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Abstract	
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Assessing Cardiovascular Comorbidities in Sleep Apnea Patients Using SpO_2

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Abstract

Several studies have demonstrated the relationship between Obstructive Sleep Apnea Syndrome (OSAS) and cardiovascular comorbidities. It is even suggested that timely OSAS treatment can prevent the development of such comorbidities. Hence, it is important to identify the patients with a high risk for cardiovascular comorbidities and prioritize their treatment. This study investigates if the blood oxygen saturation (SpO_2) signal could be used to assess the cardiovascular status of the patient. This on its turn can improve the phenotyping of OSAS patients.

SpO_2 signals from 100 OSAS patients, of which half have a known cardiovascular comorbidity, are investigated. The individual oxygen desaturations are extracted and these desaturations are classified as caused by a respiratory event or not. This classification is then used to compute patient averaged features of apneic and non-apneic desaturations. The most discriminative features to differentiate between patients with and without cardiac comorbidity are selected. Using these, a Least-squares Support Vector Machine (LS-SVM) classifier reached an accuracy of 76.7 % on separating test set patients according to their cardiac comorbidity status.

These results suggest that the analysis of the SpO_2 signal has an added value in the assessment of the cardiovascular risk of OSAS patients.

1. Introduction

Obstructive Sleep Apnea Syndrome (OSAS) is the most common sleep related breathing disorder. It affects around 13 % of men and 6 % of women, among adults between 30 and 70 years old [1]. The disease presents itself as complete or partial cessations of breathing during the night due to blockage of the upper airways or loss of respiratory drive. These events usually result in hypoxia and/or arousal, which trigger the restoration of normal breathing.

The hypoxia, arousals, and negative intrathoracic pressure swings due to respiratory events deteriorate the cardiovascular system via different pathways. Changes in both parasympathetic and sympathetic activity have been recorded, as well as a decreased cardiac output, inflammation and endothelial dysfunction [2].

These adverse effects cause patients with OSAS to have an increased risk of developing hypertension, diabetes and cardiovascular events such as myocardial infarction and stroke, even when adjusted for confounding factors such as obesity [2]. An observational study by Marin et al., showed that patients with untreated severe OSAS have an adjusted odds ratio of 3.17 for developing non-fatal cardiovascular events with respect to healthy subjects [3]. The patient group treated with continuous positive airway pressure (CPAP), however, had no significant increase in risk. These results suggest that treatment with CPAP can decrease the risk of developing cardiovascular events.

Therefore, it is important to identify high risk patients in order to avert severe cardiovascular comorbidities by timely OSAS treatment. Nowadays OSAS severity is defined by the apnea hypopnea index (AHI), which corresponds to the amount of respiratory events per hour of sleep. It has been shown, however, that the AHI is not a very good predictor for cardiovascular events, when adjusted for confounding factors [4]. In contrast, the time spent with oxygen saturation below 90 %, proved to be a significant predictor. This indicates that the SpO_2 signal contains useful information with respect to the cardiovascular comorbidity of the patient.

In this study, parameters of individual oxygen desaturations due to respiratory events will be compared for OSAS patients with and without cardiovascular comorbidity. Using the most discriminative features, an indication of the presence of cardiovascular comorbidities is automatically computed.

2. Methodology

An overview of the methodology used in this study can be found in Figure 1. The different steps will be explained in the following paragraphs, starting with a description of the used dataset.

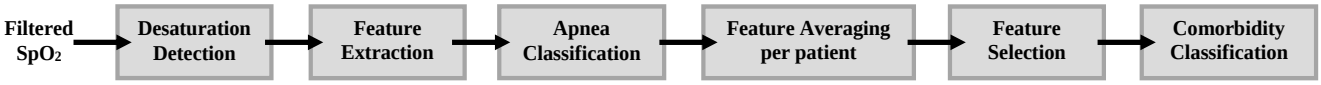

Figure 1. Overview of the proposed algorithm to create a cardiovascular comorbidity detector.

2.1. Data

In this study, SpO_2 signals extracted from polysomnography (PSG) recordings of patients referred to the University Hospitals Leuven are analysed. The SpO_2 signals were recorded using a Nonin oximeter and sampled at 500 Hz. The PSG data was annotated by sleep specialists according to the AASM 2012 scoring rules [5]. Additionally, an assessment of cardiovascular comorbidities was made for each patient. The presence of hypertension, hyperlipidaemia and diabetes were listed as well as previous occurrences of myocardial infarction or stroke. Patients with an AHI larger than 15 were selected from the hospital's database. Subjects with at least one of the above cardiovascular comorbidities were matched for age, gender, body mass index (BMI) and smoking status with a patient without any comorbidity.

A dataset of 100 patients was collected, including 78 men and 22 women with an average age of 48 ± 10.8 years and a BMI of 30 ± 4.5 kg/m^2. 24 % of the patients smoked at the time of the PSG and the average AHI is 41.3 ± 22.0. Hyperlipidaemia and hypertension were the most common comorbidities, present in, respectively, 46 and 40 subjects, 5 patients suffered from diabetes, 4 patients had a myocardial infarction and 2 a stroke.

This dataset is split into a training set of 70 patients and a test set of 30 patients, using the patient characteristics and making sure half of the patients in each set have a comorbidity.

2.2. SpO_2 preprocessing

The aim of the study is to detect changes in the SpO_2 desaturations due to cardiovascular comorbidities. Therefore, the individual desaturations need to be extracted from the SpO_2 signal. Before doing so, zero level artefacts caused by sensor disconnections are detected when the signal drops below 50 %. An interval around the drop is replaced by linear interpolation. Sharp changes and ripples due to oversampling are corrected by means of a moving average filter of 3 seconds. Afterwards the signal is down sampled to 1 Hz.

The desaturation events are detected as peaks in the derivative of this filtered signal. Each event consists of a desaturation part where the SpO_2 drops, possibly followed by a stable SpO_2 period, and ending with the resaturation where the SpO_2 tends to go back to baseline level. The start and end points of the desaturation and the following resaturation are used to segment the signals. Events with a drop of more than 1 % in SpO_2 and a total duration of less than 120 s are taken into account.

In addition, the SpO_2 baseline is defined as the 95th percentile from the last minute of artefact and desaturation free signal.

2.3. Feature extraction

A total of 143 features and their logarithmic transformation were extracted from all detected events. Simple time-domain features are extracted such as the amplitudes, lengths and slopes of the desaturation and resaturation. Furthermore, the obstruction severity, defined as the length of the event multiplied by the area under baseline is extracted [6]. Additionally, the time and area that the SpO_2 spends under baseline or 2, 3 or 4 % below baseline during the event is computed [7,8].

In addition, the minimum, maximum, mean, median and variance are extracted from the SpO_2 signal and its first, second and third order derivative. These features are extracted 3 times, for the complete event, the desaturation and the resaturation part. Moreover, deviations of the minima and maxima from the above mentioned medians and means are computed, as Koley et al. did for the detection of respiratory events in the SpO_2 signal [8].

The last group of features takes into account the fact that patients often have episodes where a sequence of respiratory events occur in close succession. To assess these quasi-periodicities, a window of five minutes around the detected desaturation is analyzed. The autocorrelation (AC) function of this segment is computed and the relative amplitude and position of the first peak, representing the delay between respiratory events, are extracted. Another way to analyze these segments is by using Phase Rectified Signal Averaging (PRSA), which detects quasi-periodicities in non-stationary data [9]. The PRSA curve is computed as the average of all 10 second downward or upward fragments in the five minute segment, representing respectively the averaged desaturation and resaturation. From this curve, the maximum amplitude difference and slope over the entire curve are extracted.

2.4. Respiratory event classification

Using these features, a classifier is built to separate the detected desaturations caused by an annotated respiratory event and desaturations not related to respiratory events. Using feature selection techniques, the six most discriminative features are selected. These contain the

duration and area under the baseline of the desaturation part, the time spent under 2 % below the baseline, the PRSA amplitude for desaturations and resaturations and the relative amplitude of the first AC peak.

With these six features, a Least Squares Support Vector Machine (LS-SVM) classifier [10], using an RBF kernel is built based on data of the 70 training patients.

2.5. Cardiac comorbidity classification

The estimated class labels obtained by the respiratory event classification are used to separate the desaturations in two groups, one containing the desaturations caused by respiratory events (apneic), the second one containing all other desaturations (non-apneic). Patient averaged features are computed for each group, once considering all desaturations, and a second time only considering desaturations with a drop from baseline larger than 3 %.

These patient averaged features are then used to classify the patients as having a cardiovascular comorbidity or not. The most discriminative features need to be selected, based on the data of the 70 training patients, before a classifier can be trained. A first selection is made based on statistical significance, features with a p-value above 0.05, computed using the Wilcoxon rank sum test, are discarded. Next highly correlated features are removed, feature couples with a correlation larger than 0.5 are inspected, starting with the highest correlation. For each couple only the feature with the highest F-test score, representing the between group variability on the within group variability, is kept. The last step is to perform a backwards wrapper on the remaining features, using an RBF LS-SVM classifier and based on the Leave One Out Cross Validation (LOO-CV) cost.

Using the selected features, an RBF LS-SVM classifier is trained using LOO-CV, to separate OSAS patients with a cardiovascular comorbidity from OSAS patients without comorbidity.

3. Results and discussion

The respiratory event classifier reached an accuracy of 80.0 % on the independent test set of 30 patients with a sensitivity of 86.0 % and a specificity of 72.7 %. This is a promising result, taking into account the facts that no sleep segmentation was performed and that the classification is only based on the SpO_2 signal. This signal is easy to acquire in a home environment and is unobtrusive for the patient, in contrast to the full PSG.

The cardiac comorbidity feature selection resulted in the selection of seven features, which are plotted in Figure 2 for patients without and with cardiovascular comorbidities. The feature set contains the logarithm of four features extracted from respiratory events with an SpO_2 drop of more than 3 % from the baseline: the mean and median of the derivative, the median of the second order derivative of the desaturation part and the deviation of the median value from the maximal value. The logarithms of three features were extracted from desaturations not associated with respiratory events: the area under baseline and the PRSA downwards slope, averaged over all desaturations, the deviation between the mean and maximum was taken over drops larger than 3 %.

The performance of the resulting cardiovascular comorbidity classifier on the training set and the independent test set can be seen in Table 1. An accuracy of 76.7 % is achieved on the independent test set, with a sensitivity of 80 % and a specificity of 73.3 %.

Table 1. Performance of the cardiovascular comorbidity classifier on the training and independent test set.

Data	Acc.	Se.	Sp.	PPV	AUC	Cohen κ
Train	97.1	97.1	97.1	97.1	0.99	94.3
Test	76.7	80.0	73.3	75.0	0.76	53.3

When analysing the features in Figure 2, one can see that the two classes are statistically different for all features on the complete dataset. If only the test set is considered, however, only features 3 and 5 have a significant difference. These features imply that OSAS patients with a cardiovascular comorbidity have a lower 2nd order derivative of the SpO_2 signal during desaturation and larger areas under the SpO_2 baseline during non-apneic desaturations.

The lower second order derivative values imply a slower change in slopes of the SpO_2 signal after a loss of oxygen supply due to a respiratory event. This effect could be due to a deterioration of the cardiovascular system, which results in a delayed oxygen desaturation in the blood.

The fact that patients with cardiovascular comorbidities have larger areas under the SpO_2 baseline is in agreement with theories that more severe hypoxias have a higher probability to cause damage to the cardiovascular system [6,7]. Features 4 and 7 can also be seen as a hypoxia severity parameter, they represent the amplitude difference between the median, respectively the mean, and the maximum SpO_2. These values increase if a patient has a cardiovascular comorbidity.

The subjects with a cardiovascular comorbidity that were misclassified as having no comorbidity all had hypertension and/or hyperlipidaemia. All patients with more severe cardiovascular comorbidities were correctly classified. It should be noted that for this study no information was available on the duration and severity of the particular cardiovascular disease of the patient. This information might have been interesting in order to see if the obtained features would differ between progressing disease stages. Moreover, patients without cardiac

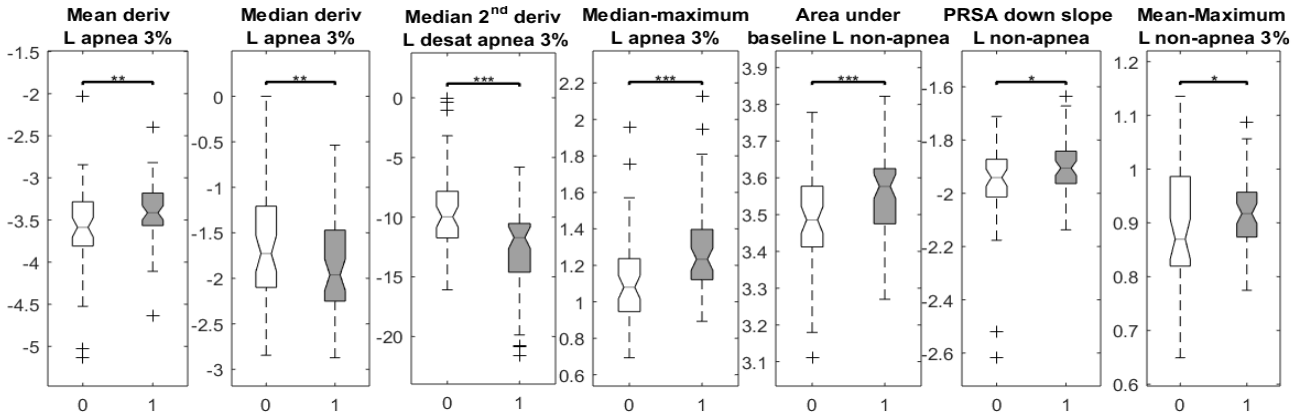

Figure 2. Features of comorbidity classification for patients without (0) and with cardiovascular comorbidity (1). Statistical significance between groups, Wilcoxon rank sum test: * p≤0.1 ** p≤0.05 *** p≤0.01.

comorbidity could already be in a late stage of development of cardiovascular disease, but without any observable symptoms yet.

The current study is performed on a limited dataset with only 30 patients used for testing. Therefore, to generalize these findings, a larger dataset should be considered. In order to move from assessing cardiovascular status to predicting the cardiovascular risk of the patient, follow-up studies should be considered to see which OSAS patients develop these comorbidities over time.

In this study only patients with an AHI larger than 15 were considered, in the future, it should be studied if the same effects in the SpO_2 signal can be seen in patients with a lower AHI. These patients are nowadays not treated with CPAP, but maybe for some of these patients CPAP treatment would decrease their risk of developing cardiovascular comorbidities.

4. Conclusion

The findings in this study suggest that cardiovascular comorbidities in OSAS patients can be detected based on changes in the SpO_2 signal. This could be interesting for the phenotyping of OSAS patients and their treatment decisions. Suggestions were made for further studies in order to be able to generalize these results.

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