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Original Research Article

Effect of Cardiac Autonomic Function in Copd - Insight from a Cross-Sectional Study in Upper Assam

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Abstract:

Background: "Chronic obstructive pulmonary disease (COPD)" is a progressive respiratory disease that induces cardiac autonomic dysfunction and adversely impacts the autonomic nervous system. 50% of COPD mortality is associated with cardiovascular disease (CVD). COPD Severity could be examined by forced expiratory volume in 1s. "Heart rate variability (HRV)" is employed for evaluating cardiac autonomic function.

Aims and Objectives: To evaluate HRV parameters including mean HR, NN50, root mean square of successive differences (RMSSD) and pNN50 across various phases of COPD and observe whether these parameters had been associated with severity of disease.

Materials and Methods: Cross-sectional research including 140 COPD patients was conducted. Pulmonary function test, HRV values, and anthropometric parameters were evaluated. Then divided into 4 categories as per "Global Initiative for Chronic Obstructive Lung Disease (GOLD)" stage criteria. Analysis of Variance (ANOVA) is employed for comparing mean ± standard deviation (SD) of continuous measurement results. When 4 groups' p values have been considered to be significant ($p < 0.05$).

Results: RMSSD levels reported lower in very severe, severe, and moderate COPD patients than in mild COPD patients. Patients with very severe, severe, and moderate COPD exhibited higher mean HR levels than those with mild COPD. Mean HR had a positive correlation with disease severity; however, RMSSD levels had a negative correlation.

Conclusion: We have demonstrated that COPD patients experience cardiac autonomic dysfunction, indicated as elevated sympathetic and decreased parasympathetic activity. This correlation became more evident as severity of disease increased.

Keywords: Forced Expiratory Volume in 1s; Cardiovascular Risk; Chronic Obstructive Pulmonary Disease; Disease Severity; Heart Rate Variability.

Introduction

COPD is frequent and advancing respiratory disorder, with globally prevalence estimated at 13.1%. [1] Asthma and COPD account for the second-highest share of India's overall mortality consequence. GOLD released reports characterizing "COPD as heterogeneous lung condition".

This condition is marked by chronic respiratory symptoms, including breathlessness, productive cough, and repeated episodes, due to airway pathology, such "as bronchitis and bronchiolitis, and or alveoli, as seen in emphysema, leading to persistent and often progressive airflow obstruction. [2] The pulmonary function test is employed to evaluate lung status. Airflow limitation is divided into different stages. Among people with FEV1/FVC ratios <0.7, FEV1>80% is considered mild, 50%≤FEV1<80% is considered moderate, 30%≤FEV1<50% is considered severe, and FEV1 <30%" is considered very severe. [3,4] COPD is a progressive respiratory disease that induces cardiac autonomic dysfunction and adversely impacts the autonomic nervous system. [5] Increased intrathoracic pressure fluctuations brought on by reduced airflow, respiratory strain, decreased oxygen, increased carbon dioxide, and adrenergic phlogosis are all linked to sympathovagal imbalance and respiratory obstructive disease. Hypoxemia is a contributing factor to cardiovascular dysautonomia. [6]

COPD impairs oxygen absorption in the bloodstream across the air blood barrier; it performs function in dysfunction of autonomic nervous system (ANS). [7,8] Right ventricle afterload rises as a result of vascular injury, increased pulmonary vascular resistance, and hypoxic constriction. In

patients with COPD, these alterations result in development of cor-pulmonale that may cause right heart failure. Disease severity may be associated with abnormal HR adjustments, which are represented by changes in HRV. These patients may experience arrhythmias and abrupt cardiac death as a result of heart autonomic dysfunction. [9]

A non-invasive method known as HRV utilizes the R-R interval in an ECG to assess the cardiac cycle-to-cycle variability in HR. HRV acts as a marker for assessing the cardiac autonomic dysfunction between the sympathetic and parasympathetic neural systems. [5] Since its initial research in 1965, HRV analysis has acquired recognition as a crucial technique for early detection of CVDs.

According to earlier research, patients with COPD had reduced HRV and the worst clinical prognosis for treatment. Impaired HRV associated with higher risk of exacerbations and greater burden of symptoms. [7] There aren't enough studies available in our nation, particularly in the northeastern population. Not only has the prevalence of COPD increased in Assam due to risk factors, but the state's higher humidity levels also contribute to it.

The OPD receives a higher volume of cases from February to October. This study aimed to identify trends in HRV parameters and their relationship to COPD severity. If the study yields positive results, HRV could be employed as non-invasive, regular diagnostic tool in COPD patients to diagnose autoimmune dysfunction early on, and it serves as a predictive indicator for therapy.

Materials and Methods

Between October 2023 - September 2024, 140 COPD patients participated in this cross-sectional investigation. 140 COPD patients admitted to pulmonary medicine department during study period would be included.

It has been developed for evaluating PFTs and HRV parameters in COPD patients and for establishing relationship between HRV parameters and disease severity. This research has been conducted at AMCH, Dibrugarh, Assam, in association with Department of Physiology and Department of Pulmonary Medicine.

Study population: Research has been conducted in COPD patients of both sexes in the age group of 40-70years. [3 attending Indoor and Outpatient Department of Pulmonary Medicine, Assam Medical College & Hospital.

Sample size calculation: Considering the mean RR (ms) to be760 ± 130 in patients with COPD [9] sample size for current research has been calculated and rounded off to be 140 with 95% confidence and 80 % power.

Inclusion Criteria: Age 40- 70 years. [3] of both sexes, stable COPD patients confirmed by spirometry, subjects who giving informed consent.

Exclusion Criteria: Patient with h/o hypertension, asthma, T2DM, coronary artery disease, having medications probably interfere with test, particularly vasodilators, angiotensin converting enzyme inhibitors. Patient with h/o malignancy, psoriasis, and renal diseases.

Case Definition: COPD patients, males and females in age group of 40-70 years attending pulmonary medicine Indoor and Outpatient Department, AMCH, Dibrugarh.

Informed Consent: Every participant received description of study, and prior to their enrolment, their informed written consent was obtained.

Ethical Clearance: When this research initiated ethical clearance had been granted from Assam Medical College's Institutional Ethics Committee (Human).

Methods

Between 9 a.m. to 1p.m., research has been conducted in Department of Physiology, AMCH, in autonomic and pulmonary function testing laboratories. Lab temperature remained between 25-27°C, there was adequate lighting, and conditions had been quiet. Enrolled participants received signed informed consent upon being clearly informed regarding study protocol in their native language.

Since it will be difficult for subjects to perform PFT and HRV while they are full, participants have been instructed to consume light breakfast about 7 a.m. and arrive for tests at 9 a.m. At least 12h before recording, individuals had been instructed to abstain from smoking, caffeine consumption, and morning dose of their COPD medications.

HRV parameters in time domain -NN50, pNN50, mean HR, RMSSD, mean RR and PFTs especially FEV1, forced vital capacity (FVC), FEV1/FVC (employing Spiro Excel) have been examined in research group. Subsequently, participants have been divided into 4 groups as per GOLD stage criteria: mild, moderate, severe, and very severe COPD.

Statistical Analysis: Microsoft Excel 2010 and computer program "Statistical Package for Social Sciences (SPSS for Windows, version 21.0. Chicago, SPSS Inc.)" have been employed in conducting statistical analysis of data. ANOVA has been employed for comparing mean ± SD of continuous measurement results. Among 4 groups, p value had been considered significant ($p<0.05$). Fischer's exact test (when cell counts had been or 0) and the Chi square test have been employed for

examining discrete data, that are expressed as number (%).

Statistical significance has been determined at 5% level (p value<0.05) for all analyses.

Results

Upon gaining informed consent from 140 COPD patients, all anthropometric, PFT, and HRV parameters have been measured, and results have been examined. Distribution of study population given in Table 1. Demographic data has been obtained and displayed in Table 2. HRV parameters have been compared across patients in various COPD severity groups employing ANOVA Test, significant differences noted among groups and shown in Table 3.

Table 1: Distribution of Study Population according to sex.

Gender	Case	
	N	%
Male	93	66.43
Female	47	33.57
TOTAL	140	100.00

Table 2: Demographic data of study Population (n=140)

Variables	**Mean ±SD**
Age (years)	57.76±7.92
Height (cm)	162.28±5.83
Weight (kg)	56.48±5.82
BMI (kg/m2)	21.43±1.71
Mean and SD has been employed for expressing values. BMI: Body mass index, SD: Standard deviation	

Table 3: Mean Heart Rate Variability of the Cases and Severity of COPD

Heart Rate Variability	GOLD 1 (n = 16)		GOLD 2 (n = 62)		GOLD 3 (n = 40)		GOLD 4 (n = 22)		p value*
	Mean	±S.D.	Mean	±S.D.	Mean	±S.D.	Mean	±S.D.	
Mean RR (ms)	860.62	54.41	646.94	57.15	539.16	9.00	511.17	7.45	<0.001*
Mean HR (bpm)	69.96	4.17	93.44	7.96	111.31	1.83	117.40	1.72	<0.001*
rMSSD (ms)	60.23	3.81	45.26	4.00	37.71	0.63	35.77	0.56	<0.001*
NN50 count	45.02	6.04	25.52	4.70	17.51	0.82	15.64	0.45	<0.001*
pNN50%	12.16	0.45	8.98	1.16	5.19	1.15	2.96	2.00	<0.001*
*ANOVA Test; The p-value is significant at 5% level of significance									

Discussion

Current research results insights into relationship between severity of COPD and HRV parameters, highlighting potential implications for disease progression and management. To assess autonomic imbalance in COPD patient that increases cardiovascular morbidity and mortality, HRV indicators had been analyzed.

In current research, mean age (years) reported that 57.76±7.92 years in COPD group. The mean (±SD) height of cases was found to be 162.28 ±5.83 cm and the mean weight, BMI were 56.48 ± 5.82kg and 21.43 ± 1.71 kg/m2 respectively. This finding were compared to those of Lalitha et al. [9], findings were similar to the present study; No significant changes noted. Paul et al. [10] also reported that no statistical significance in age, height and BMI in study population. In present study mean of mean RR (ms) was 860.62 ± 54.41ms in GOLD I. In GOLD II, III, IV, the values were 646.94 ± 57.15,539.16 ± 9.00, 511.17 ± 7.45, respectively. The values were decreasing when compared to GOLD I. That indicate mean RR was reduced with severity of disease. A et al. [11] observed those similar results in Mean RR interval, less in GOLD IV (649.47 ± 52.95) and high in GOLD stage I (809 ± 60.19).

In this Current research, observed that mean of mean HR (bpm) in GOLD I was 69.96 ± 4.17. In GOLD II, III, IV, the values were 93.44 ± 7.96,111.31 ± 1.83, and 117.40 ± 1.72, respectively. According to severity values were increasing, lowest mean HR in GOLD I- MILD COPD. The mean HR level had been considerably higher in very severe COPD patients. [5]

Stein et al.12 found that COPD patients had higher resting heart rates and shorter RR intervals, indicating chronic sympathetic activation. Carvalho et al. [13] observed that individuals with COPD with recurrent worsening showed a greater increase in Mean HR, correlating with disease severity and hypoxia levels. Volterrani et al. [14] observed to be mean HR was inversely correlated with lung function (FEV1%), suggesting lung function deteriorates, heart rate increases due to heightened sympathetic tone. COPD leads to chronic hypoxemia,

which stimulate chemoreceptor reflex, increasing heart rate. Inflammation causes elevated levels of CRP, TNF alpha and IL 6 impair vagal function, further reducing Mean RR interval and increasing Mean HR.

In current research, rMSSD (ms) in GOLD I, GOLD II, III, and IV were 60.23 ± 3.81,45.26 ± 4, 37.71 ± 0.63, and 35.77 ± 0.56, respectively. The values showed significant decrease from GOLD I TI IV. This indicated rMSSD were decrease with severity of disease. In study of Ganesan et al. [5] observed the same finding, rMSSD was decreased in 4th stage of disease than first stage decease patients. Study of A et al. [11] showed same trend in rMSSD (ms).

The rMSSD was decreasing in their studies. Carvalho et al. [13] reported that rMMSD is strongly influenced by vagal tone, which is suppressed in COPD due to chronic inflammation, oxidative stress, and prolonged sympathetic activation. COPD patient often experiences dyspnea and poor lung mechanics, which may impair normal respiratory sinus arrhythmia, leading to reduced RMSSD. In Pantoni et al. [15]'s study also showed rMSSD was decreased in COPD.

Macdonald et al. [16] reported a marked reduction in RMSSD among COPD patients, particularly in those with frequent exacerbations and cardiovascular comorbidities. Borghi-Silva et al. [17] reported that COPD patients had higher RMMSD values post-intervention, suggesting that exercise may restore autonomic balance. Ucak et al. [18] demonstrated that COPD patients with obstructive sleep apnea (OSA) had even lower RMSSD values, emphasizing the compounding effect of sleep disturbances on autonomic dysfunction.

Present study was found to be mean NN50 count was 45.02 ± 6.04 in GOLD I. In GOLD II and III, NN50 were 25.52 ± 4.70,17.51 ± 0.82. In GOLD IV value was 15.64 ± 0.45. Less value of NN50 was observed in GOLD IV. It showed that, according to severity, NN50 was decreasing.

In this study, the mean pNN50% in GOLD I was 12.16 ±0.45. In GOLD II, III, IV stages, the values were 8.98 ± 1.16,5.19 ± 1.15, and 2.96 ± 2, respectively among 4 subgroups significant difference in pNN50% noticed. The mean value is lower in GOLD IV. It indicated that, according to increased severity, pNN50% was decreased when compared to mild COPD.

A decline in pNN50 is correlated with higher disease severity and lower exercise capacity. [19] Gunduz et al. [19] observed in the study that NN50, PNN50, and rMSSD were decreased in chronic obstructive patients. When compared to healthy population, COPD patients' pNN50 and NN50 count had been considerably lower, indicating decreased vagal activity and elevated sympathetic tone. [20] Rennie et al. (2003) found that COPD patients with severe airflow limitation (FEV1< 50%) had nearly 50% lower Pnn50 and NN50 values compared to mild COPD, showing a progressive loss of parasympathetic function with disease severity. This study demonstrated a significant decrease in HRV parameters among COPD patients, indicating increased autonomic dysfunction. Specifically, time domain indices encompassing Mean RR interval, Mean HR, RMSSD, pNN50, and NN50 count were markedly reduced in COPD patients, suggesting reduced parasympathetic activity and increased sympathetic dominance.

Physical activity and pulmonary rehabilitation have been shown to improve autonomic function in COPD individual. Cohort by Zhang et al. [21] observed that pulmonary rehabilitation led to significant improvements in HRV, indicating enhanced parasympathetic activity. Encouraging COPD patients to engage in moderate exercise may help mitigate autonomic dysfunction and reduce cardiovascular risk. [17]

COPD patients with low HRV have higher cardiovascular risk and poor health outcomes. This study given the strongest association between HRV and cardiovascular risk, results suggest that HRV can be a valuable non -invasive measurement for monitoring disease progression as well as assessing treatment efficacy. Regular HRV assessments may help identify high – risk patients who require closer cardiovascular monitoring and allowing for timely interventions such as pulmonary rehabilitation, lifestyle modifications and pharmacological treatments targeting autonomic balance.

Conclusion

From current research, HRV is associated with COPD and decreases with disease severity. It is proven that impact of COPD on autonomic nervous system regulation and leading to cardiac autonomic function dysregulation in the form of decreased parasympathetic action and increased sympathetic activity. According to the results of this study, HRV could be employed as routine non-invasive assessment for identifying cardiac problems early in COPD patients. This would assist patient's live better lives by implementing appropriate management measures and follow-ups. The results' generalisability may be limited by research's limitations, which include its single-centre methodology and brief HRV analysis duration.

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