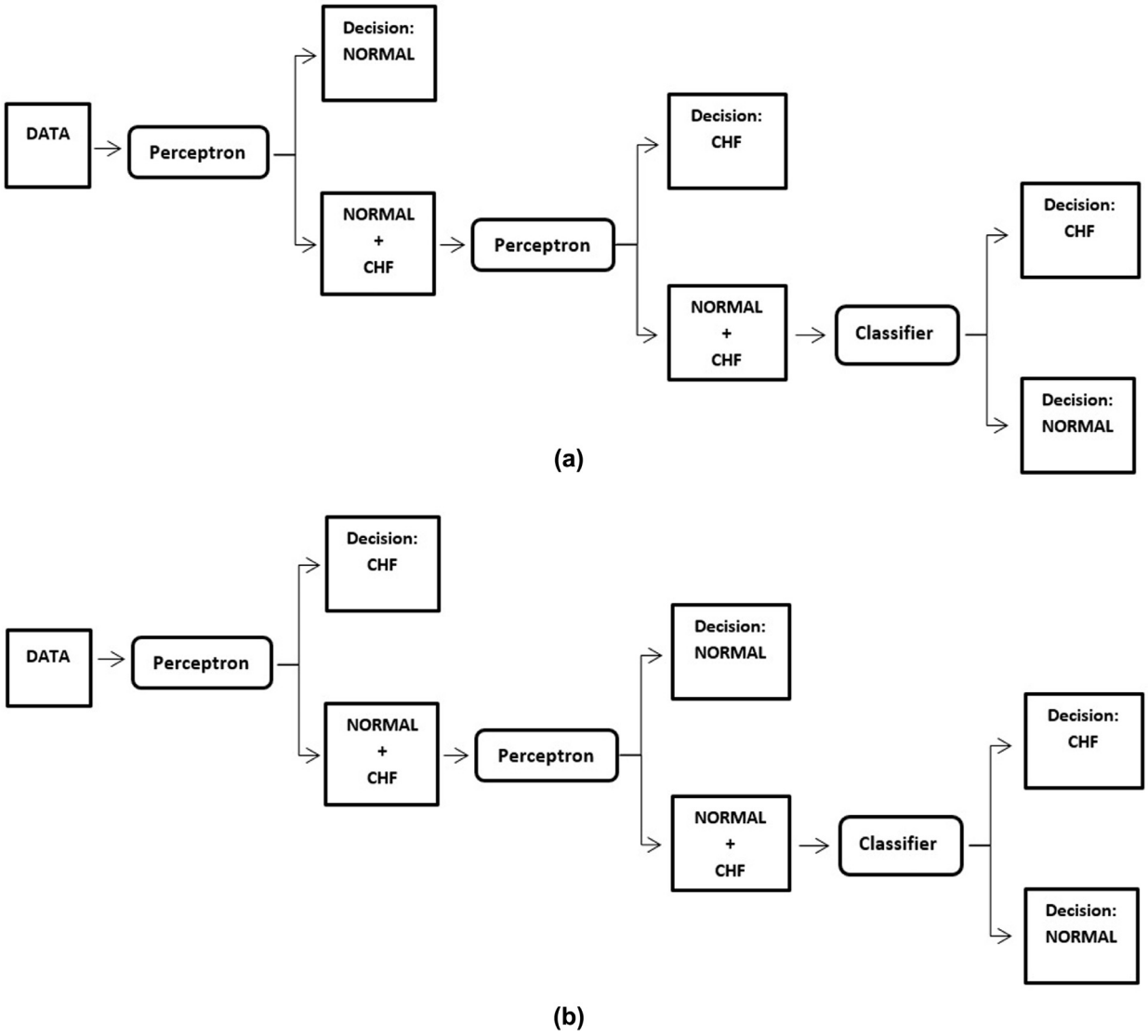

Fig. 2. The block diagram of the proposed system for (a) Normal-first and (b) CHF-first approaches. Normal subjects are perfectly classified in the normal-first approach, or vice versa. Obvious diagnoses are determined in the first two stages. If the diagnostic decision is not given in the first and the second stages, final decision is given at the last stage.

tions that give the maximum accuracy of 98.8% as shown in bold in Table 1 with the number of features of 34, 39, 48 and 59. However, since the minimum number of features is also desired, we can reach at two optimal configurations for the maximal accuracies: MLP-N and RBF ANN-N with 34 features. In the both configurations, algorithms use 34 statistically significant features of 5%. The first stage of the system involves the "Normal-first" approach while the final stage is either MLP or RBF. On the other hand, since MLP requires less computational burden than the RBF, we suggested that the Normal-first multi-stage classifier approach with the final classifier is MLP and the selected HRV features by 5% significance level yields the best performance for discriminating the CHF.

We showed the current literature to discriminate CHF patients from normal subjects using short-term HRV data in Table 2. These studies also include feature selection methods for their investigation. Li et al. [18] used a deep learning algorithm of CNN classifier and obtained a relatively lower classification performance of an accuracy of 81.9%. Isler and Kuntalp [9] used KNN classifier with a classification performance of an accuracy of 89.2%, specificity of 94.4%, and sensitivity of 79.3%. Narin et al. [14] used SVM classifier and achieved a classification performance of an accuracy of 91.5%, specificity of 96.2%, and sensitivity of 82.7%. Isler and Kuntalp [10] revisited the issue to improve the classification performance by investigating the impact of an extra preprocessing step so-called heart rate normalization in KNN classifier, reaching at a classification performance of an accuracy of 93.4%, specificity of 100%, and sensitivity of 82.7%. Pecchia et al. [13] used CART algorithm and obtained a classification performance of an accuracy of 96.4%, specificity of 100%, and sensitivity of 89.7%. Altan et al. [15] reconsidered MLP classifier and reached at a classification performance of an accuracy of 97.8%, specificity of 93.7%, and sensitivity of 100%. Kumar et al. [19] used LS-SVM classifier and achieved a classification performance of an accuracy of 98.2%, specificity of 98.3%, and sensitivity of 98.1%. Consequently, comparative results indicate that the proposed multi-stage classifier structure in this study results in better classification performance than the similar

Table 1
The system performance obtained by testing the remaining individuals from stage-1 stage -2 within whole data for selected features data by using independent *t*-test for the 1%, 2%, 5%, 10% and 20% significance values. NF is the number of features, and N.A. means that the value is not available.

Algorithm	1%			2%			5%			10%			20%			ALL		
	SEN (%)	SPE (%)	ACC (%)	SEN (%)	SPE (%)	ACC (%)	SEN (%)	SPE (%)	ACC (%)	SEN (%)	SPE (%)	ACC (%)	SEN (%)	SPE (%)	ACC (%)	SEN (%)	SPE (%)	ACC (%)
LDA-N	75.8	96.2	89.1	72.4	100	90.3	82.7	100	93.9	82.7	100	93.9	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
LDA-C	82.7	79.6	80.7	93.1	86.1	87.9	93.1	96.2	95.1	96.5	88.8	91.5	100	87.0	91.5	100	85.1	90.3
MLP-N	82.7	98.1	92.7	82.7	100	93.9	**100**	**98.1**	**98.8**	**100**	**98.1**	**98.8**	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
MLP-C	75.8	98.1	90.3	86.2	100	95.1	93.1	100	97.5	93.1	100	97.5	**96.5**	**100**	**98.8**	**96.5**	**100**	**98.8**
KNN-N	75.8	96.2	89.1	75.8	100	91.5	79.3	100	92.7	79.3	100	92.7	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
KNN-C	86.2	72.2	77.1	93.1	74.0	80.7	89.6	98.1	95.1	93.1	94.4	93.9	96.5	92.5	93.7	96.5	94.4	95.1
Linear SVM-N	68.9	98.1	87.9	72.4	100	90.3	79.3	100	92.7	79.3	100	92.7	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Linear SVM-C	82.7	70.3	74.6	93.1	51.8	66.2	93.1	88.8	90.3	93.1	90.7	91.5	100	85.1	90.3	100	85.1	90.3
RBF ANN-N	75.8	96.2	89.1	72.4	100	90.3	**100**	**98.1**	**98.8**	**100**	**98.1**	**98.8**	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
RBF ANN-C	72.4	94.4	86.7	96.5	64.8	75.9	89.6	100	96.3	93.1	100	97.5	**96.5**	**100**	**98.8**	**96.5**	**100**	**98.8**
NF	22			26			34			39			48			59		

Table 2
Relevant studies dealing with classification of CHF from 5-min HRV series. HRN means that the heart rate normalization is applied before the classification.

Authors	Method	SEN (%)	SPE (%)	ACC (%)
Li et al. [18]	CNN	–	–	81.9
Isler and Kuntalp [9]	KNN	79.3	94.4	89.2
Narin et al. [14]	SVM	82.7	96.2	91.5
Isler and Kuntalp [10]	KNN with HRN	82.7	100	93.4
Pecchia et al. [13]	CART	89.7	100	96.4
Altan et al. [15]	MLP	100	93.7	97.8
Kumar et al. [19]	LS-SVM	98.1	98.3	98.2
This study	**3-Stage Classifier**	**100**	**98.1**	**98.8**

studies in literature. Therefore, we may suggest that our approach provide better tool to predict CHF events.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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