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CLINICAL OBSERVATION

Recurrence quantification analysis on pulse morphological changes in patients with coronary heart disease

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Abstract

OBJECTIVE: To show that the pulse diagnosis used in Traditional Chinese Medicine, combined with nonlinear dynamic analysis, can help identify cardiovascular diseases.

METHODS: Recurrence quantification analysis (RQA) was used to study pulse morphological changes in 37 inpatients with coronary heart disease (CHD) and 37 normal subjects (controls). An independent sample t-test detected significant differences in RQA measures of their pulses. A support vector machine (SVM) classified the groups according to their RQA measures. Classic time-domain parameters were used for comparison.

RESULTS: RQA measures can be divided into two groups. One group of measures [ecurrence rate (RR), determinism (DEL), average diagonal line length (L), maximum length of diagonal structures (Lmax), Shannon entropy of the frequency distribution of diagonal line lengths (ENTR), laminarity (LAM), average length of vertical structures (TT), maximum length of vertical structures (Vmax)] showed significantly higher values for patients with CHD than for normal subjects (P<0.05). The other measures (RR_std, L_std, Lmax_std, TT_std, Vmax_std) showed significantly lower values for the CHD group than for normal subjects (P<0.05). SVM classification accuracy was higher with RQA measures: With RQA (16 parameters) accuracy was at 88.21%, and with RQA(12 parameters) accuracy was at 84.11%. In contrast, with classic time-domain (15 parameters) accuracy was 75.73%, and with time-domain (7 parameters) accuracy was 74.70%.

CONCLUSION: Nonlinear dynamic methods such as RQA can be used to study functional and structural changes in the pulse noninvasively. Pulse signals of individuals with CHD have greater regularity, determinism, and stability than normal subjects, and their pulse morphology displays less variability. RQA can distinguish the CHD pulse from the healthy pulse with an accuracy of 88.21%, thereby providing an early diagnosis of cardiovascular diseases such as CHD.

Key words: Pulse-taking; Cardiovascular diseases; Recurrence quantification analysis

INTRODUCTION

The pulse diagnosis of Traditional Chinese Medicine (TCM) is a noninvasive method that has been proven to be clinically valid for more than 2000 years. The pulse, usually felt by TCM doctors by placing their fingers on the radial artery, can project information about a variety of physiological and pathological conditions. Modern medical research shows that the pulse contains a great deal of information about the cardiovascular system.[1] Coronary heart disease (CHD), for example, can disrupt the pumping function of heart, causing changes in both structure and function of blood vessels, which is reflected in pulse morphology. If the changes that are linked to health and disease could be distinguished, it is possible that the distinctions could be used to diagnose cardiovascular diseases at an early stage.

A number of researchers in China and other countries have been assessing various methods and have reported their findings on pulse analysis, time-domain analysis, frequency-domain analysis, and time-frequency joint analysis, among others.[2-4] The traditional methods, based on linear concepts, are restricted to system stability. They are not particularly sensitive to changes in the pathological state and are insufficient for characterizing the complex dynamics of this nonlinear system. In contrast, nonlinear dynamic methods such as recurrence quantification analysis (RQA) can obtain nonlinear information from the pulse that the traditional analysis methods cannot. They have wide application for physiological signals such as heart rate variability and electroencephalographic and electrocardiographic changes.

We employed RQA to analyze morphological changes in the pulse at the wrist. Based on the assumption that the cardiac control system is a nonlinear biological deterministic system, we observed pulse morphological changes in patients with CHD and healthy subjects. In addition, classifications were made by means of a support vector machine (SVM) with RQA measures and using time-domain parameters for comparison.

METHODS

Material collection

The TCM pulse diagnosis refers to what the doctor senses by palpating the examinee's radial artery with his or her fingers. Simulating the actions of TCM doctors, measurement equipment (cooperatively developed by our research team and the Shanghai Asia-Pacific Computer Co., Shanghai, China) was used to acquire pulse recordings, which laid the foundation for an objective pulse analysis.

Pulse recordings used in this study were acquired from 74 volunteers for 60 s periods at a sampling rate of 720 Hz after they gave informed consent. Each subject was asked to relax for more than 5 min before pulse acquisition. The volunteers, who were ascertained to have no respiratory system or nervous system disorders, were divided into two groups. Group 1 included 37 inpatients with CHD aged (60±10) years from Longhua Hospital (Shanghai, China) and Shuguang Hospital (Shanghai, China), both affiliated with the Shanghai University of TCM. Group 2 included 37 normal subjects aged (57±4) years who were selected from among participants in the "2010 Zhangjiang ball game competition for the elderly (Shanghai, China)", and who had no documented history of a cardiovascular disorder.

The Scientific Research Section and Moral and Ethical Committee at Putuo Hospital (affiliated with Shanghai University of Traditional Chinese Medicine) approved the study. Also, following acquisition of informed consent, they approved all of the volunteers taking part in this research project.

Extraction of the pulse signal

The pulse signal was analyzed using a recurrence plot (RP). Phase space reconstruction, the basis for nonlinear time series analysis, can be used to estimate the characteristic properties of a dynamic system. Usually, the phase space has to be reconstructed from the original one-dimensional time series.[5,6] A frequently used method for reconstruction is the time-delay method. For a one-dimensional time series, such as a pulse signal of length M, a trajectory X_i is reconstructed as $X_i = \left(x(i), x(i+\tau), \cdots, x(i+(m-1)\tau)\right)^T$. The length of X_i is $N = M - (m-1)\times\tau$, where the embedding dimension m can be estimated with the method of false nearest neighbors,[7,8] and the time delay τ can be estimated with the method of mutual information.[9] All of these time trajectories $\{X_i, i = 1,2,\cdots,N\}$ make up the m-dimension phase space orbits of the system, as shown in Figure 1A,1C.

Recurrence is a fundamental property of dissipative dynamic systems. Eckmann et al. introduced a tool that enables us to investigate the m-dimensional phase space trajectory through a two-dimensional representation of its recurrences.[10] This RP representation is shown in Figure 1B,1D. Such an RP can be mathematically expressed as

$$R_{i,j} = \Theta\left(\varepsilon_i - \left\|\vec{x}_i - \vec{x}_j\right\|\right), \qquad i, j = 1,2,\cdots,N \qquad 1)$$

where N is the number of considered states, x_i, ε_i is a threshold distance, $\|\cdot\|$ is a norm, and $\Theta(\cdot)$ is the Heaviside function.

The phase space trajectories and their corresponding RPs of a CHD patient and a normal subject with 1000 sampling points are shown in Figure 1. The diagonal lines (angle $\frac{\pi}{4}$) in the two RPs mean that the evolution of states is similar at different times, and the process could be deterministic. There are more black dots in Figure 1B than in Figure 1D, which shows that the

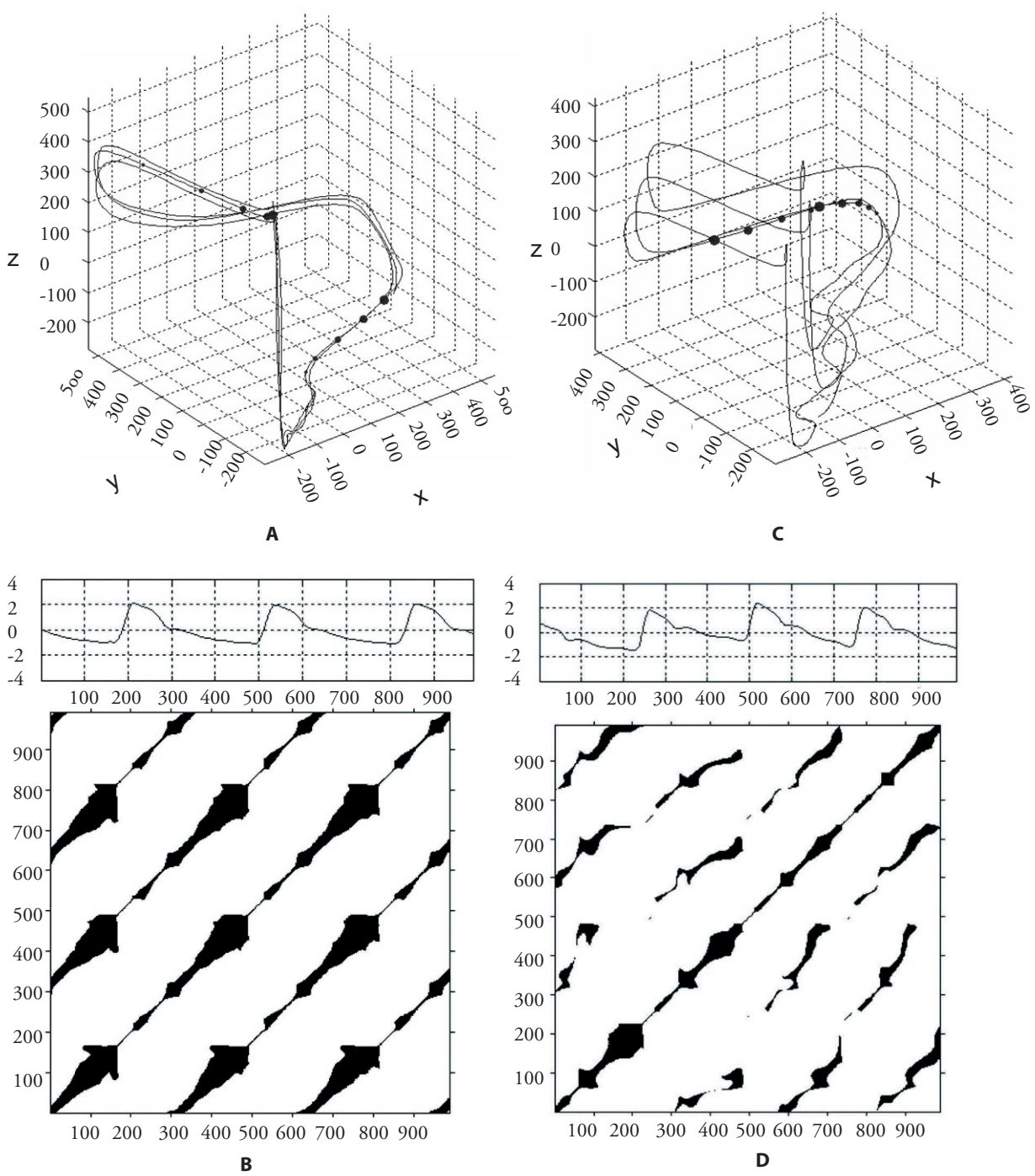

Figure 1 Reconstructed phase spaces and corresponding recurrence plots (RPs) of a pulse signal from a patient with coronary heart disease (CHD) and a healthy subject

A: segment of phase space trajectory of pulse data of a 60-year-old patient with CHD (m=3, τ=5, ε=0.2σ, where σ is variance of the time series, y=x+τ, z=x+2*τ). B: RP corresponding to Figure A. C: segment of the phase space trajectory of a pulse waveform from a 58-year-old healthy person (with embedding dimension m=3, time delay τ=5, and distance cutoff ε=0.2σ, where σ is the variance of the time series). D: RP corresponding to (c).

pulse signal of this patient with CHD had greater regularity and determinism than the healthy subject. The visual interpretation of RP requires some experience. Hence, quantitative analysis of RP is highly desirable.

Analysis of pulse data using recurrence quantification analysis

Zbilut and Webber developed RQA, a tool that quantifies structures in the RP[11,12] and has become well known, especially for physiological analyses. They defined measures of complexity using recurrence point density and diagonal structures in the RP. Gao defined the new measures based on vertical structures.[13,14] In 2004, Marwan and Meinke applied extended RQA to physiological event-related potentials (EPRs).[15] In our study, we analyzed pulse morphological changes using eight RQA measures: recurrence rate (RR), determinism (DEL), average diagonal line length (L), maximum length of diagonal structures (Lmax), Shannon entropy of the frequency distribution of diagonal line lengths (ENTR), laminarity (LAM), average length of vertical

structures (TT), maximum length of vertical structures (Vmax).

Pulse morphology refers to blood pressure, vascular resistance, and artery compliance, among other factors that are important parameters when assessing the cardiovascular system. Pulse morphological change refers to the alterations and variations in the morphology of the pulse waveform.[16] To analyze morphological changes of the pulse, we need to segment the pulse waveform. The pulse waveform was segmented using a moving window with a size of 1000 sampling points. The window moved forward by 300 sampling points each time. We then computed RQA measures of each segment for each subject. Finally, we calculated the means and standard deviations of all segments for each subject. We then obtained 16 RQA measures for each subject, characterizing the morphological change of each pulse, including RR, DET, L, Lmax, ENTR, LAM, TT, Vmax, RR_std, DET_std, L_std, Lmax_std, ENTR_std, LAM_std, TT_std, and Vmax_std. As a group, we called them RQA (16).

Extraction of time-domain parameters for comparison

The time-domain method is most commonly used in TCM pulse waveform analysis and has many applications in clinical practice. The classic time-domain parameters, which are important physiological indexes for assessing the cardiovascular system, are described via some characteristic points on the pulse waveform, as shown in Figures 2 and 3.[17]

We extracted 15 time-domain parameters—h1, h3, h4, h5, t1, t4, t5, t, w, h3/h1, h4/h1, h5/h1, w/t, As, Ad—and used them for comparisons, as shown in Figures 2 and 3. We called the group of parameters the time-domain (15).

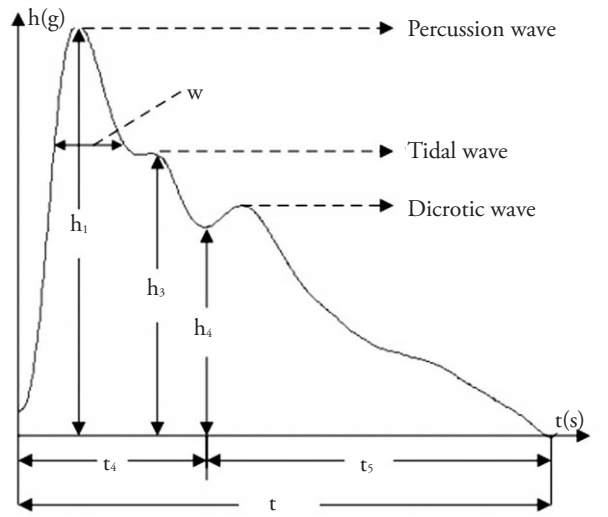

Figure 2 Height and time parameters of a typical cycle pulse
h1: height of the percussion wave; h3: height of the tidal wave; h4: height of the dicrotic notch; t4: time between the starting point of the pulse chart and the dicrotic notch; t5: time between the dicrotic notch and the ending point of the pulse chart; t: time between the starting point and the ending point; w: width of the percussion wave at its one-third height position.

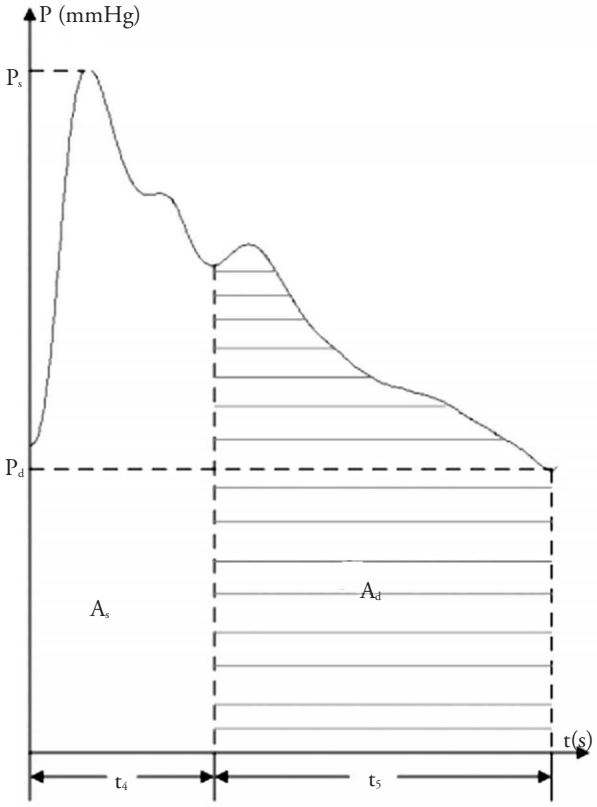

Figure 3 Area parameters of a typical cycle pulse
P_s: systolic pressure; P_d: diastolic pressure; t4: contraction phase; t5: diastolic phase. A_s: area of the contraction phase; A_d: area of the diastolic phase.

Statistical analysis

Using SPSS 16.0 software (IBM, Armonk, NY, USA), we found that the RQA measures and time-domain parameters of the pulse signals from the two groups were in nearly normal distributions. Therefore, all of the data (RQA measures and time-domain parameters) were analyzed by an independent sample t-test to detect any significant differences between the two groups (CHD patients and controls).

Classification method

Since the 1960s, Vapnik and his group have achieved a series of advancements in the field of machine learning of finite samples and constructed an integrated theory known as the support vector machine (SVM).[18] In our study, RQA measures and time-domain parameters were entered into the SVM classifier to distinguish between pulses of the patients with CHD and those of the controls. Classification was performed with LIBSVM tools[19] with the supporting vector machine C-SVM, and the radial kernel function. A good method for evaluating classification performance is the 10-fold cross examination, in which each group is divided into 10 subsets that are approximately equal in size. Nine folds are used for training and the last fold for evaluation. This process is repeated 10 times, leaving a single, different fold for evaluation each time.

RESULTS

Comparison of RQA measures

We computed the RQA(16) of the two groups using the Matlab Toolbox (developed for application of recurrence through the internet—available at: http://tocsy.pik-potsdam.de/; accessed August 4, 2011) and statistically analyzed RQA measures using an independent sample *t*-test. We found 12 RQA measures with significant differences (P<0.05) between the CHD patients and the normal subjects, as shown in Table 1. The measures included the RR, DEL, L, ENIR, LAM, TT, Vmax, RR_std, L_std, Lmax_std, TT_std,Vmax_std. We called this grouping the RQA (12).

Table 1 shows that RR, DEL, L, ENIR, LAM, TT, and Vmax are significantly higher in the CHD group than in the control group (P<0.05). In addition, PR_std, L_std, Lmax_std, TT_std, and Vmax_std are significantly lower in the CHD group than in the healthy group (P<0.05).

Table 1 RQA measures with significant differences by independent sample *t*- test

RQA measures	CHD patients	Normal subjects
RR	0.1166±0.021[a]	0.092±0.001
DEI	0.9990±0.0004[a]	0.9980±0.0003
L	44.618±10.256[a]	35.502±7.868
ENTR	4.464±0.194[a]	4.262±0.199
LAM	0.9988±0.0004[a]	0.9981±0.0006
TT	25.925±4.188[a]	20.084±3.232
Vmax	92.988±17.512[a]	67.473±12.250
RR_std	0.013±0.005[a]	0.010±0.004
L_std	6.131±2.136[a]	5.016±1.736
Lmax_std	16.590±3.800[a]	14.150±3.563
TT_std	2.905±1.075[a]	2.076±0.895
Vmax_std	17.517±10.454[a]	9.391±4.632

Notes: RR: recurrence rate; DEL: determinism; L: average diagonal line length; Lmax: maximum length of diagonal structures; ENTR: shannon entropy of the frequency distribution of diagonal line lengths; LAM: laminarity; TT: average length of vertical structures; Vmax: maximum length of vertical structures; RQA: recurrence quantification analysis; CHD:coronary heart disease; [a]P<0.05: significantly different from that of the normal subjects

Comparison of time-domain parameters

We statistically analyzed time-domain parameters using an independent sample *t*-test and found several time-domain parameters with significant differences (P<0.05) between the CHD patients and the controls, as shown in Table 2.

Table 2 Time-domain parameters with significant differences by an independent sample *t*-test

Time-domain parameters	CHD patients	Normal subjects
h1	19.075±7.084[a]	14.378±4.204
h3	14.702±5.054[a]	11.642±3.307
t5	0.534±0.123[a]	0.456±0.098
t	0.888±0.171[a]	0.795±0.138
h4/h1	0.420±0.098[a]	0.485±0.094
w/t	0.228±0.047[a]	0.255±0.032
As	3108.682±1171.332[a]	2339.767±768.201

Note: CHD:coronary heart disease; [a]P<0.05, significantly different from that of the normal subjects.

Table 2 indicates that there are seven time-domain parameters—h1, h3, t5, t, h4/h1, w/t, As—with significant differences. We call this group of time-domain parameters Time-domain (7). They are used for classification purposes.

Classification results with RQA measures and time-domain parameters

To show that RQA measures can distinguish the pulses of those with the CHD from the pulses of healthy persons, we computed the classification accuracy rate based on SVM with RQA measures. We used time-domain parameters for comparison. The classification accuracy is higher with RQA measures (84.11% and 88.21%) than with classic time-domain parameters (75.73%, 74.70%). Although the measures RQA(12) of the two groups are significantly different, the classification accuracy with RQA (12) is not the highest. The highest accuracy, 88.21%, occurred when all RQA measures, in RQA (16), was used for recognition. The same occurred for the time-domain parameters, where the accuracy with time-domain (15) was higher than that with time-domain (7). Therefore, the classification accuracy is highest when all RQA measures or time-domain parameters of pulse are used, as they include more abundant information than when only the parameters with significant differences are used.

DISCUSSION

Modern medical research shows that the arterial pulse is generated by contraction of the heart. Left ventricular contraction causes blood to flow into the aorta through the aortic valve. Thus, the pulse is affected not only by the condition of the heart but also by parameters such as blood pressure, vascular resistance, and arterial compliance, among others. This means that the pulse contains extensive information about the cardiovascular system.[1] Diseases such as CHD can disrupt the pumping function of the heart, causing changes in both structure and function of blood vessels, which in

turn is reflected in pulse wave morphology. If these changes are linked to health and disease and the examiner can distinguished the differences, it may be possible to diagnose cardiovascular diseases at an early stage.

The pulse signal is nonlinear, which is mainly caused by, for example, nonlinear excitation of the heart, nonlinearity of the vascular system geometry and mechanical properties, and nonlinearity of vessel movement.[20] Thus, nonlinear analysis of the pulse signal of CHD patients and normal subjects can help quantitative and qualitative analysis of pathological and physiological conditions.

The RP is a visual representation of nonlinear properties of deterministic dynamic systems. RQA is a tool that quantifies RP. In this study, we used RQA to analyze morphological changes in pulse signals for a group of patients with CHD and a group of healthy persons (controls). Various RQA measures representing different nonlinear dynamic characteristics were assessed. RR is a measure of density of recurrence, and a high RR indicates the presence of a strong cyclical process. DEL is a measure of the determinism of the system, which is the same as L. The higher their values, the stronger is the determinism of the system. The measure ENTR reflects the complexity of the deterministic structure in the system. The measures LAM, TT, and Vmax mark a time interval during which a state does not change or changes very slowly. Therefore, the higher their values, the more stable is the system.

By comparing RQA measures of the pulse morphological changes between the two groups, we found that these changes can be divided into two groups, as shown in Table 1. For one group of RQA parameters (RR, DET, L, ENTR, LAM, TT, Vmax), the values were higher in the CHD patients than in the healthy controls. Based on the physical significance of this group of parameters, we speculate that the pulse is more regular and stable in patients with CHD than in normal subjects. The cardiovascular system is closely connected with the pulse, which is consistent with the discovery in many studies that a cardiovascular system in a pathological state is usually more stable than in healthy individuals.[21,22] The values of another group of parameters (PR_std, L_std, Lmax_std, TT_std, Vmax_std) were lower in the CHD patients than in the controls, suggesting that the pulse morphology of patients with CHD has less variability. Therefore, we speculate that CHD patients have less ability to regulate their cardiovascular system than do healthy subjects. Based on this study, we identified physiological and pathological conditions that can be associated with pulse morphological changes characterized by RQA measures in the two groups. All of the RQA measures discussed in this article help us to better understand the nonlinear dynamic characteristics of the pulse signal system of CHD patients and normal subjects.

To demonstrate that RQA measures can distinguish the pulse of a CHD patient from that of a normal subject, we used an SVM to classify RQA measures and time-domain parameters. Time-domain parameters were chosen for comparison because the method is relatively mature, and these parameters are known to be clinically effective. Experimental results showed that the RQA measures can differentiate the CHD group from the healthy group with higher accuracy [(88.21% with RQA(16), 84.11% with RQA(12)], which is higher than that achieved using the classic time-domain parameters (75.73%, 74.70%). Although linear methods, such as the classic time-domain analysis, have won acceptance in objective studies of the pulse, nonlinear dynamic methods such as RQA have shown potential for distinguishing pulses of patients with CHD from those of healthy persons. However, more data are required for further evaluation of the accuracy, specificity, and sensitivity of classification.

Our study confirmed that a nonlinear dynamic method such as RQA has the potential to study functional and structural changes in the pulse noninvasively and can help with early screening for cardiovascular disease.

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