Coronary Artery Disease and Low Frequency Heart Sound Signatures

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Abstract

The aim of the current study was to study the low-frequency power distribution of diastolic heart sounds in patients with coronary artery disease (CAD).

Heart sound recordings were made from the 4th intercostal space in 132 patients referred for elective coronary angiography. CAD patients were defined as subjects with at least one stenosis with a diameter reduction of at least 50% as identified with quantitative coronary angiography. The diastolic heart sounds were analyzed using short-time Fourier transform (STFT) and autoregressive (AR) models. The STFT analyses showed that the energy below 100 Hz was increased approximately 150 ms after the second heart sound in CAD patients. The AR-spectra of the band-pass filtered (20-100 Hz) diastolic heart sound showed that the frequency distribution shifted towards lower frequencies in the case of CAD. The cause of these changes might be due to variations in ventricular filling patterns.

1. Introduction

Coronary artery disease (CAD) accounts for approximately 20% of the deaths in the European Union. Since established diagnostic methods, such as coronary angiography and exercise tests, are costly and time consuming, a fast and low cost non-invasive diagnostic method will provide new diagnostic opportunities.

One approach for non-invasive detection of CAD is analyses of heart sounds. Several studies have shown that CAD cause an increase in energy of the diastolic sound at higher frequencies (>100-200Hz) [1-4]. This increase is generally associated with weak murmurs caused by post-stenotic turbulence in the coronary arteries. However, recent studies by the current group showed that coronary artery disease (CAD) also alters the frequency distribution of diastolic heart sound at lower frequencies (20-125 Hz) by shifting the energy toward lower frequencies [5-7]. The origin of this phenomenon is unknown, but it might be caused by the CAD murmurs or by changes in the ventricle movements.

The aim of the current study was to further study this phenomenon in a new dataset using time-frequency analysis and AR-modelling.

2. Method

2.1. Data collection

Heart sound recordings from 132 patients were randomly selected from a database of heart sounds recorded from patients referred for coronary angiography at the Department of Cardiology at Rigshospitalet (Copenhagen University Hospital, Denmark). The recordings were made from the left 4th intercostal space on the chest of patients in supine position using a newly developed acoustic sensor and a dedicated acquisition system described elsewhere [8,9]. The sample rate of the acquisition system was 48 KHz, but the recordings were later down sampled to 16 KHz. The patient was asked to stop breathing four periods of 8 seconds. The analysis in the current study was focused on the recordings in these periods only. Coronary angiography images from the patients were analysed with quantitative coronary angiography. Patients with at least one diameter reduction of more than 50% were defined as CAD subjects and the patients without any identifiable stenosis were defined as non-CAD subjects. To simplify the analysis, patients whose largest stenosis was in the range 0-50% were excluded from the analysis. Inclusion criteria were normal heart rhythm, no diastolic murmurs due to heart valve defects and a diastolic period of at least 400 ms. The average characteristics of the patient population can be seen in table 1.

Table 1. Characteristics of patient population

<table>
<thead>
<tr>
<th></th>
<th>Non-CAD</th>
<th>CAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>42</td>
<td>90</td>
</tr>
<tr>
<td>Age (years)</td>
<td>61.1</td>
<td>65.3</td>
</tr>
<tr>
<td>Male</td>
<td>23</td>
<td>58</td>
</tr>
<tr>
<td>Females</td>
<td>19</td>
<td>32</td>
</tr>
<tr>
<td>BMI</td>
<td>28.3</td>
<td>27.9</td>
</tr>
<tr>
<td>Blood pressure (Sys/Dia)</td>
<td>143/83</td>
<td>146/82</td>
</tr>
</tbody>
</table>
2.2. Pre-processing

The recordings were automatically segmented into diastolic and systolic periods using the duration dependent hidden Markov model develop by [10]. To further optimize the segmentation each beat was aligned according to the second heart sound (S2) using cross correlation, see figure 1. The diastolic periods were high-pass filtered with a 4th order Butterworth filter with break frequencies at 20 Hz.

To limit the influence of ambient noise, noisy diastoles were discharged automatically using the following approach. The external room noise was measured using an external microphone. Using the external signal the energy of external noise was calculated for each beat and a threshold for external room noise was set as the 90% percentile of external room noise in the entire dataset. Beats which external sound pressure exceed this threshold was then excluded from analysis. Next the recordings were cleaned for internal body noise by excluding beats where the diastolic energy was 5 dB higher than the median diastole energy of all beats in the given recording. This process was repeated until no beat exceeded the threshold.

![Figure 1. Figure 2. Beats from one recording, aligned to the second heart sound (S2). The diastolic period is initialized by S2 and terminated by the first heart sound (S1). The periods analysed in the current study are indicated.](image)

3. Short time Fourier transform

To analyse the frequency distribution the diastolic sounds from 50 ms before the S2 sound to 400 ms after the S2 sound were examined using Short time Fourier transform (STFT). A subject-representative STFT estimate was generated as the median of the STFTs from the individual beats in the recording. To limit spectral leakage a Hamming window was applied. The window length in the STFT was 50 ms and a 90% overlap was used. A mean STFT was estimated for both the non-CAD group and the CAD group.

To evaluate the difference between the non-CAD and CAD groups the mean STFTs from each group was subtracted (in the logarithmic domain) from each other. The statistical significance level was estimated using one sided t-tests.

2.4. AR-models

AR models have been used successfully in several studies to model diastolic hearts sound [2,11]. 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 modelled, \( a_p \) 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 AR model is used to quantify the changes in frequency distribution in the diastole period by estimating the pole angles. To focus the analyses on the low frequency content of the signal, the diastoles were band pass filtered before modelling, using a 4th order Butterworth filter with cut off frequencies at 20 and 100 Hz. Using the Akaike information criterion the model order (\( M \)) was chosen as 11. To avoid the influence of S2 sounds and potential S3 sounds the analysis period started 250 ms after S2 sound. The analysis window ended 500 ms after S2 or in cases of shorter diastoles 50 ms before the S1 sound to avoid potential S4 sounds. The analysis window was then divided into sub-segments of 50 ms before the poles of the AR-models were estimated in each sub-segment. Representative poles were then calculated as the mean of AR-poles from the sub-segments in all beats. To evaluate the classification performance of the pole angles the area under receiver operating characteristic curve was calculated. To test if the pole angle differed significantly between the two groups a two side t-test was applied.

3. Results

Mean STFT estimates of the diastolic periods in non-CAD and CAD subjects are seen in figure 2. Furthermore, the two mean spectra were subtracted from each other (in the logarithmic domain) and shown in the right part of Figure 2. The energy is increased in the CAD subjects at frequencies below 100 Hz, approximately 200 ms after the second heart sound. Also the low frequency energy around S2 is slightly increased. Figure 3 shows the significance levels of the difference between the two groups.

As seen in table 2, the pole angles of the AR-model shift towards lower frequencies in the CAD subjects. This phenomena was significant (\( \alpha=0.05 \)) for the second, third and fourth pole.
Arbitrary amplitude (dB)
Frequency (Hz)

Figure 2. Estimates of the average time frequency distribution of diastolic heart sounds from CAD and non-CAD patients and the difference between them.

Figure 3. P-values for significance between the CAD and Non-CAD spectrums.

Figure 4. AR-based frequency spectrums of the diastolic segments.

This is further illustrated in figure 4 where the diastolic frequency spectrums were estimated by Fourier transforming the AR-models. The peaks which represent the pole locations are placed at lower frequencies in the CAD subjects compared to the non-CAD subjects.

4. Discussion

The current result confirms recent studies which showed that the diastolic energy was increased at lower frequencies in CAD subjects compared to non-CAD subjects. Not only was the energy below 100 Hz increased, but the energy was shifted to lower frequencies according to the AR-model. That there was no significant difference from 100-200 ms after the second heart sound might be due to the presence of the third heart sound in some recordings.

Why CAD increases the energy at lower frequencies is unknown. One possible source could be murmurs originating from the post-stenotic region in the coronary arteries, but these are usually expected to spread to higher frequencies [1]. Another explanation could be a change of resonance frequency of the coronary arteries. Simulations by Wang et Al. showed that a resonance component of the coronary arteries moved to lower frequencies in the case of CAD [12]. However it is uncertain if the resonance frequency from the small coronary arteries can significantly increase the already intense low frequency power at 40 dB/Hz with 3-5 dB. A more likely source is changes in ventricular filling patterns. It is known that the ventricular compliance may decrease in CAD subjects [1]. Another explanation could be a change of correlation between low frequency heart sound changes and ventricle movements.

The actual diagnostic value of the low frequency component is still unknown. Ongoing work will try to combine it with other measures estimated from the heart sounds, such as features which describe changes at higher frequencies.

<table>
<thead>
<tr>
<th>Table 2. AR-pole angles in Hz</th>
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<tbody>
<tr>
<td>1. pole</td>
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<tr>
<td>Mean (±std)</td>
</tr>
<tr>
<td>Non-CAD</td>
</tr>
<tr>
<td>CAD</td>
</tr>
<tr>
<td>p-value</td>
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<tr>
<td>AUC</td>
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Acarix is a registered trademark of Acarix A/S (www.acarix.com) committed to development of CAD-diagnostic equipment.

Conflict of interest

The authors Egon Toft and Samuel E. Schmidt are minor shareholders in Acarix A/S. Samuel E. Schmidt works as a part time consultant for Acarix A/S.

References


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