Journal of Cardiovascular Disease Research

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 02, 2024

Assessing Autonomic Dysfunction in Chronic Obstructive Pulmonary Disease Patients: A Cross-Sectional Study

[1]Dr. Roma Singh, [2]Dr. Nipun Saproo, [3]Dr. Harshul Patidar, [4]Dr. Varsha Patel

[1]Associate Professor, Department of Pathology, LN Medical College and Sewakunj Hospital, Indore, Madhya Pradesh, India
[2]Associate Professor, Department of Neurology, MGM Superspeciality Hospital, Indore, Madhya Pradesh, India
[3]Associate Professor, Department of Pathology, Government Medical College, Satna, Madhya Pradesh, India
[4]Senior Resident, Department of Pathology, Government Medical College, Satna, Madhya Pradesh, India

Corresponding Author:
Dr. Varsha Patel
Email ID: varshapatel1718@gmail.com

Received: 29-01-2024 Accepted: 10-02-2024 Published: 25-02-2024

Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) ranks as the second leading cause of mortality in India and is linked with cardiovascular dysautonomia. Heart rate variability (HRV) analysis is a common non-invasive method used to assess cardiac autonomic nervous activity. This study aimed to evaluate and compare HRV in COPD patients with healthy control subjects matched for age and sex.

Materials and Methods: This cross-sectional study was conducted at a tertiary care teaching institute in India. A total of 78 individuals participated, including 39 COPD patients and 39 healthy age- and sex-matched individuals in the control group. The unpaired Student t-test was utilized for statistical analysis.

Results: The study found non-significant differences in mean height, age, weight, body mass index, and heart rate between the COPD group and the control group. However, there was a statistically significant difference in mean RR interval, with COPD patients exhibiting lower values compared to healthy subjects. Measures of HRV, including RMSSD and SDNN, were notably lower in COPD patients compared to controls. Moreover, significant differences were observed in pNN50 and NN50 between the two groups. The COPD group showed higher mean LF nu, lower mean HF nu, and a higher mean LF/HF ratio compared to controls.

Conclusion: The study concluded that COPD patients exhibit sympathetic hyperactivity and reduced parasympathetic activity compared to healthy individuals, which is statistically significant. This underscores the importance of utilizing non-invasive methods like HRV analysis for screening autonomic function status in COPD patients.

Keywords: Autonomic functions, chronic obstructive pulmonary disease (COPD), dysautonomia, heart rate variability.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) stands as a significant health concern globally, being the second most common cause of mortality in India and contributing to approximately 8.7% of deaths in the country. It is projected to become the third leading cause of death worldwide by 2030. COPD is a non-communicable disease characterized by irreversible airflow obstruction, leading to decreased forced expiratory volume in 1 second (FEV1) and airflow restrictions. The inhalation of toxic particles and gases, notably from smoking, is a major cause of COPD [1,2].

Hypoxemia, a common consequence of COPD, plays a role in cardiovascular dysautonomia. This involves vascular inhibition induced by reduced arterial oxygen pressure, leading to endothelial remodeling and a low autonomic sympathetic response. COPD also leads to a reduction in oxygen uptake in the blood through the respiratory membrane, resulting in reduced energy production at the cellular level. These hypoxemic conditions contribute to autonomic nervous system (ANS) dysfunction [3,4].

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COPD influences the systemic autonomic system, causing an increase in sympathetic activity and resting heart rate (HR) [5]. This feedback loop may be associated with parasympathetic airway hyperactivity, bronchoconstriction, vasoconstriction, and systemic inflammation [6-8]. These extrapulmonary comorbidities can significantly affect the prognosis of COPD patients. Therefore, early cardiac assessment is recommended for these patients due to the increased risk of myocardial injury, ventricular dysfunction, functional alterations, and cardiac dysfunction, reflected in changes such as increased resting HR and/or decreased HR variability (HRV) indices [9,10].

Assessing autonomic function through HRV analysis is crucial in understanding the pathological and physiological irregularities of COPD and guiding clinical management. HRV is a non-invasive procedure that evaluates the activity of the cardiac autonomic nervous system (ANS) by analyzing the oscillations between consecutive heartbeats (RR intervals) [11]. Decreased HRV is associated with higher morbidity and mortality, while high HRV levels are linked to reduced stress and better physical fitness [12,13]. Monitoring HRV can help identify mortality risks in COPD patients due to cardiovascular system involvement [14].

The present study aims to assess and compare HRV in COPD patients with stable lung conditions and healthy age- and sex-matched controls. Analyzing HRV can aid in the early detection of cardiovascular changes in COPD patients, facilitating prompt diagnosis and treatment interventions [15].

MATERIALS AND METHODS

The cross-sectional study was conducted at an Indian tertiary care teaching institute. A total of 78 individuals participated, including 39 COPD patients and 39 healthy age- and sex-matched individuals forming the control group. The control group, aged between 30 to 50 years, was selected from the outpatient departments of allergy and pulmonology within the same institute.

Confirmed cases of COPD as per Gold Criteria, diagnosed by a physician based on clinical and spirometric criteria, in stable cardiorespiratory condition without recent respiratory tract infections or hospitalizations for pulmonary or cardiac reasons and Cooperative individuals aged ≤30 years were included as participants for the COPD group.

The exclusion criteria for this study encompass a range of conditions and characteristics. Patients undergoing acute exacerbations of COPD, those with cardiac disease, hypertension, neurological complications, and diabetes are excluded from participation. Additionally, individuals experiencing breathing discomfort, acute respiratory illnesses, or displaying uncooperative behavior are not included. Furthermore, individuals with a history of taking vasodilators, angiotensin-converting enzyme inhibitors, systemic corticosteroids, medications influencing autonomic functions, or those with a history of alcohol abuse are also excluded from the study. These criteria ensure that the study participants are free from these confounding factors, thereby enhancing the validity and reliability of the study outcomes.

All participants were advised to avoid caffeine and excessive physical exertion the day before the tests, and to ensure adequate sleep. COPD patients were instructed to take prescribed medications as usual except for inhalation corticosteroids and bronchodilators, which were discontinued for specific durations before the tests. The procedures were conducted in a comfortable environment at ambient temperature. HRV analysis was performed using a computerized polygraph. HRV parameters were assessed and reported as mean ± standard deviation.

The unpaired Student t-test was utilized for statistical analysis using the SPSS version 19.0. A probability value of ≤0.05 was considered statistically significant.

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RESULTS

In our study, each study group comprised 20 male participants and 19 female participants, ensuring a balanced representation of both genders. Table 1 presents a comparison of key variables including height, mean weight, mean age, and mean BMI between COPD patients and the control group.

A comparison of SDNN (Standard Deviation of Normal-to-Normal Intervals) and RMSSD (Root Mean Square of Successive Differences) in COPD patients and controls revealed a decrease in both parameters among COPD patients, with higher mean values observed in the control group. The lower mean SDNN in COPD cases indicates reduced heart rate variability (HRV), reflecting autonomic dysfunction. Similarly, the lower mean values of pNN50 (percentage of successive NN intervals that differ by more than 50 ms) and NN50 (number of pairs of successive

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 02, 2024

NN intervals differing by more than 50 ms) in COPD cases compared to higher means in controls further highlight this difference, as summarized in Table 2.

The frequency-domain parameter LF nu (normalized unit) was slightly higher in COPD cases compared to controls. This elevated LF nu in COPD patients indicates sympathetic overactivity when compared to healthy subjects. Conversely, the frequency-domain parameter HF nu was significantly lower in COPD patients than in controls, indicating reduced parasympathetic activity in the COPD group. The mean LF/HF ratio also showed an apparent increase in COPD cases compared to healthy subjects, suggesting a higher sympathetic-parasympathetic balance in COPD patients. While the mean LF ms2 was higher in COPD cases compared to controls (not statistically significant), the mean HF ms2 was lower in COPD cases, albeit also not statistically significant (Table 3).

The mean value of FEV1 % (forced expiratory volume in one second as a percentage of predicted value) was significantly higher in COPD cases compared to controls, with a highly significant p-value of <0.05, as indicated in Table 4.

Table 1: Anthropometric parameters of study population

Parameter	Cases (Mean ± SD)	Controls (Mean ± SD)	P-value
Height; in cm	164 ± 6.3	163 ± 6.7	0.08
Weight; in kg	62 ± 5.4	60.5 ± 7.1	0.85
BMI; in kg/m²	22.6 ± 1.6	23 ± 1.8	0.12
Age; in years	42.5 ± 6.5	41 ± 6.9	0.68

Table 2: Time domain parameters of HRV in study population

Parameter	Cases (Mean ± SD)	Controls (Mean ± SD)	P-value
Mean RR interval	620 ± 310	750 ± 135	<0.05
Mean HR; in bpm	92.05 ± 55.10	86.14 ± 16.18	0.57
NN50 count	20.41 ± 40.22	80.45 ± 140.25	<0.05
pNN50 %	5.23 ± 10.21	19.31 ± 30.35	<0.05
SDNN (m)	35.35 ± 30.7	60.14 ± 40.48	<0.05
RMSSD (m)	37.15 ± 42.1	70.48 ± 70.05	<0.05

Table 3: Frequency domain parameters of HRV in study population

Parameter	Cases (Mean ± SD)	Controls (Mean ± SD)	P-value
LF nu	66.51 ± 17.11	52.55 ± 16.13	<0.05
HF nu	33.04 ± 17.84	47.29 ± 16.23	<0.05
LF/HF	2.01 ± 3.46	1.07 ± 1.56	<0.05
LF ms2	180.12 ± 199.88	170.32 ± 131.79	0.78
HF ms2	95.42 ± 75.08	105.28 ± 60.47	0.47

Table 4: Comparison of FEV1 in study population

Parameter	Cases (Mean ± SD)	Controls (Mean ± SD)	P-value
FEV1, in %	71.52 ± 8.85	83.91 ± 3.65	<0.05

DISCUSSION

In patients with COPD, there is an elevated LF/HF ratio and a prevalence of sympathetic dominance. The increased heart rate (HR) is associated with heightened cardiac comorbidities [16-18]. The risk of autonomic imbalance escalates with the severity of shallow breathing, causing a reduction in sympathetic nervous system activity and an increase in baroreflex sensitivity among patients with chronic heart failure [19]. A study conducted by Buch et al. in the Copenhagen City Heart Study observed that the primary cause of arrhythmia in COPD patients is likely multifactorial, attributable to various risk factors including hypoxemia, acidosis, and reduced forced expiratory volume in one second (FEV1). They noted a higher risk of atrial fibrillation in patients with an FEV1 range of 60–

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 02, 2024

80% predicted compared to those with an FEV1 ≥80% [20]. Moreover, COPD is associated with distinct electrocardiographic abnormalities, characterized by an increased incidence of conduction abnormalities such as supraventricular or ventricular premature beats, atrial fibrillation (AF), flutter, multifocal atrial tachycardia, supraventricular tachycardia (SVT), and non-sustained ventricular tachycardia (VT) [21,22].

Our study reveals an elevated LF nu in COPD patients compared to controls, indicating heightened sympathetic activation. This phenomenon is attributed to factors such as intermittent or sustained hypoxemia, oxidative stress, and lung hyperinflation, which collectively lead to a loss of respiratory sinus arrhythmia and a decrease in high-frequency (HF) power among COPD patients. Heart rate (HR) is influenced by autonomic nervous system (ANS) activity, with sympathetic stimulation increasing HR while parasympathetic stimulation decreases it. The time-domain parameters including mean RR interval, RMSSD, and SDNN demonstrate patterns similar to frequency-domain (FD) parameters. The decreased mean RR intervals observed in our study indirectly reflect an increase in HR, suggesting heightened sympathetic activity. The elevated LF nu in COPD patients signifies sympathetic hyperactivity compared to controls, corroborating findings from previous studies [23,24]. Conversely, the reduced HF nu in COPD patients indicates lower parasympathetic activity. The high mean LF/HF ratio in COPD patients suggests both sympathetic hyperactivity and reduced heart rate variability (HRV), consistent with our study's results. However, our study's limitations was that HRV assessment was conducted at rest for only 5 minutes, potentially limiting the reliability compared to HRV measured over 24 hours..

CONCLUSION

COPD leads to sympathetic hyperactivity and diminished parasympathetic activity compared to individuals without the condition. Analyzing HRV in COPD patients can detect cardiac sympathovagal imbalances at an early stage, enabling appropriate management strategies. This study underscores the significance of non-invasive techniques for assessing autonomic function in COPD patients. Early identification is crucial for preventing and managing complications associated with cardiac autonomic dysfunction including sudden death. Future research exploring the interplay between respiratory and cardiovascular diseases could have significant clinical implications.

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