Turk J Elec Eng & Comp Sci, Vol.18, No.2, 2010, © TÜBİTAK
doi:10.3906/elk-0905-53

# Nonlinear dynamic analysis of mitral valve doppler signals: surrogate data analysis

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**Abstract**

*In our study, the nonlinear dynamics of mitral valve Doppler signals from 32 healthy and 28 patients with mitral valve stenosis was evaluated using by the computation of Lyapunov exponents, correlation dimension values and surrogate data analysis. Two chaotic features are compared for healthy and patient subjects. It was found that the largest Lyapunov exponent and correlation dimension values derived from patient subjects were larger than that of healthy subjects ($\rho < 0.005$). Surrogate data analysis was performed to determine the chaotic dynamics of Doppler signals. It was observed that the original and surrogate data have similar spectral features. Receiver operating characteristic (ROC) curves were used to evaluate the nonlinearity character Area Under the curve (AUC) values were obtained as 0.99 and 0.978 for the largest Lyapunov exponent and correlation dimension values, respectively. According to these results, Doppler signals have a nonlinear dynamic property and the largest Lyapunov exponent. Correlation dimension features can be used to detect the change in blood flow velocity of patients with mitral valve stenosis.*

**Key Words:** *Doppler, mitral valve, largest lyapunov exponent, correlation dimension, surrogate data, ROC.*

## 1. Introduction

The mitral valve allows blood to flow from the left atrium to the left ventricle. Mitral valve stenosis is a narrowing of the mitral valve caused by anatomical abnormalities in the valvular system and is an important disorder among the heart diseases. As a result, the blood's volume and pressure in the left atrium increases, so that the left atrium enlarges and beats rapidly in an irregular pattern.This in turn reduces the heart's pumping efficiency. If mitral valve stenosis is severe, pressure increases in the blood vessels of the lungs, resulting in heart failure with fluid accumulation in the lungs and a low level of oxygen in the blood. Mild mitral stenosis does not usually cause symptoms, but severe mitral stenosis can cause atrial fibrillation or heart failure [1].

These situations can be prevented by early diagnosis of mitral valve stenosis [2], the diagnosis of which is usually confirmed by;hest x-rays, electrocardiography (ECG), Doppler ultrasound imaging, invasive techniques such as angiography and transozefagial echocardiography [3-5], while heart sounds and murmers are detecting using stethoscopes. Nowadays, among these diagnostic techniques, color ultrasonic Doppler sonography is generally the most preferred technique used to detect cardiovascular disease because it is completely non-invasive, safe, considerably cheaper and quick. The Doppler ultrasound technique provides crucial information to estimate blood flow characteristics, to image blood flow regions, and to locate sites of arterial disease [6-8]. Doppler ultrasound systems are based on the principle of detecting the change in the frequency (i.e. Doppler shift) of sound pulses scattered from moving objects [9].

In the literature, there are many techniques relating to extracting information from Doppler signals. Techniques for spectral analysis of Doppler signals can extract information concerning blood flow [10,11]. Traditional linear spectral analysis techniques, such as;ower spectrum analysis, linear transformations, and parametric linear transformations, have been employed to extract information from Doppler ultrasound signals over the last two decades [12,13]. However, traditional spectral analysis techniques assume that the data is stationary. However, because Doppler signals are aperiodic and nonstationary, they possess complex nonlinear characteristics. Therefore, these signals can be modeled as chaotic signals occurring from a deterministic physical process.[14-15]

In this study, nonlinear analysis was applied to mitral valve Doppler signals to numerically define the time changing procedures. The Doppler signals were recorded from patients with mitral valve stenosis and healthy subjects to examine their nonlinear characteristics. The two strongest quantitative indicators of chaos, the maximum Lyapunov exponent and the correlation dimension, were calculated for each Doppler signal.

Our study proceeds as follows.;irst, the blood flow in the mitral valve is analyzed using Doppler signals from both patients with mitral valve stenosis and normal subjects. The existence of attractors for all subjects is found, and the correlation dimension and Lyapunov exponent of the Doppler time signals are compared. Therefore, possible distinguishing features of mitral valve signals were compared for healthy and patient subjects. Finally, a phase randomized surrogate data analysis is done on the Doppler data. The correlation dimension and Lyapunov exponent is found for each surrogate data set, and compared with that from the original data. Furthermore, because receiver operating characteristic (ROC) curve analysis is one of the better methods for evaluating the performance of a test and defining appropriate decision thresholds, ROC curves are analyzed to determine the classification accuracy between healthy and patient subject for largest Lyapunov exponent and correlation dimension values.

## 2. Materials and method

### 2.1. Demograptic acknowledgments and system hardware

In the present study, Doppler ultrasound signals were acquired from the mitral valve of 28 patients with mitral valve stenosis and 32 healthy subjects in the Cardiology Department of the Erciyes University Hospital. The patient group, which included 16 males and 12 females, were diagnosed with mitral valve stenosis using cardiac angiographies. The healthy volunteers had no clinical or echocardiographic demonstration of valvular disease or history of heart failure. Doppler echocardiographic examinations were carried out using a GE Vivid7 ultrasound device with a 5 MHz ultrasonic transducer in the Cardiology Department of the Erciyes University Hospital. The Doppler signal measurement system consists of a 5 MHz ultrasound probe used to transmit pulsed ultrasound signals, a digital Doppler unit, an input-output card, and a personal computer. All mitral valve signals were recorded on the PC and calculations were implemented using MATLAB software. The insonation angle and presentation of the ultrasound were kept constant, and sonograms were taken into consideration during the examinations. The sampling volume was placed within the center of the mitral valve. The amplification gain was carefully adjusted to obtain clean spectral output with minimal background noise on the spectral display. In the ultrasound unit, the audio output was sampled at 44100 Hz.

## 2.2. Nonlinear analysis

Mitral valve stenosis is the result of functional disorders in mitral valve and characterized by complex nonlinear behavior in Doppler signals. Therefore, nonlinearity and stationary tests were applied to the Doppler signals. In this study, the two strongest chaos indicators,;he maximal Lyapunov exponent and correlation dimension, were calculated for each signal. Also, the surrogate data sets method was applied to the mitral valve Doppler signals in order to detect possible nonlinearities.

### 2.2.1. Calculation of the largest lyapunov exponent

The Lyapunov exponent is an important index indicating the dynamic characteristics of nonlinear systems. The Lyapunov exponent gives the rate of exponential divergence from disordered initial conditions. The rate of exponential divergence can be distinctive for different orientations of initial separation vector. Then, the number of Lyapunov exponents' spectrum is equal to the number of the phase space's dimension. The maximal Lyapunov exponent determines the predictability of a dynamical system. A positive maximal Lyapunov exponent means that the system has chaotic characteristics. Because phase space trajectories that have nearly identical initial states will separate from each other at an exponentially increasing rate, chaotic systems show aperiodic dynamics [16-19]. The number of the Lyapunov exponents is equal to the dimension of the phase space [20]. If a dynamic system is chaotic, there is a positive value in the spectrum of Lyapunov exponents [16-19] . For a chaotic system, its largest Lyapunov exponent implies that the degree of chaos of the system is higher. In order to estimate the Lyapunov exponent and the correlation dimension, we have to provide the time delay information between embedding vectors.

The largest Lyapunov exponent of a chaotic system is calculated in a phase space. There are a number of methods for calculating the largest Lyapunov exponent in the literature [21]. We calculate the largest Lyapunov exponent of a time series as follows [22]:

It is assumed that, the time series of the experimental data is $\{x(t_i),\ i = 1, 2, \ldots, N\}$. Here, the embedding dimension is $m$, and the delay time is$\tau$. Then we have the reconstructed phase space:

$$X(t_i) = (x(t_i), x(t_i + \tau), x(t_i + 2\tau) \ldots, x(t_i + (m-1)\tau)), i = 1, 2, .., M \tag{1}$$

where, $x(t_i)$ is the phase point in m-dimension phase space, $M$ is the number of phase points, $M = N - (m-1)\tau$, and the time series set, $\{x(t_i),\ i = 1, 2, \ldots, N\}$, describes the evaluative trajectory of the system in the phase space. Related studies show that the reconstructed system has the same topologic property as the original system if the choice of $m$ and $\tau$ is suitable. If $\tau$ is chosen to be very small, data points cannot be distinguished from each other. If $\tau$ is chosen to be very large, data points are totally independent from each other in the statically sense. In our study, the time delay value $\tau$ has been obtained using Taken's method. Taken's time delay theorem is applicable to obtain the requested information from the time series [23]. In nonlinear systems, an average mutual function is used to select the $\tau$ value [24]. This function is applied to measurements taken from physical systems; e.g. if $x(t_i)$ is a set of measured values, the measurements are $x(t_i+\tau)$ after a time delay of $\tau$, and the average mutual function information between $t_i$n and $t_i+\tau$ is $x(t_i+\tau)\,x(t_i)$;

$$I(\tau)=\sum_{m=1}^{N} P(x(t_i),x(t_i+\tau))\log_2\left[\frac{P(x(t_i),x(t_i+\tau))}{P(x(t),x(t_i+\tau))}\right] \quad \tau>0 \tag{2}$$

The best value for $\tau$, proposed by Fraser and Swinney, is the first local minimum value of the mutual information. The mutual information is a measure of how much information can be derived from one point of a time series given complete information about the other [25,26]. The time delay where the mutual information takes on the first minimum value is chosen as the optimum delay. In our study, the time delay range was found as 12-15 time points. The time delay curve is shown in Figure 1.

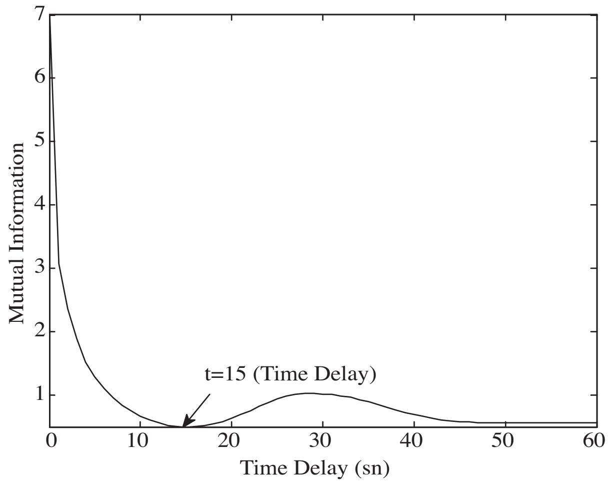


**Figure 1.** Time delay value of mitral valve Doppler signals from a healthy subject (Subj. No. 8).

The aim of phase space reconstruction is to provide a sufficiently large Euclidian space $(R_m)$, and to observe the system's attractor without any uncertainty. The higher values for $m$, two nearest points can be seen in $m$ dimension [24]. In $R_m$ space all the ambiguities can be solved. We used Cao's method [27] to find the embedded dimension. According to this method, Euclidian distance is the difference between the nearest neighborhood pairs in the $y_i(m)$ and $y_i(m+1)$. Euclidian distance is given that;

$$a(i,m)=\frac{\left\|y_i(m+1)-y_{n(i,m)}(m+1)\right\|}{\left\|y_i(m)-y_{n(i,m)}(m)\right\|} \quad i=1,2,...,N-m\tau \tag{3}$$

$$\left\|y_k(d)-y_l(d)=\max_{0\le j\le d-1}|x_{k+j\tau}-x_{l+j\tau}|\right\| \tag{4}$$

If the $m$ value is determined suitably, any two points are close to each other in $m$ dimension, and in the constructed phase space of $m+1$ dimension as well [27]. This form of pairs of points are called “right” neighbors, otherwise they are called “wrong” neighbors. If there is a wrong neighborhood, the $a(i,m)$ value is too different from the calculated threshold value. The threshold value $E(m)$ can be found from the average of all the $a(i,m)$.

$$E(m) = \frac{1}{N - mT}\sum\nolimits_{i=1}^{N-mT} a(i,m) \tag{5}$$

wherethe $E(m)$ value depends on dimension, $m$, and time delay, $\tau$.

In our study, Cao's method was applied to the Doppler signal to find the embedding dimension. The calculated embedding dimension values from mitral valve Doppler signals varies between 6-8 values. The minimum embedding dimension curve from Doppler signals is shown in Figure 2.

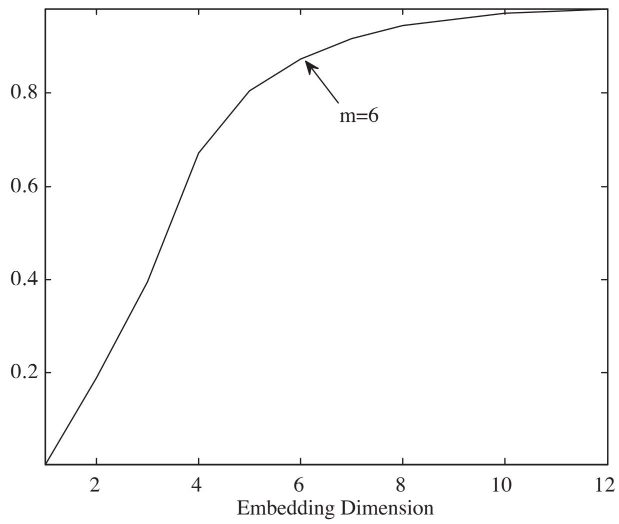


**Figure 2.** The curve of minimum embedding dimension for a healthy subject (Subj No. 8).

The nearest adjacent point $X\left(t_{\hat{j}}\right)$ for each point $X\left(t_j\right)$ on the given trajectory is searched and the temporal separation, after the phase space is reconstructed, is restricted. This shows that;

$$d_j\left(0\right) = \min_{\hat{j}} \left\| X\left(t_j\right) - X\left(t_{\hat{j}}\right) \right\| \tag{6}$$

$$\left| j - \hat{j} \right| \rangle p \tag{7}$$

where $p$ is the mean period of the time series. The largest Lyapunov exponent is computed as the mean divergence rate of the nearest adjacent point of each point on the trajectory. The distance between the pair of points after the i-th discrete time step for each point $X\left(t_j\right)$ in the phase space is calculated.

$$d_j\left(i\right) = \left| X\left(t_{j+i}\right) - X\left(t_{\hat{j}+i}\right) \right| \quad i = 1, 2, \ldots, \min\left(M - j, M - \hat{j}\right) \tag{8}$$

Then for each $i$, we calculate $y\left(i\right)$ through the $\ln d_j\left(i\right)$ mean over all j. That is,

$$y\left(i\right) = \frac{1}{q\Delta t}\sum_{j=1}^{q} \ln d_j\left(i\right) \tag{9}$$

where $q$ is the number of nonzero values of $d_j(i)$. The largest Lyapunov exponent $\lambda_l$ is the slope of the regressive line drawn using the method of least squares.

The largest Lyapunov exponent based on a time series provides a powerful tool for studying the dynamic characteristics of the physiological signals.In this study, the largest Lyapunov exponent is found for 60 data points each of both mitral valve stenosis patients and healthy subjects. The results are compared in Table 1 and the graphs shown in in Figure 3.

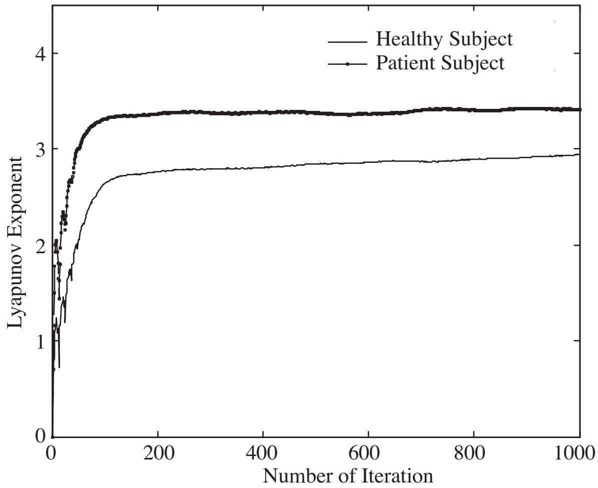


**Figure 3.** The largest Lyapunov exponent curve for a patient and healthy subject (Patient Subj. No. 24, Healthy Subj. No. 8).

**Table 1.** Largest Lyapunov exponent and correlation dimension values of original and surrogate data values.

| | Healthy Subject | Patient Subject | Surrogate Data Healthy Subject | Surrogate Data Patient Subject |
|---|---|---|---|---|
| | Mean ± std | Mean ± std | Mean ± std | Mean ± std |
| Max. Lyap. Exponent | 3.0485 ± 0.2063 | 3.9351 ± 0.4142 | 2.4680 ± 0.2321 (S=2.5011) | 3.2491 ± 0.1514 (S=4.5310) |
| Max. Correlation Dimension | 2.3013 ± 0.2184 | 3.2516 ± 0.4842 | 2.0017 ± 0.1263 (S=2.4699) | 2.7841 ± 0.1185 (S=3.9451) |

### 2.2.2. Correlation dimension

In the nonlinear analysis of dynamic systems, the correlation dimension is a measure of the dimensionality of the space, which is filled by a set of random points, often referred to as a type of fractal dimension. The correlation dimension method is calculated from time series to determine the approximate dimension of the phase space. When an attractor has chaotic behaviors, the neighboring trajectories will diverge exponentially in time and the points on these trajectories will be dynamically uncorrelated. Because the points located on the attractor are correlated in phase space, they appear as randomly scattered points. The correlation integral $C(m,\varepsilon)$ is the weight $p(\varepsilon)$ of a typical $\varepsilon$-ball covering part of steady set scales with diameter given by $p(\varepsilon) = \varepsilon^D$, where the value, D, depends on the weight factor. The correlation dimension is the square of the probability $p_i$ of the point set inside the ball. The correlation integral is defined as [28];

$$C(m,\varepsilon) = \frac{1}{N_{pairs}} \sum_{j=m}^{N} \sum_{k\langle j-w}^{N} \Theta\left(\varepsilon - |s_j - s_k|\right) \tag{10}$$

Here, the value $s_j$ is the m-dimensional time delay vector, $N_{pairs} = (N-m+1)(N-m-w+1)/2$is the number of point pairs covered by the sums, $\Theta$the Heaviside step function, and $\omega$ is the Theiler window [29]. Since appropriate elements of a time series are not usually independent, Theiler suggested omitting these temporally correlated points from the pair counting operation. This is realized by simply ignoring all points pairs whose time indices differ by less than $\omega$. According to Garssberg and Proccia, the correlation integral $C(m,\varepsilon)$ behaves as a power of $D_2$ [30]; and can be calculated as

$$C(m,\varepsilon) \propto \varepsilon^{D_2} \tag{11}$$

The $D_2$ exponent is defined as the correlation dimension and can be calculated by;

$$D_2 = \lim_{\varepsilon \to o} \frac{\log\left(C\left(\varepsilon\right)\right)}{\log\left(\varepsilon\right)} \tag{12}$$

There are many methods of measuring fractal dimension but the correlation dimension has the advantage of being straightforwardly and quickly calculated, and is often in agreement with other calculations of dimension.

## 2.3. Test of nonlinearity: surrogate data analysis

One of the important criteria for determining chaotic dynamics is nonlinearity analysis. The surrogate data analysis method developed by Theiler determines any nonlinearity present in a time series [31]. This technique is used to determine whether an observed time series is statistically different from a specified class of system [31], known as the null hypothesis. The surrogate time series is constructed from an original time series to obtain information about the dynamic behavior of the time series. Surrogate data is produced by phase randomizing of the original data and has similar spectral features, such as;ean, variance, and autocorrelation, and a power spectrum similar to that of the original data. This analysis technique involves the following steps [31]. First, ; surrogate time series is configured from the original time series by calculating its Discrete Fourier Transform (DFT). Second, ;ts phase is randomly varied and the inverse transformation of the resulting series is computed. The new series formed in this way will have the same autocorrelation and power spectral density as the original time series for nonlinear signals. The final step is to test against the null hypothesis using measurements of chaotic dynamics, such as the correlation dimensionand largest Lyapunov exponent. As a result, the values computed from the original time series is not significantly different from that computed from the surrogate time series. If the difference is statistically significant, the null hypothesis is rejected. A “significance” measure of this difference obtained from the correlation dimension (CD) and largest Lyapunov exponent may be defined as

$$S = \frac{\left| CD_{original} - \bar{CD}_{surrogate} \right|}{\sigma_{CD_{surrogate}}} \tag{13}$$

To improve the robustness of the test, several surrogate sets are formed and their average correlation dimension and largest Lypunov exponent is computed. Hoyer [25] and Theiler [32] found that if S > 10, the null hypothesis can be rejected.

## 3. Results and discussion

During echocardiographic assessments, the Doppler ultrasound technique provides crucial information for estimating the blood flow characteristics of mitral valve stenosis. Unlike traditional spectral analysis techniques, in our study, mitral valve Doppler signals were analyzed as chaotic signals to examine the blood flow, because of their aperiodic and nonstationary behavior. Time delay was determined using the mutual information method, as shown in Figure 1, and the first minimum value of the time delay graph was found to be the optimum time delay for calculating the Lyapunov exponent, an indicator of the dynamic characteristics of nonlinear systems. After that, the minimum embedding dimension was calculated by Cao's method, as shown in Figure 2, in which there is a kink. The largest Lyapunov exponent values are found for 60 data pointseach of both mitral valve stenosis patients and healthy subjects. The Lyapunov exponents are shown in Figure 3. The largest Lyapunov exponent found for healthy subjects and patients is compared in Figure 4.

In this study, random surrogate mitral valve data sets are constructed for each signal. Nonlinearity is tested by comparing the chaotic dynamic measures obtained from the original data with those obtained from surrogate data sets. The results of these comparisons, the largest Lyapunov exponent and correlation dimension values for real and surrogate data, are given in Table 1 for both patients with mitral valve stenosis and healthy subjects. The mean values of the largest Lyapunov exponent computed from original data for healthy subjects and patients with mitral valve stenosis are calculated as $3.0485 \pm 0.2063$ and $3.9351 \pm 0.4142$, respectively, as shown in Table 1. The mean values of the correlation dimension computed from original data for healthy subjects and patients are found as $2.3013 \pm 0.2184$ and $3.2516 \pm 0.4842$, respectively, also shown in Table 1. The mean values of the largest Lyapunov exponent derived from surrogate data for healthy subjects and patients with mitral valve stenosis are calculated as $2.468 \pm 0.2321$ and $3.2491 \pm 0.1514$, respectively, as shown in Table 1.

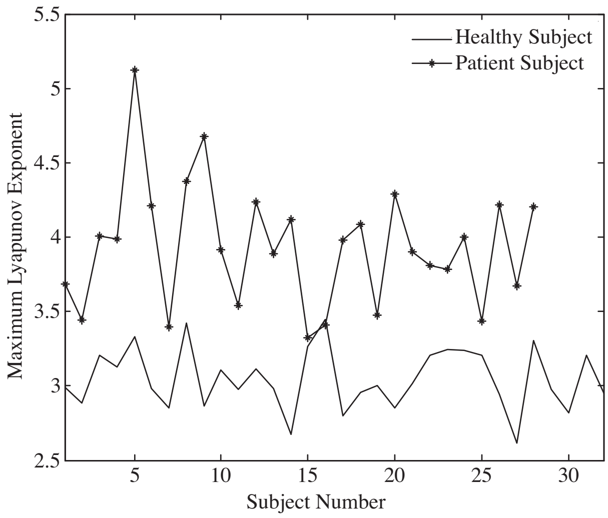


**Figure 4.** Graph comparing the value of the largest Lyapunov exponent of healthy subjects and patients.

The mean values of the correlation dimension derived from surrogate data for healthy subjects and patients are computed as 2.0017±0.1263 and 2.7841±0.1185, respectively, also shown in Table 1. The values of S, defined in Eq. 13, were determined from original and surrogate data (see Table 1). All $S$ values are smaller than 10, therefore, the null hypothesis can be accepted.

A raised value of correlation dimension indicates that the randomness of the mitral valve activity has increased during mitral valve stenosis. The largest Lyapunov exponent behaves as an indicator long-range behavior. The largest Lyapunov exponent rises during mitral valve stenosis. So, from this result, it was determined that nonlinearity also increases during mitral valve stenosis. ROC curves, which are shown in Figure 5 and Figure 6, represent the performance of the test parameter, i.e. the largest Lyapunov exponent and correlation dimension values derived from the time series Doppler signals. Area under the ROC curve (AUC) values are calculated as 0.99 and 0.978. For AUC values approaching 1, the classification accuracy is very high. These results indicate that nonlinear analysis of mitral valve Doppler signals is an effective interpretation method for diagnosing mitral valve stenosis.

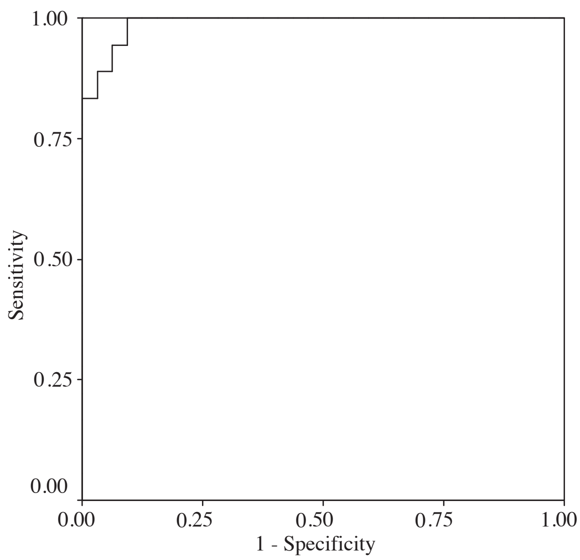


**Figure 5.** ROC curve for largest Lyapunov exponent (AUC for largest Lyapunov exponent=0.99).

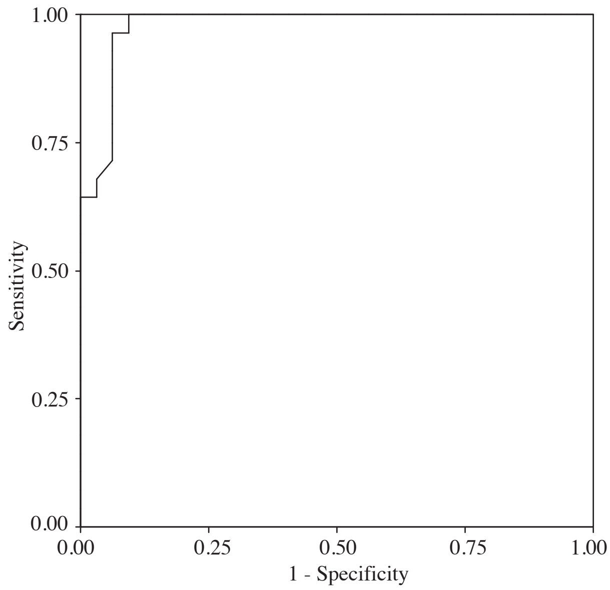


**Figure 6.** ROC curve for correlation dimension (AUC for correlation dimension=0.978).

## 4. Conclusion

In this study, nonlinear feature extraction from mitral valve Doppler signals was performed by computing Lyapunov exponents and correlation dimension values. Based on nonlinear analysis, we calculated that two chaotic invariant measures could be used for determining the blood flow velocity variation due to mitral valve stenosis. The discrimination of Doppler ultrasound signals was accomplished using the method of nonlinear analysis. It was shown that the largest Lyapunov exponent and correlation dimension values increase in the case of mitral valve stenosis. Furthermore, using surrogate data analysis it was found that mitral valve Doppler signals showed a nonlinear character for $S < 10$. The ROC curves also suggested that the classification performance of two chaotic invariants was very promising, indicating the success of the feature extraction method. In future studies, the number of patients may be increased and classified with respect to the degree of mitral valve stenosis.

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