Section: Miscellaneous

Original Research Article

ASSESSMENT OF AUTONOMIC FUNCTION USING HEART RATE VARIABILITY AMONG MILD AND MODERATE CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Chronic Obstructive Pulmonary Disease (COPD) is a progressive respiratory condition characterized by airflow limitation and systemic involvement, including cardiovascular complications. Autonomic dysfunction is a recognized contributor to increased cardiovascular morbidity and mortality in COPD patients. Heart Rate Variability (HRV) is a non-invasive measure of autonomic nervous system activity and may serve as an early indicator of such dysfunction. This study aimed to assess pulmonary function and HRV in mild and moderate COPD and explore their association. The objective is to evaluate Autonomic function using HRV parameters among individuals with mild and moderate COPD compared to normal and (ii) To determine the association between HRV and pulmonary function test (PFT) parameters across different grades of COPD. **Materials and Methods:** A cross-sectional hospital-based study was conducted in 90 subjects divided into three groups: normal (n=30), mild COPD (n=30), and moderate COPD (n=30). PFT was done using spirometry, and HRV was assessed through 5-minute lead II ECG using LabChart software. HRV indices included frequency-domain (LF, HF, LF/HF ratio) and time-domain (SDRR, RMSSD) parameters. Statistical analysis was performed using SPSS v26.0; $p < 0.05$ was considered significant. **Result:** Mean FEV1% was significantly lower in mild (88.8 ± 7.0) and moderate COPD (69.7 ± 7.0) compared to normal (113.5 ± 22.4), with $p = 0.001$. FEV1/FVC ratio also declined significantly (normal: 107.0 ± 12.7 vs moderate COPD: 67.6 ± 3.9; $p = 0.011$). HRV parameters showed marked reductions: SDRR was significantly lower in mild (20.8 ± 11.0 ms) and moderate COPD (16.7 ± 13.3 ms) compared to normal (39.7 ± 12.6 ms; $p < 0.05$). Similarly, HF power decreased from 540.3 ± 246.9 ms² (normal) to 246.9 ± 275.3 ms² (mild) and 90.2 ± 114.0 ms² (moderate), with significant intergroup differences ($p < 0.05$). FEV1% showed strong positive correlations with LF ($r = 0.509$), HF ($r = 0.538$), SDRR ($r = 0.522$), and RMSSD ($r = 0.529$), all $p < 0.01$. **Conclusion:** Mild and moderate COPD are associated with significant reductions in HRV parameters, indicating early autonomic dysfunction. The strong correlation between lung function and HRV underscores the systemic nature of COPD and suggests HRV as a potential non-invasive marker for early cardiovascular involvement.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is defined by Global Initiative for Obstructive Lung Disease (GOLD) as a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.[1] It is the 2nd leading cause of death and disability adjusted life years (DALYs) in India, with an estimated prevalence across India of 37.8 million.[2,3]

Spirometry is a method used to assess lung function.4 It is more sensitive than any clinical symptoms or examinations in making the diagnosis of obstructive respiratory pathology and is thus, recommended by several guidelines, remains the gold standard for

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accurate diagnosis and determination of severity in COPD, based on FEV1/FVC <0.7 after bronchodilator and FEV1 with mild ≥80% predicted, moderate 50-80%, severe 30-49% predicted, very severe <30% predicted.[4,5] FEV1 normally decreases with age, and the rate of fall is an important indicator of disease progression in COPD.[6] The most common respiratory symptoms include dyspnea, cough and/or sputum production.[7]

Patients of COPD often are associated with comorbidities and include worse outcomes such as impaired quality of life, increased frequency of hospital admissions, decreased therapeutic response, and increased mortality.[8] Many comorbid conditions are seen in people with chronic obstructive pulmonary disease, with cardiovascular diseases (CVDs) perceived to be the most important. CVDs are associated with an increased risk of death in patients with COPD.[9]

The autonomic nervous system (ANS) regulates various physiological processes, and dysfunctions of the autonomic nervous system are recognized by symptoms that result from the failure of the sympathetic or parasympathetic components.[10] The disruption of autonomic reflexes with increased sympathetic tone, loss of parasympathetic tone and altered baroreceptor sensitivity (BRS) are considered major risk factors for cardiac morbidity and mortality.[11,12]

Autonomic dysfunction is postulated as a pathway in both respiratory and cardiovascular morbidity in COPD.[13] The Ewing test battery is time consuming and requires patient cooperation. Due to this, assessment of heart rate variability has been replaced as a diagnostic tool for autonomic dysfunction.[14] The variations in ANS function are assessed non-invasively using heart rate variability (HRV).[15]

Heart rate variability is defined as the fluctuation in the time intervals between adjacent heartbeats and is generated by heart-brain interactions and dynamic, non-linear autonomic nervous system processes.[16,17] Higher value of HRV indicates a greater adaptation by the cardiovascular system for intrinsic and extrinsic changes such as exercise or stress, whereas, lower HRV value indicates a greater risk/predisposition for cardiovascular mortality and morbidity.[18] Cardiac autonomic dysfunction is seen in patients of COPD, with various studies showing reduced HRV in patients with COPD compared to matched healthy controls.[19]

The present study was conducted to evaluate Autonomic function using HRV among individuals with mild and moderate COPD as compared to normal.

Objectives:

1. To evaluate Autonomic function using HRV parameters among individuals with mild and moderate COPD compared to normal
2. To determine the association between HRV and pulmonary function test (PFT) parameters across different grades of COPD.

MATERIALS AND METHODS

The study was a hospital-based Observational cross - sectional study conducted in the Department of Physiology, in collaboration with Department of Respiratory Medicine, Jawaharlal Nehru Institute of Medical Science, Imphal from June 2023 to March 2025. between 35 to75 years of all gender and those who were willing to participate in the study were included in the study. Adult patients diagnosed as a case of COPD according to GOLD guidelines were the study groups along with apparently healthy controls. Those patients with (i) any risk of increased in intracranial, intraocular, intrathoracic and intraabdominal pressure (ii) any form of acute respiratory infection and pain inside the mouth or on the face while biting the mouth piece (iii) on bronchodilator or any medication that can alter the autonomic function in the last 6 hours and (iv) those who are not willing to give consent were excluded from the study.

The study population were divided into three groups of 30 individual each.

1. **Normal:** Age and sex-matched control among the staffs of JNIMS who are not suffering from any form of respiratory disease.
2. **Mild COPD:** Patients with FEV1 ≥ 80% (GOLD guidelines) and
3. **Moderate COPD:** Patients with 50% ≤ FEV1 < 80% (GOLD guidelines).[4,5]

After taking informed consent, subjects were explained about the procedure and the purpose of the study. They were subjected to thorough general physical and clinical examinations. Detailed history regarding the duration of disease, history and duration of smoking, occupational or environmental exposures, past history, presence of comorbidities and associated symptoms were taken.

The following tests were done:

1. Pulmonary functions were assessed by using Spirometry:

It was done once for the normal group and twice for the mild and moderate COPD patients, first before administration of a bronchodilator and the later 20 minutes after the administration of 400mcg of salbutamol given by a metered dose inhaler using a spacer.

Steps for performing Spirometry: Before starting the procedure, the patient's age, sex, and height were recorded and entered into the spirometer so that predicted curves and values can be calculated by the spirometer. The patient was made comfortable after having recently emptied their bladder. Spirometry was performed with the patient in sitting position by using Medicaid Spiro Excel.

A clean, disposable, one-way mouthpiece was attached to the spirometer. The patient was instructed to breathe in maximally and asked to hold their breath long enough to seal their lips tightly around the mouthpiece. The air was blast out as forcibly and fast as possible until there is no more air left to expel.

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The procedure was repeated until three acceptable and repeatable blows were obtained with a maximum of eight efforts. Out of the three readings, the best two within 150 mL or 5% of each other were taken. The best readings of FEV1 and FVC were taken for data analysis.

2. Assessment of Heart Rate Variability (HRV):

Short term HRV measurements was performed according to European Society of Cardiology Guidelines (1996) where five minutes electrocardiogram (ECG) was recorded for analysis. The patients were asked to lie comfortably on the couch where electrodes for lead II ECG acquisition by Labchart Prov8.1.13 (AD Instrument, Australia) were attached. A five-minute lead II ECG (sampling rate 1KHz) was recorded after taking rest for 10 minutes. The subjects were instructed to breathe regularly and calmly with normal breathing rate of 12-16 breaths per minute and stay awake to prevent artefacts in the recording. The ECG signal was kept by data acquisition software (Lab Chart Prov8.1.13) with HRV module version 2.0; (AD Instruments, Australia) using PowerLab 26T (AD Instruments, Australia). "R" waves were detected, and artefact free signals were kept. Then, time-domain and frequency-domain components of HRV were analyzed using Lomb Scargle Periodogram. Time domain components of HRV are SDRR (standard deviation of interbeat interval for all sinus beats) and RMSSD (square root of the mean squares differences between adjacent RR intervals) which denote overall HRV and vagal activity respectively. Under frequency-domain, low frequency (LF: 0.04–0.15Hz) and high frequency (HF: 0.15–0.40Hz) power in absolute values of power (ms2) and LF/HF ratio were calculated. The high frequency power denotes parasympathetic activity; low frequency denotes combination of sympathetic and parasympathetic input while LF/HF ratio indicates sympathovagal balance

The data was entered in MS Excel and analyzed by using Statistical Package for Social Science (SPSS) version 26. Descriptive statistics were expressed in terms of mean, standard deviation and percentage. Inferential statistics was done using independent sample t test to compare HRV indices between normal individuals and mild COPD, normal and moderate COPD and mild and moderate COPD. Paired t test was used to compare between Pre and Post bronchodilator among the COPD patients. Correlation between PFT and HRV parameters were done using Pearson correlation test. p value less than 0.05 were taken as statistically significant.

Ethical clearance was obtained from the Institutional Ethical Committee, JNIMS vide letter No. Ac/03/IEC/JNIMS/2018-PGT before the conduct of the study.

RESULTS

The mean age of the participants with normal individuals (60.8 ± 8.61 years), mild COPD patients (59.6 ± 6.83 years) and moderate COPD patients being (64.23 ± 7.92 years). The height did not differ significantly across the study population but weight and Body Mass Index (BMI) showed a progressive decline from normal individuals to those with moderate COPD. The mean BMI was highest among normal (26.79 ± 3.58 kg/m²), followed by mild COPD (25.2 ± 5.14 kg/m²) and lowest in moderate COPD (23.06 ± 4.34 kg/m²). [Table 1]

Table 1: Demographic profile

Demographics	Normal (n=30) (Mean ± SD)	Mild COPD(n=30) (Mean ± SD)	Moderate COPD (n=30) (Mean ± SD)
Age (years)	60.8 ± 8.61	59.6 ± 6.83	64.23 ± 7.92
Height (cm)	154.77 ± 4.15	154.4 ± 7.2	160.1 ± 6.4
Weight (kg)	64.13 ± 9.45	63.1 ± 12.1	58.5 ± 7.9
BMI (Mean ± SD)	26.79 ± 3.58	25.2 ± 5.14	23.06 ± 4.34

Table 2: Pulmonary function test among the study participants

Parameters	Normal	Mild COPD		Moderate COPD		p- value
		Pre	Post	Pre	Post	
FEV1(litre)	2.1 ± 0.60	1.7 ± 0.4	1.9 ± 0.4	1.5 ± 0.4	1.8 ± 0.4	0.242
FVC(litre)	2.4 ± 0.7	2.2 ± 0.5	2.5 ± 0.5	2.2 ± 0.5	2.3 ± 0.5	0.062
FEV1/ FVC	107.0 ± 12.7	63.2 ± 4.5	65.5± 3.9	64.2 ± 2.7	67.6 ± 3.9	0.011*
FEV1%	113.5 ± 22.4	81.7 ± 8.2	88.8± 7.0	60.08± 10.2	69.7 ± 7.0	0.001ŧ
* Significant, ŧ highly significant						

Pulmonary function tests showed progressive decline from normal to moderate COPD groups (Table 2). Though the decline in absolute values of FEV1 and FVC was not statistically significant, the FEV1/FVC ratio and FEV1% predicted showed significant reductions ($p = 0.011$ and $p = 0.001$, respectively). This supports the obstructive nature of the disease and the usefulness of these parameters in distinguishing disease severity. Interestingly, the post-bronchodilator FEV1/FVC ratio was reduced even in mild COPD, emphasizing that airflow limitation can occur early in the disease course.

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Table 3: Comparison of time domain and frequency domain of HRV in Normal vs Mild COPD, Normal vs Moderate COPD and Mild COPD vs Moderate COPD

Variables	Normal	Mild COPD	Moderate COPD
LF (ms2)	521.6 ± 332.3	128.6 ± 114.1*	163.6 ± 206.5*
HF (ms2)	540.3 ± 246.9	246.9 ± 275.3*	90.2 ± 114.0*ŧ
LF/HF ratio	1.7 ± 1.7	1.2 ± 1.1	1.5 ± 1.4*
SDRR (ms)	39.7 ± 12.6	20.8 ± 11*	16.7 ± 13.3*
RMSSD (ms)	34.1 ± 13.8	19.3 ± 12.8*	12.6 ± 14.9

*p value <0.05 (normal and mild COPD; normal and moderate COPD)
ŧ p value < 0.05 (mild COPD and moderate COPD)

There was a significant reduction in both parasympathetic and sympathetic activity in COPD groups compared to normal (Table 3). Both LF and HF parameters of HRV were significantly lower in mild and moderate COPD. RMSSD and SDRR, indicators of parasympathetic tone and overall variability respectively, were markedly reduced in COPD, with the most pronounced reduction in moderate disease. These findings suggest autonomic dysfunction in COPD, which worsens with disease severity. The LF/HF ratio showed significant reduction in moderate COPD (1.5 ± 1.4) as compared to normal (1.7 ± 1.7), possibly reflecting an impaired sympathovagal balance.

Table 4: Correlation between Pulmonary function test and Heart rate variability

Pulmonary Function Test Variable	Heart rate Variability Parameters ('r')				
	LF	HF	LF/HF	SDRR	RMSSD
Post FEV1	0.278*	0.210	0.453ŧ	0.378ŧ	0.059
Post FVC	0.113	0.102	0.326*	0.206	0.136
Post FEV1/FVC	0.425ŧ	0.140	0.323*	0.280*	0.145
Post FEV1%	0.509ŧ	0.538ŧ	0.323*	0.522ŧ	0.529ŧ

'r'- Pearsons correlation; * significant, ŧ highly significant

[Table 4] highlights significant correlations between pulmonary function and HRV indices. Post-bronchodilator FEV1% showed strong positive correlations with LF (r = 0.509), HF (r = 0.538), SDRR (r = 0.522), and RMSSD (r = 0.529), all statistically significant ($p < 0.01$). This indicates that better lung function is associated with better autonomic regulation. Post FEV1/FVC and FEV1 also correlated with several HRV parameters, particularly LF/HF ratio and SDRR. These results suggest that worsening airflow obstruction is associated with increasing autonomic imbalance and reduced HRV.

DISCUSSION

The present study evaluated the differences in pulmonary function and heart rate variability (HRV) among normal individuals and patients with mild and moderate Chronic Obstructive Pulmonary Disease (COPD). The results not only confirmed the expected deterioration in pulmonary function with increasing COPD severity but also revealed significant alterations in autonomic cardiac modulation, even at early stages of the disease. These findings underline the systemic nature of COPD, where the impact extends beyond the lungs to affect autonomic cardiovascular control.[10]

The mean age of the participants with normal individuals (60.8 ± 8.61 years), mild COPD patients (59.6 ± 6.83 years) and moderate COPD patients being (64.23 ± 7.92 years). The height did not differ significantly across the study population but weight and Body Mass Index (BMI) showed a progressive decline from normal individuals to those with moderate COPD. The mean BMI was highest among normal (26.79 ± 3.58 kg/m²), followed by mild COPD (25.2 ± 5.14 kg/m²) and lowest in moderate COPD (23.06 ± 4.34 kg/m²). The progressive decline in body weight and BMI with increasing COPD severity is in line with previous reports suggesting that patients with more advanced COPD often experience weight loss and muscle wasting, possibly due to increased energy expenditure during breathing, systemic inflammation, and reduced nutritional intake.[20]

Pulmonary Function Changes

Pulmonary function parameters showed a gradual decline from normal individuals to those with moderate COPD. The FEV_1/FVC ratio and $FEV_1\%$ predicted values demonstrated statistically significant reductions, which are hallmark indicators of airflow obstruction. Although FEV_1 and FVC themselves did not show significant differences across groups, their decline followed a clinically relevant trend. The FEV_1/FVC ratio was particularly reduced in COPD groups, reflecting impaired expiratory airflow and airway obstruction, fundamental features in COPD pathophysiology. The reduction in post-bronchodilator $FEV_1\%$ highlights persistent airflow limitation even after bronchodilation, which supports the diagnosis and severity classification of COPD per GOLD criteria.[21]

Heart Rate Variability: Evidence of Autonomic Dysfunction

The study also assessed HRV, a non-invasive marker of autonomic nervous system function. HRV parameters, both in time and frequency domains, showed marked reductions in the COPD groups

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compared to normals. LF and HF power, which reflect sympathetic and parasympathetic activity respectively, were significantly reduced in both mild and moderate COPD.[22] This suggests that COPD is associated with autonomic impairment characterized by blunting of both sympathetic and parasympathetic responses.[10]

Time domain parameters like SDRR and RMSSD, which assess beat-to-beat variability, were significantly lower in COPD patients.[23] This indicates a reduction in vagal tone and a possible impaired adaptability of the heart to physiological demands, highlighting the systemic implications of the disease.[24]

The reduced HF power and RMSSD particularly point toward parasympathetic withdrawal.[17] In contrast, while LF is traditionally associated with sympathetic modulation, it also has parasympathetic components,[25] its reduction here may reflect a global autonomic blunting rather than a sympathetic overdrive. The LF/HF ratio, although not statistically different among all groups, showed a non-significant trend toward sympathetic predominance in moderate COPD which may suggest an impairment in the sympathovagal balance which may be due to increase in sympathetic or decrease in parasympathetic activity.[26]

There was an increase in LF/HF ratio in moderate COPD as compared to mild COPD which shows that the sympathvagal imbalance increases with the progression of disease which is similar to the findings of Ganesan R.[27] Kiviniemi et al and Thayer et al in their studies showed that the reduction in total power of HRV was associated with mortality and morbidity.[28,29] These findings suggested that among the COPD patients, moderate COPD patients has more sympathetic dysfunction and increased cardiovascular risk when compared to mild COPD

These alterations in HRV could predispose patients to increased cardiovascular risks, including arrhythmias and sudden cardiac death, as previously reported in COPD literature.[30]

Correlations Between Pulmonary Function and HRV

Strong correlations were found between post-bronchodilator pulmonary function parameters and HRV indices. FEV_1% predicted was significantly positively correlated with most HRV markers, including LF, HF, SDRR, and RMSSD, indicating that better lung function is associated with better autonomic control. The FEV_1/FVC ratio also showed significant positive correlations with LF, LF/HF ratio, and SDRR. These associations support the hypothesis that as pulmonary function deteriorates, so does the autonomic regulatory capacity of the cardiovascular system.[31] These results suggest that worsening airflow obstruction is associated with increasing autonomic imbalance and reduced HRV.

This finding is clinically important because it provides a non-invasive physiological linkage between lung mechanics and cardiac autonomic function, suggesting that HRV might be used as an early marker of systemic involvement in COPD. Autonomic dysfunction, particularly vagal withdrawal, may precede overt cardiovascular events and therefore offers a potential target for early intervention and risk stratification.

Pathophysiological Implications

The autonomic imbalance observed in COPD can be attributed to several mechanisms including chronic hypoxia, systemic inflammation, oxidative stress, and hyperinflation. Chronic lung hyperinflation may cause mechanical stress on the heart and baroreceptors, altering autonomic tone.10 Moreover, hypoxaemia and systemic inflammation may directly impair neural regulation through central and peripheral pathways.

Clinical Implications

The findings support the growing evidence that COPD is not merely a pulmonary disease but a systemic disorder with cardiovascular implications. Reduced HRV in COPD patients signifies autonomic dysfunction, which has been associated with increased cardiovascular morbidity and mortality. Early recognition and intervention may help reduce risk and improve quality of life.

The cross-sectional design of the study limits the assessment of causal relationship or progression of autonomic dysfunction over time. Exclusion of the severe and very severe COPD due to the inability of the patients to perform PFT and AFT due to morbidity also limits the study in providing a comprehensive view of HRV changes along the progression of the disease.

CONCLUSION

This study demonstrates that patients with COPD, even in its mild form, exhibit significant impairment in pulmonary function and heart rate variability (HRV) compared to normal individuals. The severity of COPD correlates with progressive autonomic dysfunction, as evidenced by reduced HRV parameters, part. Significant correlations between pulmonary function (especially FEV1% and FEV1/FVC) and HRV indices highlight the interplay between respiratory impairment and autonomic regulation. These findings underscore the importance of early detection of autonomic dysfunction in COPD, which may have implications for cardiovascular risk stratification and comprehensive disease management.

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