DETERMININATION OF THE FREQUENCY OF ALTERED CARDIAC REPOLARIZATION BY MEASURING THE HEART RATE CORRECTED QT INTERVAL IN COPD PATIENTS

ABSTRACT

Objectives: - To determine the frequency of altered cardiac repolarization by measuring the heart rate corrected QT interval in COPD patients.

Setting: - Department of Medicine at LUMHS hospital Hyderabad/Jamshoro

Study design: - Descriptive Cross sectional study

Duration of study: 6 months from 01-03-2019 to 31-08-2019

Methods: A total of 232 patients with severe acute exacerbation of COPD were included in this study. A 12 lead ECG was performed. QT intervals were measured on a resting ECG tracing in lead II. The QT interval was measured manually from the starting point of the QRS complex to the terminal point of the down slope of the T wave.

Results: A total of 232 patients with COPD were included in this study. Most of the cases were above 50 years of age. The average age of the patients was 53.74±4.35 years. There were 92.67% (215/232) male and 7.33% (17/232) female. Out of 232 patients, 21.14% were current smoker and 75.86% were ex-smoker. A QTc interval >0.44 seconds was considered abnormally prolonged. Frequency of altered cardiac repolarization by measuring the heart rate corrected QT interval in COPD patients was 31.47% (73/232) . Rate of altered cardiac repolarization was not significant among different age groups (p=0.641) . Rate of altered cardiac repolarization was significantly high in male as compare to female (33.5% vs. 5.9%; p=0.018). This was not significant between obese and non-obese groups (p=0.100) . Rate of altered cardiac repolarization was significantly high in former smoker (p=0.0005) and those patients whose duration of COPD was above 15 years (p=0.0005) .

Conclusion: Patients with hypoxic chronic obstructive pulmonary disease (COPD) have evidence of a subclinical parasympathetic autonomic neuropathy, with apparent preservation of sympathetic function. Measuring heart rate corrected QT interval (QTc) test is repeatable, easy to perform and a sensitive indicator for autonomic dysfunction in breathlessness individuals with COPD.

Key Words: Chronic obstructive pulmonary disease, QT interval, Altered cardiac repolarization

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) remains a major public health problem. It has significant extra pulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with abnormal inflammatory response of the lung to noxious particles or gases. The chronic airflow limitation characteristic of COPD is caused by a mixture of small airway disease (obstructive bronchiolitis) and parenchymal destruction (emphysema), the relative contributions of which vary from person to person.[1]

Chronic obstructive pulmonary disease(COPD) is the third leading cause of death globally.[2] Progressive air flow limitation is the hall mark of COPD which is associated with local chronic inflammatory response in the airways and lungs.[3] The exact prevalence of COPD in Pakistan is unknown. However, it has been suggested that the risk of undetected airflow obstruction in smokers is associated with increasing age and the number of pack years of smoking.[4]

COPD patients also have a higher rate of cardiovascular morbidity and mortality than the general population , Moreover, half of the deaths of COPD patients are attributable to cardiovascular disease.[5] Finkelstein et al. demonstrated that COPD patients had a higher risk of myocardial infarction and arrhythmia than non-COPD controls.[6] Chronic obstructive pulmonary disease (COPD) is associated with an increased risk of cardiovascular morbidity and mortality.[7-9] Previous population-based studies suggested that patients with COPD have a two to three fold increased risk of sudden cardiac death (SCD).[10] Alteration of cardiac repolarization is an important mechanism for the development of malignant arrhythmias and the occurrence of SCD.[11-13]

Study conducted by Sievi et al. in 2014 showed that one third of a typical COPD population has altered cardiac repolarization and increased dispersion of repolarization, which may be related to hypoxia.

Altered cardiac repolarization may result in an increased risk of malignant ventricular arrhythmias and sudden cardiac death. And they found that QT interval was prolonged in 31.9% of the COPD patients.[14]

OBJECTIVES

To determine the frequency of altered cardiac repolarization by measuring the heart rate corrected QT interval in COPD patients.

MATERIAL AND METHODS

Study setting: - Department of Medicine at LUMHS hospital Hyderabad/Jamshoro

Study design: - Cross sectional descriptive study

Duration of study: 6 months from 01-03-2019 to 31-08-2019

Sample size: - The sample size is calculated by Raosoft sample size calculator. With confidence interval 95%, margin of error 6% and anticipated proportion of patients with altered cardiac repolarization in COPD is 31.9%, Sample size is 232 required for study.

Sample selection: Non – Probability consecutive Sampling.

Inclusion criteria

- All patients with COPD
- 40 t0 70 years of age, of either gender.
- current as well as Ex-smoker , with duration of disease more than 10 years, willing to participate in the study .

Exclusion criteria.

1) Age less than 40 years.

2) Patients with reversible airway obstruction (>12% Change in FEV1 after bronchodilator therapy on spirometery).

METHOD OF DATA COLLECTION

All consecutive patients admitted to the medical ward for severe acute exacerbation of COPD were for included in the study and written informed consent was obtained from all. A 12 lead ECG including 3 bipolar limb leads, 3 unipolar limb leads and 6 unipolar precordial leads was performed. For all electrocardiographic recordings a commercially available 12-lead ECG machine was used and set at 25-mm/s paper speed and 10-mm/mV amplitude. QT intervals was measured on a resting ECG tracing in lead II. The QT interval was measured manually from the starting point of the QRS complex to the terminal point of the down slope of the T wave. If the T waves are inverted, the end was taken at the point where the trace return to the baseline between the T wave and the P wave. In the presence of U wave, the end of the T wave was taken as the lowest point between the T wave and the U wave. As the QT interval varies inversely with the heart rate, the corrected QT interval (QTc) was calculated using Bazett's formula: QTc = measured QT interval /(√R-R interval), where QT and R-R interval are expressed in seconds. A QTc interval >0.44 seconds was considered abnormally prolonged.

Ethical consideration.

This is a zero risk study as there was no collection of identity information from the patient. Written informed consent was obtained before administering the questionnaire from all enrolled patients. Confidentiality and privacy was maintained throughout the process.

DATA ANALYSIS PROCEDURE:-

Statistics was calculated by SPSS, Version 16.0. Data was calculated by SPSS, Version 16.0. Continuous variables such as age, weight, Height, BMI, QT interval and duration of COPD were calculated as mean ± standard deviation (SD). Frequency and Percentage was computed for qualitative variables like gender, smoker,

altered cardiac repolarization. Effect modifiers like age, BMI, gender, smoker and duration of COPD was controlled by post stratification. Statistical significance was calculated using Chi-square test. A P-value ≤ 0.05 was considered to be statistically significant.

RESULTS

A total of 232 patients with COPD were included in this study. Most of the cases were above 50 years of age as shown in figure 1. The average age of the patients was 53.74±4.35 years. Other demographic and duration of COPD is also reported in table 1. There were 92.67% (215/232) male and 7.33% (17/232) female as shown in figure 2. Out of 232 patients, 21.14% were current smoker and 75.86% were Ex-smoker as presented in figure 3. The frequency of altered cardiac repolarization by measuring the heart rate corrected QT interval in COPD patients by duration of COPD as shown in table 2.

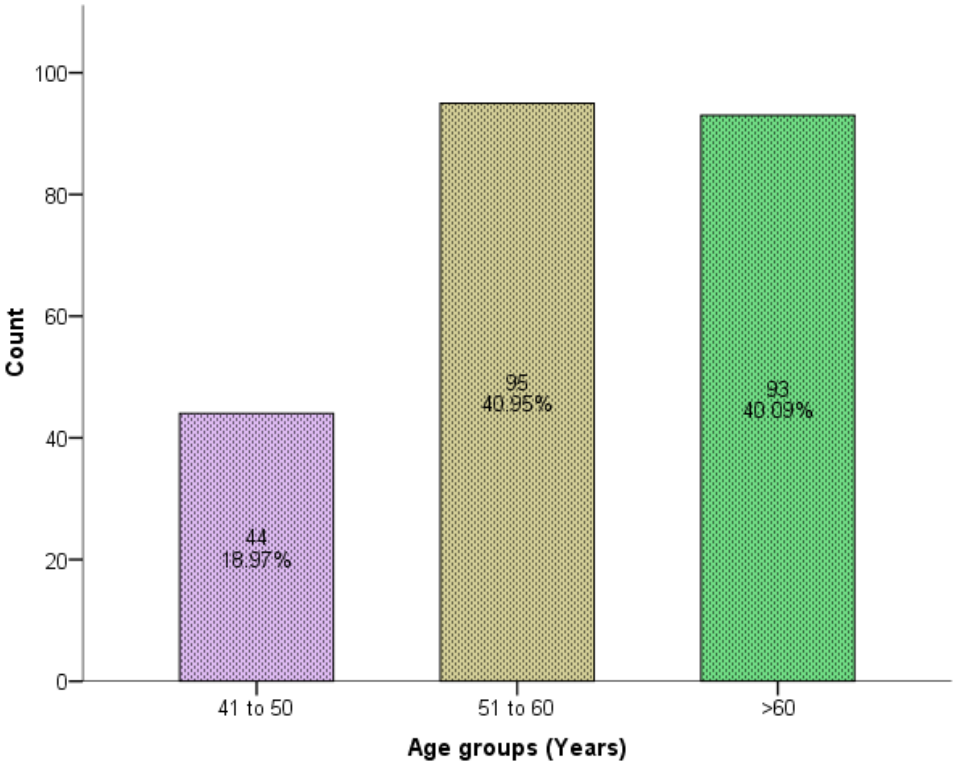

FIGURE 1 AGE DISTRIBUTION OF THE PATIENTS n= 232

TABLE 1

DESCRIPTIVE STATISTICS OF DEMOGRAPHIC VARIABLES

Age Groups (Years)	Mean	95% Confidence Interval for Mean		Std. Deviation
		Lower Bound	Upper Bound	
Age (Years)	53.74	53.18	54.31	4.35
Height (cm)	154.52	153.82	155.21	5.38
Weight (kg)	67.10	65.55	68.66	12.04
BMI (kg/m^2)	28.07	27.46	28.68	4.70
duration of COPD	13.66	13.39	14.92	2.04

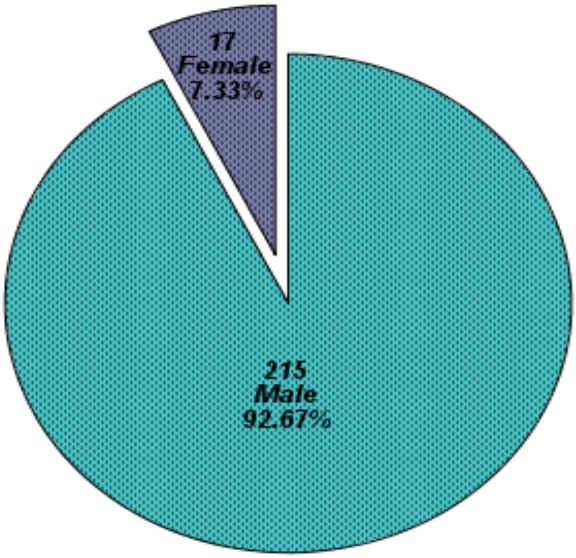

FIGURE 2 GENDER DISTRIBUTION OF THE PATIENTS n= 232

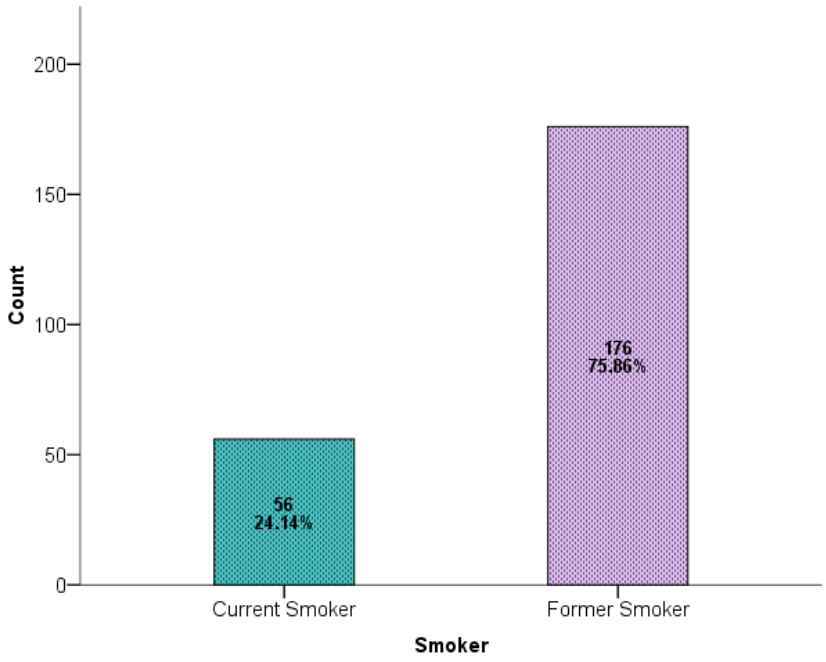

FIGURE 3SMOKING STATUS OF THE PATIENTS n=232

TABLE 2

FREQUENCY OF ALTERED CARDIAC REPOLARIZATION BY MEASURING THE HEART RATE CORRECTED QT INTERVAL IN COPD PATIENTS BY DURATION OF COPD

n=232 Chi-Square= 30.96

Duration Of COPD	Altered Cardiac Repolarization		**Total**	**P-Value**
	Yes	**No**		
11-15 years	31(19.7%)	126(80.3%)	157	0.0005
>15 years	42(56.0%)	33(44.0%)	75	

DISCUSSION:

COPD represents a significant and increasing healthcare concern and is predicted to be the third leading cause of mortality worldwide by 2020.[15,16] COPD is responsible for approximately 2.75 million deaths worldwide. According to the Global Burden of Disease (GBD) study 2006, a systematic review and meta-analysis was conducted based on the published medical literature and it was found that the global prevalence of chronic obstructive pulmonary disease in adults aged ≥40 years was 9-10%.[17] The prevalence of COPD is explored in many community-based projects; and is found to be 16.4% for Spanish, 2.8% for population from England and Wales, and 13.8% for population of Karachi.[18] Previous population-based studies suggested that patients with COPD have a two to three fold increased risk of sudden cardiac death (SCD). However, the mechanisms underlying the association between COPD and SCD are currently unclear and predictors of malignant cardiac arrhythmias and SCD in COPD have not been defined. To determine the frequency of altered cardiac repolarization by measuring the heart rate corrected QT interval in all COPD patients included in this study. Timing of illness is a central component of the experience of living with a chronic illness. Older individuals are more likely than younger individuals to expect illness as a normative part of aging.[19] In the past, chronic obstructive pulmonary disease (COPD) was always considered to be a disease that mainly affected elderly men, reflecting the high prevalence of smoking among men. However ,COPD has now more prevalence in women than men,[20] although diagnosis is less likely than in men with the same degree of lung function impairment. In our study most of the cases were above 50 years of age and the average age of the patients was 53.74±4.35 years. There were 92.67% male and 7.33% female. There are multiple risk factors for developing COPD; and associations of some factors are already established like cigarette smoking,[21] and exposure to biomass fuel. Cigarette smokers complained of more frequent respiratory symptoms and lung function abnormalities. Out of 232 patients in our study, 21.14% were current smoker and 75.86% were Ex-smoker. The sex difference in our study is wholly attributable to differences in smoking habits: in fact, the difference increases with advancing age because of the cumulative effects of long-term smoking in men. According to a national survey, in Pakistan, the

prevalence of chronic bronchitis in the population over 65 years of age was 14% in rural females and 6% in rural males. In urban population, the prevalence was less than 2%in the age group of 15-24 and greater than 9% above 65 years of age, higher prevalence in female might be due to exposure to household smoke, use of biomass and wood as fuel.[22]

Prolonged cardiac repolarization is associated with the development of fatal arrhythmias and the occurrence of Sudden Cardiac Death. Different measures derived from electrocardiography (ECG) represent repolarization in homogeneities of the myocardium such as QT interval and QT dispersion. In diverse patient populations, an association between altered cardiac repolarization and the development of malignant arrhythmia and SCD, respectively, has been documented. In our study the frequency of altered cardiac repolarization by measuring the heart rate corrected QT interval in COPD patients was 31.47% (73/232). Our results are supported by a recently published cross-sectional study which reported that a high prevalence of COPD patients showed altered cardiac repolarization and increased dispersion of repolarization, potentially exposing these patients to an increased risk of malignant ventricular arrhythmias and SCD. In a recent study Oliver Van Oekelen et al reported recalculating the QTc duration using the Fridericia formula resulted in a lower prevalence of only 11% for COPD in large population-based studies including elderly subjects, the prevalence of an altered QTc interval has been estimated to be approximately 8%.[23] In contrast, the COPD patients in the current study showed a fourfold higher prevalence of an altered QTc interval compared to the general population. In a case-control study, investigating the risk of SCD in patients with coronary heart disease with and without prolonged QTc interval, the prevalence of prolonged QTc interval was 39% in the group with subsequent SCD. This prevalence of altered QTc in SCD patients is comparable with the findings of the current study in COPD patients.

As a limitation of this study, no continuous 24-hour ECG was performed, and therefore, it is not possible to evaluate cardiac repolarization both during a longer daytime period and during sleep.

CONCLUSION : Patients with hypoxic chronic obstructive pulmonary disease (COPD) have evidence of a subclinical parasympathetic autonomic neuropathy, with apparent preservation of sympathetic function. Measuring heart rate corrected QT interval (QTc) test is repeatable, easy to perform and a sensitive indicator for autonomic dysfunction in individuals with COPD.

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