Original article :

Differentiation of COPD from Normal Population using ECG Derived Respiration: a Pilot Observation

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ABSTRACT

Background: The respiration pattern (waveform) in different diseases may differ from normal population. These characteristics may help to differentiate COPD from normal population.

Aim of the study: To discriminate normal subjects and COPD patients using ECG derived respiration (EDR).

Methods : A group of 'normal' persons and 'COPD' sufferers were selected based on objective evaluations including chest X-ray and spirometry. Their respiratory patterns were collected from their ECG tracing (ECG Derived Respiration). Further, different qualities of the respiration pattern of both the groups were analyzed based on area ratio, time ratio and P/R ratio from EDR and ECG. Support Vector Machine (SVM) classifier was used to differentiate the equalities of both the groups.

Results: The features, as area ratio, time ratio, P/R ratio, extracted from the EDR of COPD patients are found to be different compared to the features extracted from normal subjects (p-value < 0.0001). The classification demonstrated 100% accuracy in case of area ratio vs. time ratio, 96.67% accuracy in case of time ratio vs. P/R ratio and 93.33% accuracy in case of area ratio vs. P/R ratio .

Conclusion: EDR can differentiate COPD from normal population. The study needs further validation before being adopted in clinical use.

Keywords: Chronic obstructive pulmonary disease (COPD), Electrocardiogram (ECG), ECG derived respiration (EDR), Peak amplitude variation (PAV), Support vector machine (SVM)

INTRODUCTION:

Chronic obstructive pulmonary disease (COPD) is a common respiratory and systemic morbidity. It is one of the leading causes of morbidity and mortality worldwide representing a substantial economic and social burden [1,2]. According to the World Health Organization (WHO), COPD is presently the fourth leading cause of death [3]. Often under-diagnosed and undertreated, this obstructive airway disease leads to severe airflow limitation with progressive shortness of breath and / or other symptoms leading to respiratory failure [4,5]. Since there is no curative treatment till date, the best way to deal with the disease is to prevent COPD before its development or at its early stage. Incidentally, the early detection of COPD; though important, is not accomplished in most of the situations. This is because of factors like (a) lack of awareness, (b) constant adjustment of the patients' functional life with disability, thus presenting late to seek help in the course of the disease, and (c) lack of easy and reliable diagnostic modality and others [6]. The standard method of COPD diagnosis through spirometry is often sparsely applied and spirometric evaluation needs thorough training to the technicians to ensure reliability and validity of the test. In addition, the availability of the instrument outside cities and towns in the developing world is also sparse. Thus the scope of the investigation is further restricted. Hence we need a simple, easily performable and interpretable method for day to day diagnosis of COPD. ECG is a commonly performed simple test

been practiced for long time and it can electro-physiologically express some of the effects of COPD on cardiac function [7,8]. Incidentally again, patients suffering from COPD are at increased risk of having cardiovascular diseases and other comorbidities [8,9]. Apart from arrhythmia, Electrocardiogram (ECG) of COPD patients clearly demonstrate specific changes like decreased heart rate variability (HRV), low amplitude of QRS complex and peaked P wave. The impact of COPD is appreciable in respiration pattern and also on the cardiac function. Previous studies have shown that ECG derived respiration can be an effective tool for monitoring respiration and ECG signal simultaneously. Here we have taken EDR signal and tried to analyze that to identify COPD.

MATERIAL AND METHOD

1. Study population

The study was done based on a protocol been approved by the Institutional Ethics Committee of the Institute of Pulmocare and Research, Kolkata. Each of the participants signed a proper informed consent. All of them underwent a medical history taking, physical examination by an expert prior to enrolment. All the subjects were evaluated by chest x-ray and spirometry, been done observing the ATS guideline [10]. In this study, ten healthy subjects with normal ECG, chest X-ray and spirometry were included in 'normal group', whereas, twenty COPD patients previously diagnosed clinicoradiologically and with pulmonary function test constituted 'COPD group'. The recordings were done at the Institute and further analysis was carried out in the Biomedical Instrumentation Laboratory of Department of Applied Physics, University of Calcutta. Subjects having arrhythmia, severe cardiovascular or pulmonary diseases like pneumonia, tuberculosis, interstitial lung disease etc. were excluded from this study. Furthermore, patients with permanent pacemaker, unwilling to give consent, sick to remain comfortably supine for 5-10 minutes and having repeated cough were also excluded.

2. Data acquisition

In this work, data acquisition was done based on a protocol. Each subject was allowed to rest for 10 minutes before the ECG and respiration were measured on a relaxed state. A data acquisition system MP-45, designed by Biopac Systems Inc., was used to collect the ECG data from each subject [11]. Respiration signal was acquired simultaneously using the respiratory effort transducer (SS5LB) by measuring the volume change in thoracic cavity and lungs during inspiration and expiration. The real-time data was recorded for 300 seconds time-duration with the signals being sampled at a frequency of 1000 Hz.

3. Preprocessing of acquired ECG data

During pre-processing, unwanted noises like powerline interference and baseline wander of the ECG signal were filtered out using a second order IIR Butterworth filter with a pass-band of 1Hz to 45 Hz. The respiration signal was filtered using a same filter with a pass-band of 0.2-0.7 Hz to eliminate the unwanted noise.

4. Extraction of EDR from R Peak Amplitude Variation (PAV)

Previous studies have established that respiration regulates the ECG measurements mainly in two ways: beat occurrence and beat morphology. Beat occurrence or heart rate variability is influenced by an effect called Respiratory Sinus Arrhythmia (RSA), where the heart rate increases during inspiration and decreases during expiration [12,13]. In beat morphology, the expansion and contraction of the chest wall during respiration, imparts motion to the heart. It changes the apparent cardiac axis during the respiratory cycle which leads to the modulation of the QRS amplitude [14]. In this study, the EDR signal was derived using R peak amplitude variation. Peak of each R-wave in the ECG were detected using multi-resolution wavelet algorithm [15].The detected R peaks were re-sampled using cubic-spline interpolation of 4 Hz frequency. The frequency band of respiration signal is generally within the range of 0.1 Hz to 0.7 Hz. As the respiration is a very slow varying signal, cubic spline interpolation was used to reconstruct data similar to original respiration signal. The sampling frequency of interpolation is found to be

adequate for extraction of respiratory information. The EDR signal was normalized between 0-1 before further processing. The ECG signal along with the EDR signal of a COPD patient is shown in figure 1.

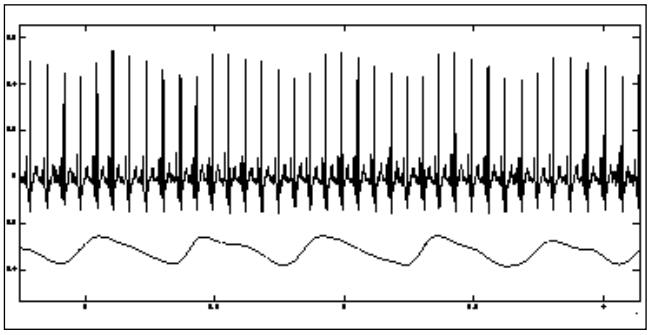

Figure 1: ECG signal (above) and ECG Derived Respiration signal (below)

The derived EDR signal was validated with the original respiration signal for each individual. A previous study showed that the ECG derived respiration rate was almost same in all the subjects with directly recorded respiration rate [16]. A trace of EDR signal followed by the original respiration signal of a subject is shown below in figure 2.

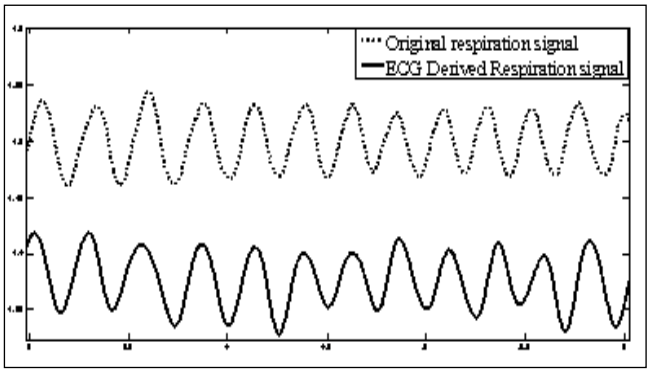

Figure 2: Original respiration signal (dotted line) and EDR signal (solid line)

5. Feature extraction

From the EDR and ECG signal we have calculated the following features described below.

a. Time ratio

Inspiration time (TI) and expiration time (TE) were derived by calculating the time interval between the starting point to the peak and peak to the ending point of one EDR cycle (shown in figure 3). The time ratio (F1) can be written as F1=T1/A

(1)

b. Area ratio

To compute area ratio, the area under the curve against baseline for both inspiration and expiration of an EDR cycle were calculated to derive inspiration area (AI) and expiration area (AE) as shown in figure 3. The area ratio (F2) can be represented as F2 =A1/Ag, (2)

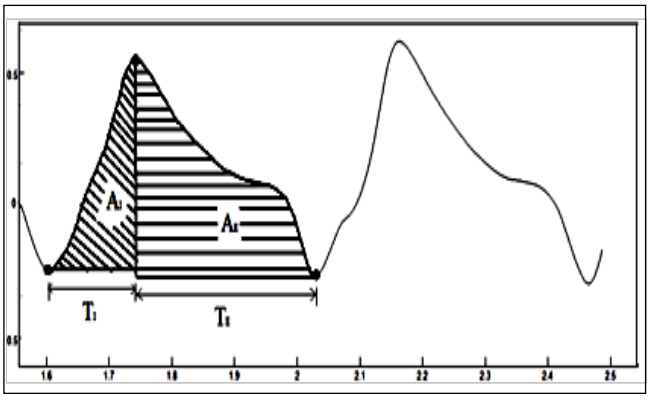

Figure 3: TI, TE of time ratio and AI , AE of are ratio are shown within an EDR cycle

c. P/R ratio

After calculating the P wave amplitude (PA) and the R wave amplitude (RA) of a filtered ECG cycle the P/R ratio (F3) can be written as F3=PA/RA,

(3)

Two spirometric parameters- FEV1 (post bronchodilator % value) and FEV1/FVC (post bronchodilator absolute value), were used as standard feature set for validation of the extracted features discussed earlier.

6. Classification

In this study binary-class support vector machine (SVM) classifier was used. The SVM maps the input features into a higher dimensional feature space through some non-linear mapping and a decision surface is constructed over there [17,18]. The training data was constructed as, (Where, = Radius of a hyper-sphere enclosing all data points; N=Number of parameters).

The test performance of the classifier was determined by calculating specificity, sensitivity, and accuracy based on the number of true negative, true positive, false positive and false negative incidents occurred during classification.

RESULTS

A total of 30 subjects (10 normal and 20 COPD) were included in this study. 70% of the COPD patients were smoker and the rest had long term exposure to indoor or outdoor pollution.

Five features (two features from spirometric values and three features from EDR signal) have been selected so far for all 30 subjects. Table 1 elaborates their mean age, male to female ratio and the mean value of FEV1, FEV1/FVC, area ratio, time ratio and P/R ratio.

The p-values from table 1 imply that like two spirometric parameters, area ratio, time ratio and P/R ratio are also very significant.

In figure 4, the classification between two spirometric parameters, FEV1 (post BD % value) and FEV1/FVC (post BD absolute value), using SVM classifier is shown. The graph shows a clear distinction between normal subjects and COPD patients. The normal subjects are denoted using black triangle and the COPD patients are denoted using black square.

The output of the SVM classifier using the extracted features is illustrated below in figure 5 with two feature sets at a time.

Based on the number of true negative, true positive, false negative and false positive incidents of each classification graph, the specificity, sensitivity and accuracy of each set of parameters were calculated (shown in table 2).

The result shows that in case of spirometric parameters and area ratio vs. time ratio feature the accuracy is 100% with no false negative or false positive incidents. But in case of area ratio vs. P/R ratio there are 2 false negative cases and for time ratio vs. P/R ratio there is 1 false positive case resulting 93.33% and 96.67% accuracy respectively. The accuracy level will increase with the increase in total number of subjects.

	Normal (N=10)	COPD (N=20)	p value
Mean Age	32.60±10.59	66.20±5.12	5.69 x 10-7
Male : Female	3:2	17:3	-
Smoker : Non-smoker	2:3	7:3	-
Mean FEV1 (post bronchodilator % value)	85±5.06	41.25±15.72	1.22 x 10-11
Mean FEV1/FVC (post bronchodilator absolute value)	83.3±5.35	51.4±1.41	2.36 x 10-11
Mean Area Ratio	0.91±0.14	1.59±0.39	8.34 x 10-8
Mean Time Ratio	0.84±0.12	1.58±0.41	2.75 x 10-8
Mean P/R Ratio	0.07±0.04	0.22±0.14	1.91 x 10-5

Table 1: Illustrates the age, male to female ratio, spirometric parameters and extracted features along with their p-value

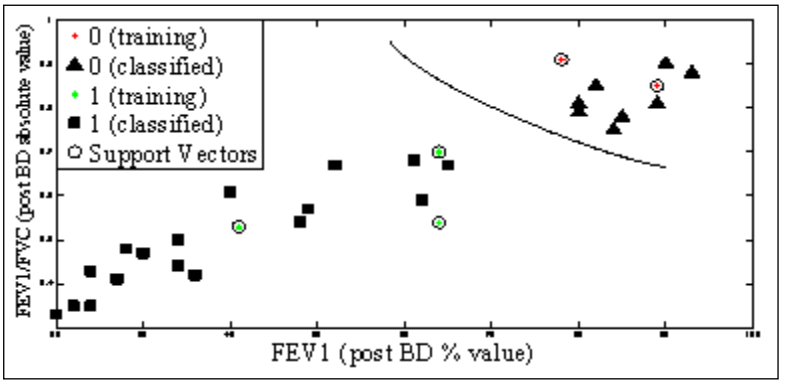

Figure 4: Classification of FEV1 (post bronchodilator % value) vs. FEV1/FVC (post bronchodilator absolute value)

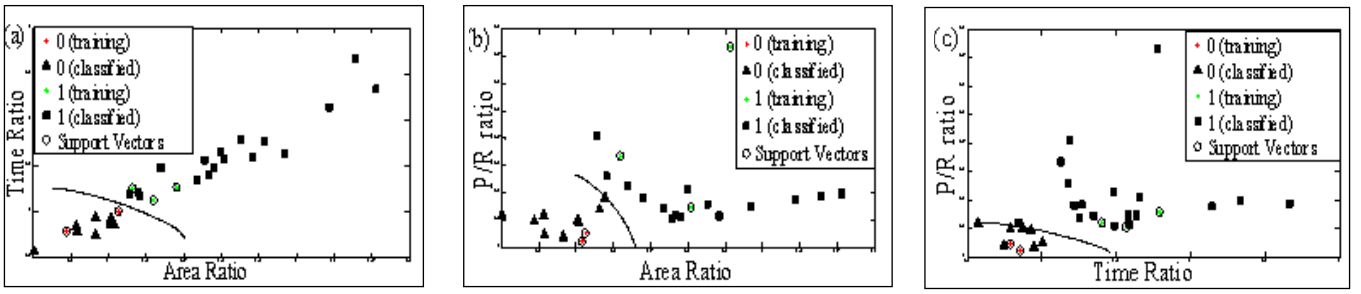

Figure 5: Classification of (a) area ratio vs. time ratio, (b) P/R ratio vs. area ratio, (c) P/R ratio vs. time ratio. The normal subject is denoted using black triangle and COPD patient is denoted using black square.

	FEV1(post BD % value) vs. FEV1/ FVC (post BD absolute value)	Area ratio vs. Time ratio	Area ratio vs. P/R ratio	Time ratio vs. P/R ratio
Specificity	100%	100%	100%	90%
Sensitivity	100%	100%	90%	100%
Accuracy	100%	100%	93.33%	96.67%

Table 2: Depicts the specificity, sensitivity and accuracy calculated from the classification using different features

DISCUSSION

COPD is a state of airflow limitations. Hence the waveform of respiration is going to be different in COPD compared to that of normal population. A prolonged expiration is likely with inspiration/ expiration ratio been smaller in COPD.

The method of EDR is actually extrapolation of respiration signal from the ECG where the 'R wave' amplitude variation is extrapolated from sinus arrhythmia. It is interesting to note that EDR cycles also follow the qualities and characteristics of airflow obstruction. Although, the results point towards successful identification of COPD from EDR characteristics, we must admit that the patients of COPD were mostly from advanced stages (Gold III & IV). Hence, it will be worthwhile to see the predictivity of the measurements for early COPD. Moreover, we have to see the changes in other airway obstruction like asthma, bronchiectasis etc. where we expect similar changes in the respiratory cycles. Hence, early detection of COPD and differentiation from its contenders will remain the next challenge of the work. Till date, various techniques are developed for COPD detection and diagnosis. Among all these methods, the most reliable and widely used conventional method is spirometry [19]. But instead of its vast use, spirometry often performs poorly because of its high patient-effort dependency and poor performance-guidance by untrained technician [20]. Spirometry is also non-suitable in case of non-ambulatory and ICU patients, patients having ora-facial and denture defects, and even sometimes for children and elderly patients. Other than spirometry, methods like volatile organic compound analysis [21,22] and electronic nose for respiratory disease detection [23,24] from exhaled breath, lung imaging technique using X-ray and CT scan [25,26,27], quantitative analysis of capnogram shape by analyzing CO2 concentration[28] are also developed. But these methods are mostly costly, time consuming, and most of them are still in state of development in research laboratories. Hence, a simple and easily performable method without any subjective bias from the performer is welcome. The EDR based diagnosis seemingly fulfills these prerequisites.

CONCLUSION

From our study it appears that analysis of EDR can give a fairly specific diagram of advanced

COPD. As the method appears to have an applied prospect, further work is needed to validate it and further research deems necessary to explore its applicability in real life clinical practice.

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