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Association between Short term Heart Rate Variability and Different Grades of Chronic Obstructive Pulmonary Disease

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Abstract

Chronic obstructive pulmonary disease (COPD) is a broad spectrum respiratory illness where there are structural and functional changes in the lungs. According to WHO, COPD is a leading global burden and by 2030 it will be the third leading cause of death worldwide. The structural and functional changes in the lungs in COPD patients tend to influence the cardiac autonomic functions and heart rate variability (HRV). Previous studies show that there is decrease in heart rate variability in COPD patients. In many previous studies, it is found that results of short term HRV analysis of 5minutes is comparable to standard 24hours HRV analysis and is very patient friendly and reproducible procedure to analyse the cardiac autonomic functions. So determination of parameters of cardiac autonomic functions with the help of short term HRV analysis in COPD patients is helpful in determining the pathophysiology and subsequent management of such patients. A descriptive and observational study was conducted upon 100 previously diagnosed COPD patients at the Autonomic function research Laboratory, Department of Physiology, R G Kar Medical College and Hospital, Kolkata, West Bengal. The study includes short term (5min) HRV analysis in COPD patients between the age group 18years and 60years after fulfilling appropriate inclusion and exclusion criteria and the results were analyzed using proper statistical software. After analysis of different data it was found that there is decrease in heart rate variability (in both Time domain and Frequency domain analysis) in case of COPD and also the decrease is more in case of increasing severity grading of COPD. Sympathetic activity increases and vagal or parasympathetic activity upon heart rate decreases with the increase in COPD grading. Further studies with more number of subjects will be helpful in assessing pathophysiology and management of COPD patients with the help of HRV analysis.

Keywords: Heart rate variability, Chronic obstructive pulmonary disease, Low frequency, High frequency, Standard deviation of NN interval

Introduction

Heart Rate Variability (HRV) analysis is the analysis of variation in heart-rate between two successive heart beat and a very sensitive procedure for evaluation of autonomic functions.[1] HRV is an index of the influence of both the sympathetic and parasympathetic nervous systems (SNS and PNS respectively).[2] The PNS quickly decreases heart rate, while the SNS slowly increase heart rate and the activity of the Vagus nerve reflects the physiological modulation of the PNS and SNS.[3] High HRV may reflect increased PNS activity, and someone with low

HRV may reflect increased SNS activity.[4] Earlier studies suggest that 24 hours HRV measurements can minutely identify changes in cardiac autonomic functions and being a snapshot of 5minutes, Short term HRV analysis also provide comparable results to that of 24 hour HRV analysis.[5 6]

Reduced HRV can be a predictor of morbidity and mortality in various diseases like Ischemic heart disease (IHD), Chronic Obstructive Pulmonary Disease (COPD), after myocardial infarction congestive heart failure, post–cardiac-transplant depression, diabetic neuropathy, susceptibility to acute respiratory distress syndrome etc.[7 8 9]

Chronic obstructive pulmonary diseases (COPD), a broad spectrum of respiratory diseases represents a worldwide problem.[10] By 2030, COPD deaths related to COPD will be projected to be the third leading cause of death worldwide. According to the WHO, prevalence of COPD among Indian adults is ranging from 4% to 20% .[11] COPD is a type of obstructive lung disease characterized by long-term breathing difficulty and reduced airflow to and from lungs.[12 13] COPD patients can be grouped stagewise as per Global Initiative for Obstructive Lung Disease (GOLD) criteria.[14 15 16 17] According to GOLD criteria, a person having COPD has FEV_1 (Forced expiratory volume)/FVC (Forced vital capacity) ratio < 0.70 in spirometry.

Classification of airflow limitation severity in COPD (based on post-bronchodilator FEV_1): In patients with FEV_1/FVC < **0.70**:

1. GOLD 1 - **mild**: FEV_1 ≥ **80%** predicted
2. GOLD 2 - **moderate**: **50%** ≤ FEV_1 < **80%** predicted
3. GOLD 3 - **severe**: **30%** ≤ FEV_1 < **50%** predicted
4. GOLD 4 - **very severe**: FEV_1 < **30%** predicted

Advanced COPD causes increased pulmonary arterial pressure which strains the right ventricle of the heart leading to cor pulmonale, pedal edema, increased jugular venous pressure and bulging neck veins.[18 19 20 21] COPD is the most common cause of lung disease producing cor pulmonale. In COPD, there are functional and structural changes in respiratory system which also greatly influence cardiac autonomic function .[22]

So parameters of cardiovascular autonomic function, in terms of short term HRV analysis within different grades of COPD can be helpful to determine the pathophysiology and further management of COPD patients. Data regarding heart rate variability analysis in case of COPD patients is very much lacking in eastern India specifically in West Bengal. Thus our study was aimed at this paucity and to enrich the data.

Aims And Objectives

1. To find out changes in different short term HRV parameters in COPD patients.

2. To find out any co-relation between the HRV parameters and severity grading of COPD patients.

Materials And Methods

An observational, descriptive and cross-sectional study was conducted for a period of one year among 100 diagnosed COPD patients within the age group of 18 and 60 years (both genders) attending for Pulmonary function test (PFT) examination in the Department of Physiology, R.G. Kar Medical College and Hospital, Kolkata, West Bengal, India.

Inclusion Criteria:

1. Patients of both genders diagnosed with COPD attending for PFT examination in the Department of Physiology, R.G. Kar Medical College and Hospital, Kolkata, West Bengal, India
2. Patients with age range between 18yrs and 60yrs.
3. Patients willing to undergo the study.

Exclusion criteria:

1. Age below 18yrs and above 60 yrs
2. Any recent illness during the past 3weeks.
3. Any deformity of thoracic cage.
4. Patients who had not given consent to perform the tests
5. Debilitating and severely ill patients
6. Patients with sputum positive pulmonary TB
7. Pregnant and menstruating women
8. Known cardiac illness like arrhythmia etc.
9. Other lung diseases e.g. Interstitial Lung Disease, Carcinoma, Asthma, Brochiectasis etc.

All patients were first grouped stagewise according to GOLD criteria after selecting the patients as per

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inclusion and exclusion criteria. Ethical clearance has been obtained from the "Institutional Ethics Committee" of R.G. Kar Medical College, prior to study. Written consents were taken from the selected patients and they were being assured of the confidentiality of their personal information.

HRV analysis were done in the Autonomic function research laboratory, R.G. Kar Medical college, Kolkata, West Bengal, India using Physiograph Polyrite-D instrument with bio-amplifiers, 4channels and accessories (RMS software-Version 3.0.16.). Frequency domain HRV parameters such as Low Frequency(LF), High Frequency(HF), LF/HF ratio and time domain parameters such as Standard deviation of NN intervals (SDNN) were taken into account.

Frequency domain (power spectral density) analysis describes the periodic oscillations of the heart rate signal. These periodic oscillations in heart's sinus rhythm contain different frequencies with different amplitudes. A simple and rapid method to analyze the frequency domain or spectral density of heart rate variability is by Fast Fourier Transformation (FFT) method which is characterized by discreet peaks for the several frequency components of heart's sinus rhythm and individual RR intervals stored in the computer are transformed into bands with different spectral frequencies.The power spectrum consists of frequency bands ranging from 0 to 0.5 Hz and can be classified into four bands: the ultra low frequency band (ULF), the very low frequency band (VLF), the low frequency band (LF) and the high frequency band (HF).[23 24]

Time domain analysis measures the heart rate changes over time or the intervals between successive normal cardiac cycles. A continuous ECG recording is obtained and each QRS complex is detected and the normal RR intervals due to instantaneous heart rate are then determined. Normal sinus intervals or NN intervals are obtained after eliminating artifacts (such as abnormal beats, ectopic beats, omitted beats, noise from the machine etc.). Standard Deviation (SD) of RR or NN intervals is generally considered to reflect the day-night changes of heart rate variability. SDNN is an index of heart rate variability and reflects circadian rhythms and long-term components which are responsible for variability of heart rate within the period of recording ECG.[23 24]

In earlier studies it was observed that cardiac autonomic and respiratory influences can be recorded by analyzing SDNN and LF/HF ratio. The HF component is generally defined as a marker of vagal or parasympathetic influence. This component is respiration mediated and frequency of breathing regulates this component. The LF component is modulated by both the sympathetic and parasympathetic nervous systems. In practical sense, LF component increases with sympathetic overdrive (physical or mental stress, sympathomimetic agents etc). The LF/HF ratio reflects sympatho-vagal balance and can be used as a measure of this balance.[23 24] SDNN usually reflects long term and circadian variation in heart rate variability in 24hours HRV analysis. It may correspond with HF component of HRV analysis. So in case of autonomic and respiratory modulation of heart rate variability, LF/HF ratio is more sensitive than SDNN values when the assessment was done with short term 5minutes HRV analysis.[23 24]

Data were tabulated in MS-Excel sheet and results were analysed by performing multivariate ANOVA using standard statistical software (SPSS version 23)

Results

Following results are obtained from the study after proper statistical analysis.

Table – 1:

COPD Grading (GOLD criteria)	Number of subjects
GOLD – 1	**18**
GOLD – 2	**27**

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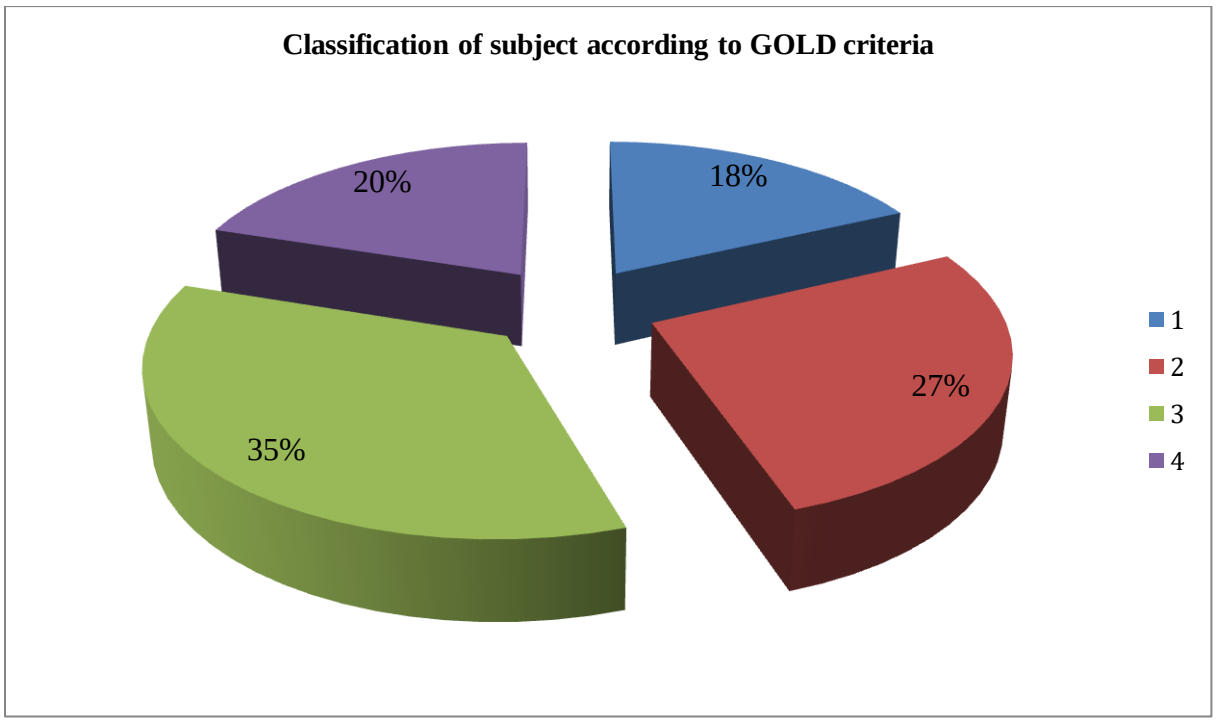
GOLD – 3	**35**
GOLD – 4	**20**
TOTAL	100

Table – 1 showing the number of subjects between different groups of COPD as sorted by GOLD criteria

Pie chart – 1



Pie chart – 1 showing classification of subjects according to GOLD criteria in which number 1,2,3,4 are the percentage of subjects classified under GOLD-1, GOLD-2, GOLD-3 and GOLD-4 respectively

Table – 2:

COPD Grading	Mean ± SD of SDNN	P value
GOLD-1	**32.58±4.43**	**0.025**
GOLD-2	**28.17±2.37**	
GOLD-3	**26.9±1.59**	
GOLD-4	**20.21±2.24**	

Mean and SD of SDNN values and their significance in different grades of COPD are shown in Table – 2.

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Table – 3:

COPD Grading	Mean ± SD of LF/HF ratio	P value
GOLD-1	**0.78±0.11**	**0.027**
GOLD-2	**0.95±0.12**	
GOLD-3	**1.06±0.12**	
GOLD-4	**1.43±0.20**	

Table- 3 is all about the mean and standard deviation data of LF/HF ratio among different grades of COPD and it also shows significance of change of LF/HF ratio among those groups.

Analysis Of Results

Time domain parameter which has been analyzed was SDNN. Mean and standard deviation of SDNN values in case of subjects with mild COPD or GOLD-1 is 32.58±4.43, in moderate COPD or GOLD-2 is 28.17±2.37, in severe COPD or GOLD-3 is 26.9±1.59 and in very severe COPD or GOLD-4 is 20.21±2.24 respectively. Mean SDNN values decrease over advancement of COPD grades, the p-value of the mean and standard deviation of SDNN in different COPD grades is 0.025 which is very much statistically significant.

Frequency domain parameters analyzed were LF, HF and LF/HF ratio. Mean and standard deviation of LF/HF ratio in mild or GOLD-1 COPD is 0.78±0.11, in moderate or GOLD-2 COPD is 0.95±0.12, in severe or GOLD-3 COPD is 1.06±0.12 and in very severe or GOLD-4 COPD grade is 1.43±0.20 respectively. Mean and standard deviation values of LF/HF ratio increase along with increase in severity grading of COPD. p – value of mean and standard deviation of LF/HF ratio in different grades of COPD is 0.027 and it is very much statistically significant.

Discussion

Heart rate variability is considered to be one of the sensitive methods for analyzing the cardiac activity. COPD is a chronic disease where there is anatomical and physiological obstruction in airways. Now, respiratory influence plays a major role in heart rate variability via the vagus nerve which is very much dedicated to the atria and the SA node. As we all know that respiratory and cardiovascular system are in a series connection within human body, so if one system is affected, there is very much probability that other system will also be affected and vice-versa. On the contrary, sympathetic influence is seen in both atria and ventricles.

In our study set-up, subjects were mainly coming from rural areas and were mainly of lower middle-class to poor social economic class. Social and economic stress, both physical and mental, leads to increased sympathetic drive which can hamper the normal homeostasis.

In our study; the mean SDNN values significantly decrease over advancement of COPD grades. As the SDNN component generally corresponds with the vagal influence over the heart rate variability; it may be said that with advancement of the disease severity of COPD there is decrease in vagal influence and increase in sympathetic dominance and thus there is decrease in heart rate variability. This finding is in tune with earlier studies showing sympathetic over-activity and decreased vagal or parasympathetic with increasing severity of COPD.[23 25 26 27]

Frequency domain parameters of HRV analysis such as LF, HF and particularly LF/HF ratio play a key role in assessing the respiratory, sympathetic and parasympathetic modulation of heart rate variability. As we all know that with increasing severity of COPD, there is increased physical or mental stress, anxiety, sympathetic over-activity. Due to the fact that LF value reflects both sympathetic and

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parasympathetic activity and HF value reflects only the vagal or respiratoy activity over heart rate variability; their single values cannot precisely reflect the autonomic influence over heart rate. Thus LF/HF ratio is used to assess the autonomic balance upon heart rate variability.[23 25] Increase in the LF/HF ratio corresponds with increase in the sympathetic activity and decreased vagal or parasympathetic activity. In our study; Mean and standard deviation values of LF/HF ratio also increases along with increase in severity grading of COPD. The subjects we tested, as we told earlier, were of lower middle class to poor economic class. They attended the OPD of the hospital and were largely treated with hospital-supply medicines. They include both sympathomimetics or beta-agonists and anticholinergics. As the severity of COPD increases, the dose of those medicines also increases which in turn can to some extent modulate the autonomic nervous system. Beta- agonists and anticholinergics can increase the sympathetic drive and decrease the parasympathetic drive. This phenomena increase with increasing dosage of those drugs which is also reflected in our study (Increased severity of COPD leads to increased dosage of those drugs which leads to increase in sympathetic activity and decrease in parasympathetic activity). Socio-economic crisis is also a major problem in these groups of people. Socio-economic stress related to day to day earning and maintenance of proper livelihood also leads to physical and mental stress among them. This can also affect the stress level and can cause sympathetic and parasympathetic imbalance which further induce heart rate variability.

So our study reflects that there is significant change in heart rate variability among different grades of COPD and there is increased sympathetic activity and heart rate variability is decreased with increasing severity of COPD. Future study with much more number of subjects regarding effect of chronic respiratory illness upon cardiovascular system can be demonstrated using HRV analysis. Cardiovascular illness may also act as a forerunner of respiratory illness which might also be demonstrated by HRV analysis as both respiratory and cardiovascular systems are in series connection.

Conclusion

In this study after proper analysis of data, it is evident that there is definite change in heart rate variability among different grades of COPD. Heart rate variability decreases significantly with increasing severity of COPD which suggests that there is significant increase in sympathetic activity and decreased parasympathetic activity upon heart rate along with increasing severity grading of COPD. Further study in this topic with much more number of subjects can be helpful for further understanding the pathophysiology and assessment of HRV in COPD patients.

Limitations

1. This study is conducted in a short time period and only the diagnosed COPD patients referred to the Department of Physiology for PFT examination were enrolled in this study. So a limited number of subjects whoever available were enrolled for the study.
2. SDNN values correspond with only HF component. So overall autonomic imbalance cannot be properly assessed by this value. LF/HF ratio is much more sensitive in this regard.
3. Though short term HRV analysis is a 5minutes snapshot of overall 24hours long term HRV analysis and is very much comparable with that, time domain methods are more sensitive in case of 24hours HRV analysis.

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