Comparison of Sample Entropy and AR-models for Heart Sound-based Detection of Coronary Artery Disease

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Abstract

The first reported observations of rare diastolic murmurs in patients with coronary artery disease (CAD) date back to the late sixties. Subsequently several studies have the examined signal processing methods for identification of the weak murmurs. One such method is autoregressive (AR) models. A recent study showed that CAD changes the entropy of the diastolic sound. The aim of the current study is to analyze the relationship between features from an AR-model and features describing signal entropy. Sample entropy and the poles of AR models were calculated from diastolic intervals in heart sound recordings randomly selected from a database of stethoscope recordings of good quality. In total 100 recordings were analyzed (50 patients with two recordings from each). The recordings were band pass filtered with a 8 order Chebyshev filter with pass band edge frequency at 50 Hz and 500 Hz. The result shows that both measures equally separates the CAD patients from non-CAD patients, but the measures are strongly correlated.

1. Introduction

Coronary artery disease is the top single cause of death in the western world. But established diagnostic methods, such as coronary angiography and exercise tests, are costly, time consuming and they are a burden for the patients. Previous studies have shown that heart sounds may contain weak murmurs caused by turbulence in poststenotic blood flow in the coronary arteries and that this turbulence related sound is a potential diagnostic indicator of CAD [1]. The murmurs are rarely audible, but several signal processing algorithms to automatically detect the murmurs have been proposed [1-3]. Diastolic heart sounds may thus be the basis for a cheap, fast, noninvasive diagnostic method for CAD, with minimal inconvenience for the patient.

Previous studies have examined various signal processing methods for identification of the weak heart murmurs. An established method for quantifying the diastolic heart sounds is autoregressive (AR) modeling of the diastolic sounds. Akay et al. found that poles in AR-models of diastolic heart sounds from CAD patients differed from non-CAD patients [1]. The presumption for the application of AR-models is that the Murmur results from a linear stochastic process.

Recent studies have applied methods for nonlinear signals to analyze various types of cardiovascular murmurs. For example, using the method of approximate entropy Akay et al. found that CAD increases the entropy of the diastolic heart sound[3]. The advantage of such methods is their ability to handle nonlinear dynamics. Power spectra methods such as AR-models will not separate nonlinear and linear processes since the phase of the signal is required for identification of nonlinearity in the frequency domain.

In a recent study [4,5] no evidence of nonlinearity in cardiovascular murmurs was found since the murmurs showed great similarity with a linear stochastic process. If the murmur can be described as a linear stochastic process its statistical properties are fully described by its power spectrum and the nonlinear methods will not yield additional information.

The aim of the current study is to examine if sample entropy yields additional information related to classification of CAD compared to AR-models. Sample entropy is a measure of signal regularity, similar to approximate entropy, but less sensitive to the length of signal [6].

2. Method

2.1. Data collection

Two heart sound recordings from each of 50 patients (100 recordings in total) were randomly selected from a database of heart sounds recorded from patients referred for coronary angiography at the Department of Cardiology at Aalborg Hospital. The recordings were made from the left 4th intercostal space on the chest of patients using a commercially available electronic stethoscope (3M Littmann E4000). Coronary angiography

images from the patients were analyzed with quantitative coronary angiography. Patients with at least one diameter reduction of more than 50% were defined as CAD subjects and the remaining patients were defined as non-CAD subjects. Inclusion criteria were normal heart rhythm and recordings being free of significant noise.

2.2. Preprocessing

The recordings were automatically segmented into diastolic and systolic periods using the duration dependent hidden Markov model develop by the current authors[7,8]. The second heart sound plus 20 ms was excluded from the diastolic period to avoid influence of the second heart sound. The diastolic periods were forward-backward band-pass filtered with a 4th order Chebyshev filter with pass-band edge frequencies at 50 Hz and 500 Hz.

Heart sound recordings obtained with a handheld stethoscope often are contaminated with noise spikes caused by friction between the stethoscope and the skin. To avoid the noise spikes the sub-segmentation method by Schmidt et al. [2] was applied before extraction of the AR-poles and the Sample entropy. The sub-segmentation method divided the diastolic periods into sub-segments of short duration and removed sub-segments with high variance. In the current implementation the duration of the sub-segments was 512 samples (128 ms) and the threshold for the allowed variance in the sub-segment was 3 times the median variance of all sub-segments.

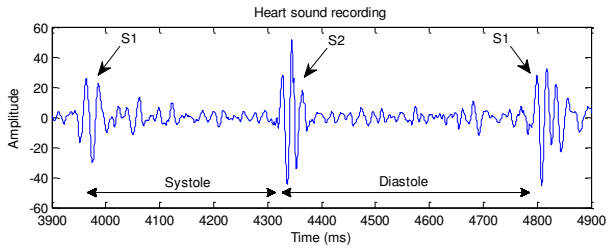

Figure 1. Typical heart sound recording illustrating first (S1) and second heart sound (S2).

2.3. Sample Entropy

Sample entropy depends on reconstruction of the m dimension phase space. The phase space of a multi dimensional dynamic system may be reconstructed from a single-dimension signal using the delay method, where each point in the reconstructed phase space consists of a vector of m signal points, sampled from the signal at intervals τ:.

$$X_i = [x(t_i), x(t_{i+\tau}), \ldots . x(t_{i+(m-1)\tau})]^T$$

Sample entropy is the negative logarithm of the conditional probability that a point which repeats itself within a tolerance of ϵ in an m dimensional phase space will repeat itself in an m+1 dimensional phase space.

$$SampEn(m, \varepsilon) = -\log\left(\frac{\mathrm{C(m+1,\varepsilon)}}{\mathrm{C(m,\varepsilon)}}\right)$$

C(m, ε) is the number of repeating points in the m dimensional phase space. Repeating was defined as points closer in a Euclidean sense than ε to the examined point. Sample entropy were calculated using two different tolerances ε=0.2 and ε=0.5 times the standard deviation of the signal. To fully represent the dynamic system, the embedding dimension, m, and embedding delay, τ, must be proper. In the current study a systematic approach was applied, by calculating the embedding matrix for Sample entropy with several combinations of embedding dimensions and embedding delays and afterward the main components was extracted using principle component analysis (PCA). Sample entropy was calculated with embedding dimensions from m =2 to 8 and embedding delays τ=1, 3, 5, 8, 12. In total 70 features were calculated using sample entropy.

2.4. AR-models

The presumption of the AR model is that each sample of the signal is an expression of a linear combination of the previous samples plus noise.

$$y(n) = -\sum_{p=1}^{M} a_p\, y(n-p) + e(n)$$

where y(n) is the signal to be modeled, a_p are the model coefficients, M is the model order and e(n) is the noise which is independent from the previous samples. In the current application the coefficients of the AR-model were adjusted with the forward-backward method to maximize the models capacity to model the signal. The features were calculated as the pole magnitudes and the pole angles of the coefficients. The AR features were calculated using model orders of M=2, 4, 6, 8, 10, 12. In total 42 features were calculated from the AR-models.

2.5. Comparison of AR-poles and sample entropy

The purpose of the analysis is to compare the classification potential and the relation between the two types of features. The similarity between AR and sample entroy migth not be expressed between two single features. Therefor were the dominating components extracted from the two feature groups by PCA.The classification performance of the six most dominating PCA components was analyzed.

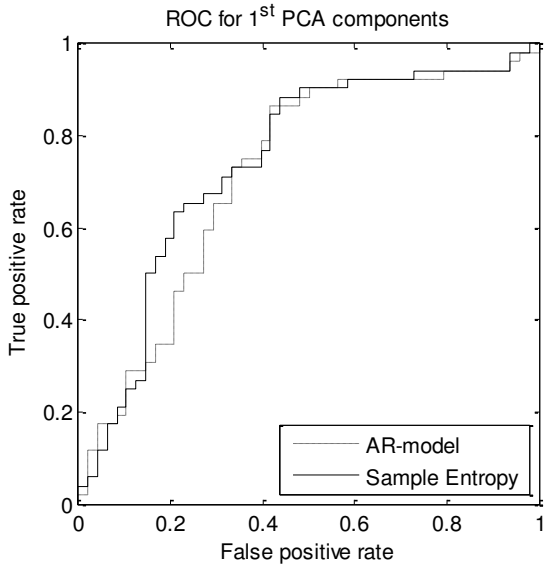

Figure 2. Receiver operating characteristic (ROC) of the 1st PCA components

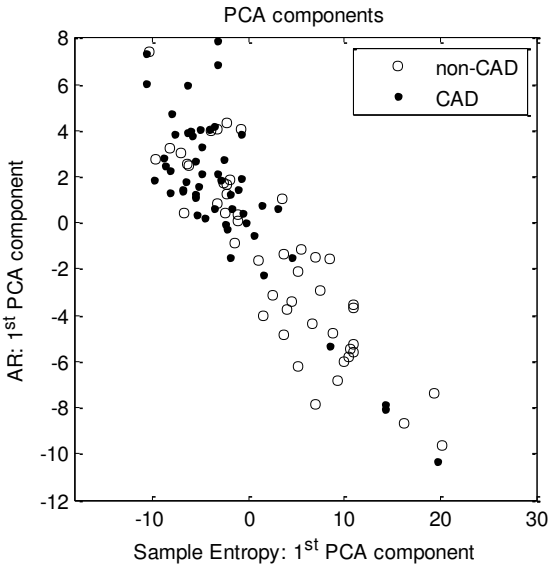

Figure 3. Scatter plots of the relationship between the 1st PCA components of each feature type.

The classification performance was measured as the area under the receiver operating characteristic (AUC). The receiver operating characteristic (ROC) was calculated using the Wilcoxon non-parametric method and the 0.95% confidence intervals (CI) were calculated using a bootstrapping method for repeated measurement [9]. The significance levels used in the the estimation of the CI were Bonferroni corrected to account for the high number of features.

The difference between the AUC two measures was calculated by subtraction of the two measures and the CI intervals for the area differences was estimated with the U-statistics approach by DeLong et al. [10].

3. Results

In both feature groups the first principle component was the component with the best classification potential, the AUC was 0.719 (CI: 0.53-0.88) for the 1st principle component of the AR features and 0.743 (CI: 0.57-0.89) for the 1st principle component from Sample entropy, see figure 2. The difference between the two areas was 0.024 (CI:-0.046-0.095). Since zero was in included in the confidence interval the difference between the areas was not significant.

The correlation between the two components was -0.88, see figure 3. Table 1 lists AUC for the 6 dominating components from each feature type.

Table 1. The AUC and the cumulative eigenvalues for the 6 dominating PCA components from both AR- and Sample entropy.

PCA component	AUC	Cumulative eigenvalues
AR-PCA1	0.72	0.39
AR-PCA2	0.55	0.56
AR-PCA3	0.57	0.69
AR-PCA4	0.50	0.81
AR-PCA5	0.51	0.85
AR-PCA6	0.60	0.90
SE-PCA1	0.74	0.85
SE-PCA2	0.57	0.89
SE-PCA3	0.52	0.91
SE-PCA4	0.58	0.93
SE-PCA5	0.55	0.94
SE-PCA6	0.60	0.95

4. Discussion

PCA components from both the AR-models and sample entropy identified a significant difference between CAD and non-CAD subjects. There was no significant difference between the classification performance of sample entropy and the AR-model and the correlation between the best features from each of the two groups was high. This indicates that Sample entropy and the AR-poles are equivalent in the current data and that sample entropy is not affected by a significant nonlinear component.

In conclusion, the current study compares sample entropy's capability to separate CAD patient from non-CAD patients with features from AR-models. The result shows that both measures equally separate CAD patients from non-CAD patients, and that the measures are strongly correlated. The information gained by complementary use of both features may thus be limited.

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