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Multiple Time Scales Analysis for Identifying Congestive Heart Failure Based on Heart Rate Variability

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ABSTRACT It is well known that electrocardiogram heartbeats are substantial for cardiac disease diagnosis. In this paper, the best time scale was investigated to recognize congestive heart failure (CHF) based on heart rate variability (HRV) measures. The classifications were performed on seven different time scales with a support vector machine classifier. Nine HRV measures, including three time-domain measures, three frequency-domain measures, and three nonlinear-domain measures, were taken as feature vectors for classifier on each time scale. A total of 83 subjects with RR intervals were analyzed, of which 54 cases were normal and 29 patients were suffering from CHF in PhysioNet databases. The classifying results using tenfold cross-validation method achieved the best performance of a sensitivity, specificity, and accuracy of 86.7%, 98.3%, and 94.4%, respectively, on the 2-h time scale. Moreover, by introducing only three nonstandard HRV features extracted from the trends of HRV measures on time scales, it achieved a better performance of a sensitivity of 93.3%, specificity of 98.3%, and an accuracy of 96.7%. The impressive performance of discrimination power on the 2-h time scale and the trends of HRV measures on time scales indicate that multiple time scales play significant roles in detecting CHF and can be valuable in expressing useful knowledge in medicine.

INDEX TERMS Electrocardiogram (ECG), heart rate variability (HRV), congestive heart failure (CHF), multiple time scales, support vector machine (SVM).

I. INTRODUCTION

Congestive heart failure (CHF) is one of cardiac disease as a result of the inability of heart to deliver enough blood to the body and it may be asymptomatic in its early stages [1]. There is no single definitive diagnosis of heart failure, but some diagnosis combinations including chest radiography, echocardiography and electrocardiography (ECG) are effective for diagnosis the congestive heart failure [1], [2]. Heart rate variability (HRV) analysis is considered as a broadly used tool for studying the difference between the healthy and cardiovascular diseases in ECG signals [3]. Task Force of the European Society of Cardiology the North American Society of Pacing Electrophysiology published standards in HRV analysis in 1996 [4]. In the last two decades, numerous studies have focused on diagnosis purpose with HRV measures, especially in detecting patients with CHF from normal sinus rhythms (NSR) subjects [5]–[16]. Depressed HRV measures such as standard deviation of NN intervals (SDNN) in time domain or low frequency power (LF) in frequency domain has been reported as a risk assessment factor for CHF [17]–[19] and the nonlinear HRV measures including Poincare plot and sample entropy (SampEn, SE) also performed significant roles between the healthy and patients with cardiovascular disease [20], [21]. There are many flaws for traditional clinical ECG such as missing the intermittent characteristics,

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limited time length signals or asymptomatic of cardiovascular diseases [22]. Thus, long-term 24-hour ECG digital time series collected via Holter monitors was analyzed for detecting CHF based on HRV measures in this work.

HRV measures are very popular in the study of classifying patients with CHF using various classification algorithms. Asyali took 9 long-term HRV measures as the discrimination features with a linear discriminant analysis (LDA) and applied a Bayesian classifier for validation [6]. Işler and Kuntalp [8] combined wavelet entropies and classical short-term HRV measures to identify the features of 54 healthy subjects and 29 patients with CHF by using a k-nearest neighbor (KNN) classifier. They also used heart rate normalization and genetic algorithm feature selection to improve the performance of the KNN classifier [9]. Pecchia *et al*. [15] applied time and frequency domain analysis to measure short-term HRV features with a classification and regression tree (CART) classifier. Liu *et al*. [12] presented a approach with nonstandard HRV measures based on KNN classifier in MIT/BIH database. Narin *et al*. [14] used standard short-term HRV measures and wavelet packet transform in addition to several non-linear parameters as feature vector in five typical classifiers. Cornforth and Jelinek [5] combined time-domain HRV measures of 1000 RR intervals and Renyi entropy exponents to identify CHF patients with five classifiers. Kumar *et al*. [11] computed Accumulated Fuzzy Entropy (AFEnt) and Accumulated Permutation Entropy (APEnt) on three different lengths of HRV signals and the extracted features ranked by a Bhattacharyya method were fed to a Least Squares SVM (LS-SVM) classifier. Wang *et al*. [16] applied a SVM classification algorithm to nine features of the short-term HRV measures including time domain, frequency domain and nonlinear domain. Isler *et al*. [10] proposed a 3-stage classification structure consisted of two simple perceptron classifiers and a kind of typical classifiers based on short-term HRV measures. The existing methods mentioned above extracted the HRV measures based on only one or two types of time scale and some methods with complex feature selection algorithms need to calculate a large number of HRV measures. In our work, we focused on nine HRV measures of RR intervals on multiple time scales.

Multiple scale analysis that contains multiple spatial scales and multiple temporal scales has been widely used in many fields [23]. For the spatial scales that may need to be considered from the size of atom to cosmos range. For the temporal scales, there is microsecond, second, minute, hour, month and year that we can record. Multiple time scales analysis is suitable for many different natural time series including climate [24], hydrology [25], [26], power systems [27], [28] and survival data [29]. As for physiological time series, Peng *et al*. [30] discussed neurophysiological control mechanisms based on gait regulation and heart rate as model systems on multiple time scales and concluded that the scaling exponents can indicate some prognostic information for CHF. Chladekova *et al*. [31] used different data segments on four time scales to calculate three different time irreversibility indices. These indices suggested that time irreversibility of blood pressure variability (BPV) and beat-to-beat HRV was significantly altered and autonomous nervous system involved in its generation [31]. Multiple time scales analysis perhaps can make progress in identifying CHF compared to single time scale analysis.

TABLE 1. The measures of HRV in time, frequency and nonlinear domain.

Domains	Variable	Unit	Definition
Time domain	MEAN	ms	the mean value of all NN intervals
	SDNN	ms	the standard deviation of all NN intervals (or RR intervals)
	RMSSD	ms	the square root of the mean of the sum of the squares of differences between adjacent NN intervals
Frequency domain	LF_n	nu	low frequency (0.04-0.15Hz) power in normalized units
	HF_n	nu	high frequency (0.15-0.4Hz) power in normalized units
	Ratio_LH		ratio LF_n / HF_n
Nonlinear domain	VAI	degree	the mean of all the absolute value of angular differences between the lines plotted from every scatter point to the original point and the diagonal line in Poincare plot
	VLI	ms	the standard deviation of all distances of scatter points from the original point in Poincare plot
	SampEn		a measure of system complexity of physiological time-series signals

Short-term 5-minute recordings and nominal 24-hour long-term recordings are the two most popular time scales for the HRV analysis [4]. We extended seven time scales between 5-minute and 24-hour according to the power of two and the habit of recording time scale. The seven time scales, namely 5-minute, 10-minute, 30-minute, 1-hour, 2-hour, 5-hour and 10-hour were applied to measure the HRV indices. Three indices included the mean value of NN intervals (MEAN), the standard deviation of NN intervals (SDNN), the square root of the mean of the sum of the squares of differences between adjacent NN intervals (RMSSD) in time domain; three indices included low frequency power with normalization (LF_n), high frequency power with normalization (HF_n), ratio of LF_n and HF_n (Ratio_LH) in frequency domain and three indices included vector length index (VLI), vector angle index (VAI), Sample Entropy (SampEn) in nonlinear domain were calculated on each time scale. The detailed descriptions of nine HRV measures used in this study were showed on Table 1. The HRV measures on each time scales was deployed to classify the CHF patients from the normal subjects with a SVM classifier based on 10-fold cross-validation. Furthermore, the trends of SDNN and VLI over seven time scales were characterized by linear function, exponential function and logarithmic function. The coefficients of fitting functions were acted as nonstandard HRV measures. These nonstandard HRV measures were used as feature vectors of SVM classifier to improve the discrimination performance. The best classification performance of

sensitivity, specificity and accuracy of 86.7%, 98.3% and 94.4% were achieved on 2-hour time scale and nine standard HRV measures. A better performance used three nonstandard features was performed with sensitivity, specificity and accuracy of 93.3%, 98.3% and 96.7%, respectively.

II. METHOD

A. DATABASE

The dataset used in this study was retrieved from the MIT/BIH database (http://www.physionet.org) [32]. We selected the Normal Sinus Rhythm (NSR) RR Interval Database (nsr2db) as a dataset for healthy human heart rate, including 54 long-term ECG signals with normal rhythms (30 males, aged from 28.5 to 76, and 24 females, aged from 58 to 73). The Congestive Heart Failure (CHF) RR Interval Database (chf2db) is the source for patients with congestive heart failure. It contains 29 long-term ECG signals (8 males, 2 females and remaining 19 unknown, aged 34 to 79) with NYHA class I, II and III. The length of each ECG recording in both datasets is nominal 24 hours. The original ECG signals were digitized at 128 Hz, and the beat annotations were obtained by automated analysis with manual review and correction.

B. PREPROCESSING

The RR interval (or NN interval) time series was directly derived from PhysioBank ATM (https://physionet.org/cgi-bin/atm/ATM). The derived RR interval time series was automatically identified by computer algorithm and contained some ectopic beats when the PQRS waveform was irregular. The ectopic beats have been annotated in the databases and the total length of time of the ectopic data is only 3% of the length of entire data, we simply deleted these beats without interpolation. Because there were four recordings which short than 20-hour after preprocessing, we set the 10-hour to be the largest time scale. According to the length of RR intervals on each time scale, we divided the entire long-term RR intervals into numerous segments which of the length were closest to the time scale. Nine HRV indices were calculated for each segment separately, and then the same indices were averaged to obtain the index results of the entire long-term RR interval time series on this time scale. Figure 1 shows the detailed steps of method used in this study.

C. HRV MEASURES CALCULATION

Time-domain indices: There are three HRV measures commonly used in time domain [4], including the mean value (MEAN) of NN intervals, the standard deviation (SDNN) of NN intervals and the square root of the mean of the sum of the squares of differences between adjacent NN intervals (RMSSD). The definitions were shown below referred to [33]:

$$\mathrm{MEAN} = \sum_{n=1}^{N} RR_n/N \tag{1}$$

$$\mathrm{SDNN} = \sqrt{E\left[(RR_n - E\left(RR_n\right))^2\right]} \tag{2}$$

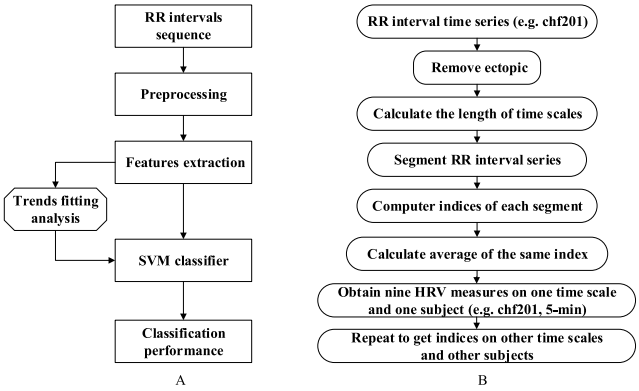

FIGURE 1. (A) The flow diagram of the method used in this study, (B) the detailed steps of preprocessing and features extraction.

$$\mathrm{RMSSD} = \sqrt{E\left[(RR_n - RR_{n+1})^2\right]} \tag{3}$$

where RR_n denotes the n^{th} NN interval, $E(*)$ denotes the average value, N is the number of NN interval.

Frequency-domain indices: The frequency-domain indices of RR interval time series were analyzed based on the autoregressive (AR) method. AR method can be expressed as the following equation with order p referred to [34]:

$$\mathrm{x}\left[\mathrm{n}\right] = -\sum_{k=1}^{p} a\left(k\right) x\left[\mathrm{n\text{-}k}\right] + w\left[n\right] \tag{4}$$

where x[n] denotes the n^{th} NN interval in NN interval time series, $a\left(k\right)$ are the AR coefficients, p is the order of AR model and $w[n]$ is white noise time series that satisfy the normal distribution with $w\left[n\right] \sim N(0, \sigma^2)$. An AR process can be presented as an all-pole filter:

$$\mathrm{H}\left(\mathrm{z}\right) = \frac{1}{1 + \sum_{k=1}^{p} a(k) z^{-k}} \tag{5}$$

To obtain the coefficients of AR model, we used a Burg method [35] in this study. The power spectrum formula of an p^{th} order AR model is referred to [34]:

$$\mathrm{PSD}^{Burg}\left(f\right) = \frac{\sigma^2}{\left|1 + \sum_{k=1}^{p} a_p(k) e^{-j2\pi fk}\right|^2} \tag{6}$$

where f is the frequency which to study in HRV measures,σ^2 denotes total least square error of noise, $a_p(k)$ is the coefficients of AR model with an order of p. The HRV frequency spectrum was produced by Burg's method with an order of 16 [36]. The low-frequency power (LF) was integrated across 0.04-0.15Hz and high-frequency power (HF) cross 0.15-0.40 Hz spectra [4]. The normalized low-frequency power (LF_n) is the proportion of LF to the sum of LF and HF, and normalized high-frequency power (HF_n) is the other, and their ratio (Ratio_LH) was defined as the proportion of LF_n to HF_n.

Nonlinear-domain indices: We extracted two non-linear indices named the vector angle index (VAI) and vector length

index (VLI) from Poincare scatter plots. The mathematical formulas of VLI and VAI are defined in [20]:

$$\mathrm{VLI} = \sqrt{\sum_{i=1}^{N} (l_i - L)^2 / N} \tag{7}$$

$$\mathrm{VAI} = \sum_{i=1}^{N} |\theta_i - 45| / N \tag{8}$$

The l_i is the vector length of each point from the original point in Poincare plot, L is the mean vector length, θ_i is the angle difference between the lines plotted from every scatter point to the original point and the x-axis, and N is the total point number in the Poincare plot.

Sample entropy (SampEn, SE) was first studied as a nonlinear index by Richman and Moorman [37]. For a time series of N points, $\mathrm{X} = \{x_1, x_2, \cdots, x_N\}$, the detailed calculation of SampEn(m, r, N) can refer to the following steps [38]:

1) Choosing the embedding dimension m:

$$\mathrm{X}_m(i) = \{X(i+k) | 0 \le k \le m-1, 1 \le i \le N-m-1\} \tag{9}$$

2) Choosing the tolerance r^*SD of accepting matches:

$$C_i^m(r) = \frac{\#\left(d\left[X_m(i), X_m(j)\right] \le r * SD\right)}{N-m+1} \tag{10}$$

where $1 \le i, j \le N-m, i \ne j$ and the distance between two such vectors defined as $d\left[X_m(i), X_m(j)\right] = \max\left(\left|x_{i+k}, x_{j+k}\right|\right), 0 \le k \le m-1$, SD is the standard variation of total time series, #(∗) is the number of vectors less than the tolerance.

1) Calculating the average of the functions $C_i^m(r)$:

$$\emptyset^m(r) = \frac{\sum_{i=1}^{N-m+1} C_i^m(r)}{N-m+1} \tag{11}$$

2) Sample entropy can be express as [34]:

$$\mathrm{SampEn}(m, r, N) = -ln[\emptyset^m(r)/\emptyset^{m+1}(r)] \tag{12}$$

The tolerance threshold r was set as 0.10, 0.15, 0.20, 0.25 and embedding dimension m as 1, 2, 3 generally [21]. The different parameter combinations could influence the value of SampEn. In this work, we set $r = 0.10$ and $m = 1$ for less computation and best distinguishing performance [16].

D. STATISTICAL ANALYSIS

After obtained the values of HRV measures of NSR and CHF groups on seven time scales, we applied Student's t-test to determine if two sets of NSR and CHF data were significantly different from each other. Before the t-test statistic, the Kolmogorov-Smirnov test was used to confirm whether all HRV indices for the two groups satisfied the normal distribution or not. We performed all statistical analyses in MATLAB software (Ver. 2014a, MathWorks) and p-value of 0.05 was accepted as the statistical significance threshold in this study.

E. TREND FITTING ANALYSIS

Trend fitting is the process of constructing a curve or mathematical function that has the best fit to a series of data points [39]. In order to characterize the trends of SDNN and VLI on seven time scales, three common functions, namely linear function, exponential function and logarithmic function, were used to fit the trends on time scales.

Linear Function:

$$y_i = \alpha x_i + \beta + \varepsilon_i \tag{13}$$

Exponential Function:

$$y_i = \alpha e^{\beta x_i} + \varepsilon_i \tag{14}$$

Logarithmic Function:

$$y_i = \alpha ln x_i + \beta + \varepsilon_i \tag{15}$$

where α and β are the coefficients of fitting functions, ε_i is the residual between predicted and actual value. The ordinary least squares estimation method was used to obtain the coefficients α and β that characterize the fitting functions [40].

$$\text{Find min } E(\alpha, \beta) = \sum_{i=1}^{n} \varepsilon_i^2 \tag{16}$$

The minimum is determined by calculating the partial derivatives of $E(\alpha, \beta)$ with respect to α and β and setting them to zero.

$$\frac{\partial E}{\partial \alpha} = \frac{\partial}{\partial \alpha}\left(\sum_{i=1}^{n} \varepsilon_i^2\right) = 0 \tag{17}$$

$$\frac{\partial E}{\partial \beta} = \frac{\partial}{\partial \beta}\left(\sum_{i=1}^{n} \varepsilon_i^2\right) = 0 \tag{18}$$

The coefficients were used as nonstandard HRV measures and the residual value as the evaluation factor. Here we used the decision coefficient R^2 to evaluate the effect of the fitting [41].

$$R^2 = 1 - \frac{\sum_{i=1}^{n} \varepsilon_i^2}{\sum_{i=1}^{n} \left(y_i - \frac{1}{n}\sum_{i=1}^{n} y_i\right)^2} \tag{19}$$

When the residual is smaller, the closer R^2 is to 1 anda the better the fitting effect is.

F. CLASSIFICATION ALGORITHM

Support Vector Machine (SVM) has been successfully applied to classification on many occasions as a machine learning algorithm. It aims at maximizing the margin between the separating hyperplane and the data to minimize an upper bound of the generalization error [42], [43]. The advantages of SVM are effective in high dimensional spaces and still effective in cases where number of dimensions is greater than the number of samples. Since a subset of training points (called support vectors) is used in the decision function, it is also memory effective. In addition, the kernel trick in SVM algorithm is used to build in expert knowledge about the problem via engineering the kernel. The more detailed information about SVM is presented in [42]. In our work,

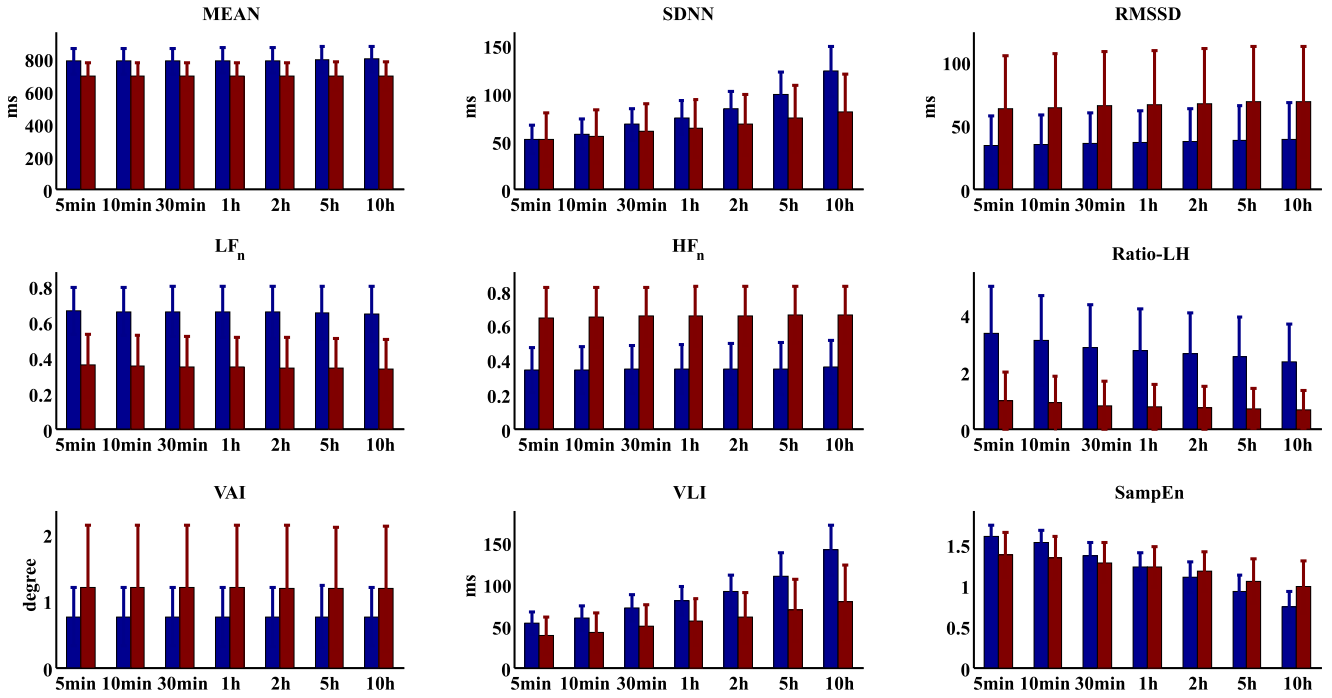

FIGURE 2. Differences (mean and standard deviation) of nine HRV measures between NSR group (blue bar) and CHF group (red bar).

the SVM classifier was performed using scikit-learn machine learning package (Ver. 0.19.1) [44] in Spyder software (Ver. Python 3.6) and the grid search was used to find out the best two parameters (C and gamma) combinations of SVM classifier with the Radial Basis Function (RBF) kernel. The two parameters to logarithmic grids ranged from 10^{-5} to 10^{5} and there were 121 kinds of different combinations.

G. THE CLASSIFIER PERFORMANCE

The data were divided into the training set and testing set to obtain the performance. To avoid the overfitting phenomenon in machine learning, 10-fold cross-validation method for SVM were conducted [45]. The SVM model performance was evaluated by sensitivity (Se), specificity (Sp) and accuracy (Acc) referred to [42].

Sensitivity (Se): (true positive rate)

$$\mathrm{Se} = \frac{\mathrm{TP}}{\mathrm{TP}+\mathrm{FN}} \times 100\% \tag{20}$$

Specificity (Sp): (true negative rate)

$$\mathrm{Sp} = \frac{\mathrm{TN}}{\mathrm{TN}+\mathrm{FP}} \times 100\% \tag{21}$$

Accuracy (Acc):

$$\mathrm{Acc} = \frac{\mathrm{TP}+\mathrm{TN}}{\mathrm{TP}+\mathrm{FP}+\mathrm{FN}+\mathrm{TN}} \times 100\% \tag{22}$$

where TP, FP, FN, TN denote the number of true positives, false positives, false negatives and true negatives in confusion matrix. The higher the average accuracy of 10-fold cross-validation is, the better the classification effect.

III. RESULTS

Figure 2 shows the differences in the performance of nine indices in time domain, frequency domain, and non-linear domain between NSR and CHF. The MEAN, RMSSD, LF_n, HF_n and VAI indices of RR intervals time series were almost constant with each other along with seven time scales for NSR and CHF subjects, but these indices in CHF subjects were different with the same indices in NSR subjects on each timescales. The mean value of RR intervals in NSR subjects was about 785±78ms that larger than 688±85ms in CHF subjects. The SDNN and VLI were increasing with the time scale lengthening while Ratio_LH and SE showed decreasing trend in contrast. The differences of SDNN or VLI indices values between CHF and NSR increased from 5-min time scale to 10-hour time scale. The values of SE index in NSR subjects on 5-min, 10-min and 30-min time scales were larger than the values in CHF subjects on the same time scales, but the values of SE index in NSR and CHF subjects reversed on 2-hour, 5-hour and 10-hour time scales. It was indicated that the SE values of NSR subjects decreased fast than the SE values of CHF.

All HRV indices of the two groups were confirmed in normal distributions by Kolmogorov-Smirnov test. The result was also reported in [16]. Table 2 shows the p-value of statistical significance between NSR and CHF subjects on seven time scales. It is intuitive and obvious that the p-value would be smaller when the distributions of NSR subjects differ much than those of CHF subjects on the same indices and time scales in Figure 2. The p-value of statistical significance almost keeps the same values on different time

TABLE 2. The statistical significance between NSR and CHF on seven time scales ("∗": $p < 0.05$, "∗∗": $p < 0.01$, "∗∗∗": $p < 0.001$).

p-value	5-m	10-m	30-m	1-h	2-h	5-h	10-h
MEAN	6.75E-06 ***	6.63E-06 ***	6.09E-06 ***	5.41E-06 ***	3.92E-06 ***	3.05E-06 ***	2.92E-06 ***
SDNN	0.957	0.644	0.206	0.0794	0.0173 *	0.00157 **	6.01E-06 ***
RMSSD	0.00167 **	0.00143 **	0.00125 **	0.00122 **	0.00129 **	0.00143 **	0.00172 **
LF_n	1.90E-10 ***	1.14E-10 ***	5.48E-11 ***	4.71E-11 ***	4.02E-11 ***	2.95E-11 ***	4.52E-11 ***
HF_n	1.90E-10 ***	1.14E-10 ***	5.48E-11 ***	4.71E-11 ***	4.02E-11 ***	2.95E-11 ***	4.52E-11 ***
Ratio_LH	1.26E-11 ***	1.59E-11 ***	1.06E-11 ***	9.04E-12 ***	1.40E-11 ***	1.25E-11 ***	1.94E-11 ***
VAI	0.0247 *	0.0246 *	0.0247 *	0.0245 *	0.0249 *	0.0257 *	0.0281 *
VLI	0.00258 **	0.00106 **	1.82E-04 ***	8.56E-05 ***	1.22E-05 ***	3.51E-06 ***	2.40E-08 ***
SampEn	1.43E-04 ***	0.00131 **	0.120	0.881	0.164	0.0260 *	4.73E-04 ***

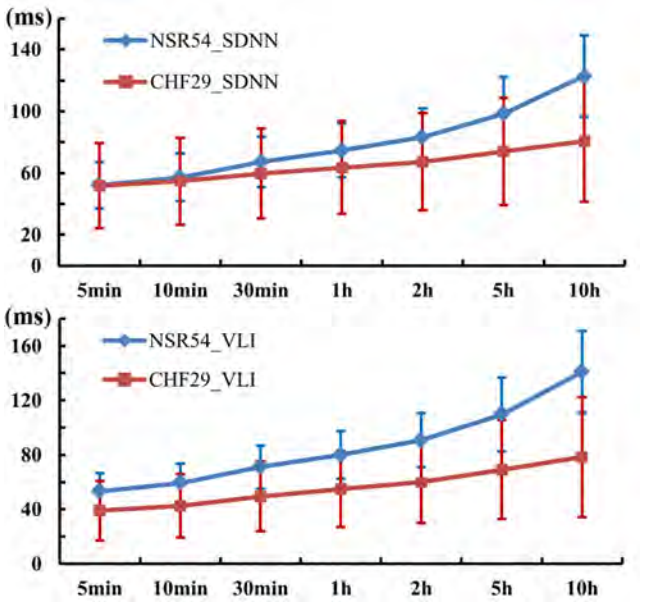

FIGURE 3. The trends of SDNN and VLI on time scales. NSR54_SDNN denotes the average and standard deviation of SDNN in NSR group. CHF29_VLI denotes the average and standard deviation of VLI in CHF group.

scales for MEAN, RMSSD, LF_n, HF_n, Ratio_LH and VAI, respectively. The p-value of SDNN and VLI both show decreasing trends with the time scale increasing. The p-value of SampEn behaves rising on short-term time scale and falling on long-term time scale. The trends of p-value are consistent with the difference of distributions of HRV indices between NSR and CHF. The p-value of frequency-domain indices indicates that the statistical significance level is best than those of time-domain and nonlinear-domain indices.

TABLE 3. The performance of SVM model on seven time scales.

RBF_SVM (%)	Se ± std	Sp ± std	Acc ± std
5min	70.00 ± 17.95	98.33 ± 5.00	88.89 ± 8.61
10min	80.00 ± 16.33	96.67 ± 6.67	91.11 ± 8.31
30min	83.33 ± 16.67	98.33 ± 5.00	93.33 ± 7.37
1h	83.33 ± 16.67	98.33 ± 5.00	93.33 ± 7.37
2h	86.67 ± 16.33	98.33 ± 5.00	94.44 ± 7.45
5h	86.67 ± 16.33	91.67 ± 8.33	90.00 ± 7.78
10h	83.33 ± 22.36	96.67 ± 6.67	92.22 ± 10.00

Table 3 shows the performance of classification model based on SVM machine learning using all nine indices on seven timescales. The classification performances using other six time scales except for short-term 5-min time scale are all better than that with 5-min time scale. We obtained the best classification performance with an accuracy of 94.44% on 2-hour time scale.

According to the difference compared CHF indices with NSR indices on the timescale from Figure 2, we could obviously see that the increasing trends showed different slopes for SDNN and VLI in Figure 3, moreover, the SDNN and VLI show that the p-value is smaller on larger time scales in Table 2. So we fitted the trends of SDNN and VLI using three common functions including linear function, logarithm function and exponent function to extract the features.

Table 4 shows the R-squared values of decision coefficient using three different functions to fit the trends. The R-squared value of goodness of fit using logarithm function to fit SDNN and VLI trends was about 0.87, it was the worst performance than others, so logarithm function is not appropriate to fit in this situation and we didn't take it for the next step. The coefficients of linear and exponent fitting functions were considered as nonstandard HRV measures. The slope α of linear function fitting SDNN trend was denoted as SDNN_α_linear and the intercept β as SDNN_β_linear. The slope α of linear function fitting VLI trend was denoted as VLI_α_linear and the intercept β as VLI_β_linear. The coefficient α of exponent function fitting SDNN trend was denoted as SDNN_α_exponent and the coefficient β as SDNN_β_exponent. The coefficient α of exponent function fitting VLI trend was denoted as VLI_α_exponent and the coefficient β as VLI_β_exponent. Table 5 shows the performance of the SVM models using the combinations of nonstandard HRV measures from fitting functions. We obtained the best classification performance with 96.67% accuracy when combining SDNN slope (SDNN_α_linear) and VLI exponent (VLI_α_exponent and VLI_β_exponent) as only three features to SVM classifier. All classification performances based on the fit of the time scales are better than the performances on every single time scale.

TABLE 4. The R-squared in three fitting functions.

R^2	linear	logarithm	exponent
SDNN Fitting	0.9319 ± 0.0453	0.8720 ± 0.0639	0.9656 ± 0.0252
VLI Fitting	0.9252 ± 0.0488	0.8740 ± 0.0609	0.9642 ± 0.0244

TABLE 5. The performance of SVM model based on time scales.

Combination of features	Number of features	SVM_RBF (%)		
		Se	Sp	Acc
All features	63	93.33	90.00	91.11
SDNN timescales VLI timescales	14	90.00	98.33	95.56
SDNN slope VLI slope	2	93.33	96.67	95.56
SDNN slope VLI exponent	3	93.33	98.33	96.67
SDNN exponent VLI slope	3	86.67	1.00	95.56
SDNN exponent VLI exponent	4	86.67	1.00	95.56
SDNN linear VLI linear	4	90.00	98.33	95.56

All features: 63 features including all nine standard HRV measures on each of seven time scales; VLI timescales: 7 features including each VLI value on each of seven time scales; SDNN timescales: 7 features including each SDNN value on each of seven time scales; SDNN slope: SDNN_α_linear; VLI slope: VLI_α_linear; SDNN linear: SDNN_α_linear and SDNN_β_linear; SDNN exponent: SDNN_α_exponent and SDNN_β_exponent; VLI linear: VLI_α_linear and VLI_β_linear; VLI exponent: VLI_α_exponent and VLI_β_exponent.

All features: 63 features including all nine standard HRV measures on each of seven time scales; VLI timescales: 7 features including each VLI value on each of seven time scales; SDNN timescales: 7 features including each SDNN value on each of seven time scales; SDNN slope: SDNN_α_linear; VLI slope: VLI_α_linear; SDNN linear: SDNN_α_linear and SDNN_β_linear; SDNN exponent: SDNN_α_exponent and SDNN_β_exponent; VLI linear: VLI_α_linear and VLI_β_linear; VLI exponent: VLI_α_exponent and VLI_β_exponent.

In this study, all of the calculations except for the classifier construction were implemented in MATLAB R2014a (The MathWorks, Inc., Natick, MA, USA). The SVM classifier construction was performed in Spyder software (Ver. Python 3.6) using scikit-learn machine learning package (Ver. 0.19.1). Both of them were deployed on Intel Core^{TM}i5 3.30 GHz CPU and Windows 10.

IV. DISCUSSION

There are many publications mainly concentrating on the HRV measures of either 5-min short-term or 24-hour long-term time scales [6], [12], [13], [15], [46]–[48], the difference of the HRV measures on other time scales have no definite studies so far. This study is the first time to investigate the HRV measures on seven time scales and the results showed in Figure 2. It was indicated that the value of SDNN on short-term time scale was much smaller than the value on long-term time scale [49], [50]. The value of SDNN with CHF was decreased compared to the healthy subjects on the same time scales and the decreased indices of HRV indicated the abnormalities of autonomic input of heart associated with increased susceptibility to ventricular arrhythmias [19]. Regarding frequency-domain measures, the power of low frequency accounts for the major component in NSR group, but the majority in CHF group is high frequency. The Ratio_LH in NSR group is always larger than that in CHF group. These results are consistent with conclusions in [4] and [50]. Wang *et al*. [16] analyzed three identical nonlinear-domain measures on 5-min time scale and drawn the similar difference between NSR and CHF group. On the other hand, Signorini *et al*. [51] obtained that SampEn value in CHF subjects is higher than in the healthy and is potentially related to an increase of unpredictability of RR interval time series in CHF group. Because the parameters in sample entropy analysis are critical, our studies show that a deeper investigation about SampEn between NSR and CHF is required to fit the existing gap.

In Table 3, the best performance in distinguishing CHF was obtained on 2-hour time scale with sensitivity of 86.67%, specificity of 98.33% and accuracy of 94.44% with the SVM classifier. The CHF classification's performances on other time scales were better than that on 5-min short-term time scale, but it was best on 2-hour timescales. It was suggested that the 2-hour time scale may be the better choice for detecting CHF patient with HRV measures than traditional 5-min time scale. The best performance on 2-hour time scale may be associated with the period of heart rate regulation in cardiovascular system with CHF. Furthermore, the different trends in SDNN and VLI indices between CHF and NSR were fitted by three common functions to extract the features. We achieved the improvement to an accuracy of 96.67% based on only three nonstandard features.

Table 6 shows the literature to discriminate CHF from NSR using HRV measures on different time scales. Asyali used 9 long-term HRV measures as the discrimination features with LDA classifier and applied Bayesian classifier for validation. The Bayesian classifier achieved sensitivity, specificity and accuracy value of 81.8%, 98.1% and 93.2%, respectively [6]. Işler and Kuntalp [9] selected 13 features by genetic algorithm (GA) as the inputs of KNN classifier and improved the performance of sensitivity value of 82.76%, specificity value of 100% and accuracy value of 93.98%. Pecchia *et al*. [15] added two nonstandard HRV indices as features of CART classifier and obtained a better accuracy value of 96.4% with 6 features. Liu *et al*. [12] presented a new approach based on combination SVM and three nonstandard heart rate variability measures and finally achieved the best performance with the CHF classification accuracy, sensitivity and specificity of 100%, 100%, 100%, respectively. Narin *et al*. [14] selected 27 features by backward elimination to SVM classifier and obtained the best performance of sensitivity of 82.75%, specificity of 96.29% and accuracy of 91.56%. Cornforth and Jelinek [5] used only four features of HRV measures on the length of 1000 RR intervals. The KNN classifier achieved a

TABLE 6. The CHF classification performance comparison using HRV measures.

Author (year)	Data	HRV measures	Number of features	Timescale	Classifier	Performance
Asyali *et al.*[6] (2003)	Physionet nsr2db(52) chf2db(22)	SDNN, SDANN, SDNN_index, SDSD, TP, ULF, VLF, LF, HF	9	Long term 24 hours	Bayesian	Se: 81.82% Sp: 98.08% Acc: 93.24%
Isler *et al.*[9] (2010)	Physionet nsr2db(54) chf2db(29)	SDNN, RMSSD, PNN20, PNN50, SDSD, SD1, SD2, LS_NLF, FFT_VLF, FFT_LF, FFT_LF/HF, WS_LF, WS_NLF	13(with genetic algorithm)	Short term 5 minutes	KNN	Se: 82.76% Sp: 100% Acc: 93.98%
Pecchia *et al.*[15] (2011)	Physionet nsr2db(54) chf2db(29)	RMSSD, TOTPWR, HF, LF/HF, ΔAVNN, ΔLF/HF	6	Short term 5 minutes	CART	Se: 89.7% Sp: 100% Acc: 96.4%
Liu *et al.*[12] (2014)	Physionet nsr2db(30) chf2db(17)	SDNN, RMSSD, pNN50%, CVrr, ApEn, SampEn, VLF, VHF, LF, HF, LF/HF, TP	12	Short term 5 minutes	KNN	Se: 100% Sp: 100% Acc: 100%
Narin *et al.*[14] (2014)	Physionet nsr2db(54) chf2db(29)	Age, RMSSD, SDSD, Symbolic dynamics, SD2, SD1/SD2, frequency-domain measures	27(with backward elimination)	Short term 5 minutes	SVM	Se: 82.75% Sp: 96.29% Acc: 91.56%
David *et al.*[5] (2016)	Physionet nsrdb(18) chfdb(15)	Renyi entropy exponents, SDNN, RMSSD	4	1000 R-R intervals	KNN	Se: 80.0% Sp: 94.4% Acc: 87.9%
Kumar *et al.*[11] (2017)	Physionet nsrdb(18) chfdb(15)	Accumulated Fuzzy Entropy (AFEnt), Accumulated Permutation Entropy (APEnt)	18(with Bhattacharyya ranking method)	500 samples	LS-SVM	Se: 98.07% Sp: 98.33% Acc: 98.21%
Wang *et al.*[16] (2018)	Physionet nsr2db(52) chf2db(18)	Mean, SDNN, RMSSD, LF_n, HF_n, Ratio_LH, VAI, VLI, SampEn	9	Short term 5 minutes	SVM	Se: 91.31% Sp: 90.04% Acc: 90.95%
Isler *et al.*[10] (2019)	Physionet nsr2db(54) chf2db(29)	time-domain measures, frequency-domain measures, Poincare plot, DFA, symbolic dynamics, ApEn, SampEn	34(with statistical significances)	Short term 5 minutes	3-Stage classifier	Se: 100% Sp: 98.1% Acc: 98.8%
The proposal method	Physionet nsr2db(54) chf2db(29)	MEAN, SDNN, RMSSD, LF_n, HF_n, Ratio_LH, VLI, VAI, SampEn	9	2 hour	SVM	Se: 86.67% Sp: 98.33% Acc: 94.44%
The proposal method	Physionet nsr2db(54) chf2db(29)	SDNN slope VLI exponent	3	From 5 minutes to 10 hours	SVM	Se: 93.33% Sp: 98.33% Acc: 96.67%

sensitivity of 80.0%, specificity of 94.4% and accuracy of 87.9%. Kumar *et al.* [11] selected 18 features of AFEnt and APEnt by Bhattacharyya ranking method on 500 samples of HRV signals. The LS-SVM classifier performed a sensitivity of 98.07%, specificity of 98.33% and accuracy of 98.22%. Isler *et al.* [10] selected 34 features from HRV measures including time-domain measures, frequency-domain measures, Poincare plot, detrended fluctuation analysis (DFA), symbolic dynamic and entropy measures. They constructed a 3-stage classifier with two simple perceptron classifiers and a multilayer perceptron. The proposed classification system resulted in the performance of a sensitivity of 100%, specificity of 98.1% and accuracy of 98.8%. The approach that Liu *et al.* [12] presented was tested by only 30 NSR subject and 17 CHF subjects selected from the datasets used in this study. The performances in [11] were presented on BIDMC CHF database with severe congestive heart failure (NYHA class III, IV). Isler *et al.* [10] and Kumar *et al.* [11] both used a large number of features after feature selection algorithm to train the classifiers, these can be high cost of hardware and time consuming.

V. CONCLUSION

In this study, a novel method was developed to detect CHF automatically with the SVM classifier. Unlikely existing HRV studies using only one or two types of time scale, it is the first time to evaluate seven types of time scale of HRV signals for identification the CHF and NSR. The feature vectors were extracted by nine HRV measures in time, frequency and nonlinear domain analysis on seven time scales for all 54 NSR and 29 CHF subjects. The 10-folds cross validation of the SVM classifier was used to classify the CHF subjects from NSR subjects with the feature vectors on different time scales. Compared to existing preferred short-term time scale studies (such as 5-minutes), the results indicated that the HRV measures extracted from 2-hour time scale showed the better discrimination performance with sensitivity of 86.67%, specificity of 98.33% and accuracy of 94.44%. In addition, by fitting the increasing trends of SDNN and VLI on time scales, the performance were improved to sensitivity of 93.33%, specificity of 98.33% and accuracy of 96.67% based on only three nonstandard HRV measures consisted of the coefficients of SDNN slope and VLI exponent.

The performance on 2-hour time scale suggested that it may be more suitable for distinguishing CHF from NSR on 2-hour time scale instead of 5-min short-term time scale. The performance based on the fitting of time scale trends demonstrated that multiple time scale on HRV analysis can be valuable to apply potentially other biomedical signal processing.

There are some flaws in this study. The number of data used in this study is small, besides, the number of NSR group and CHF group are imbalanced. Both of flaws are potentially related to the performance of classifier. It is reported that the leave-one-out method is better than other cross-validation methods [52]. It is possible to make an optimization in classification performance using a wide-spread, balanced data and leave-one-out cross-validation method.

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CONFLICT OF INTEREST STATEMENT

The authors declare that there are no conflicts of interest to this work.

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