



## The Effect of Effort Test on QT Dispersion in Patients with New Diagnosis COPD

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Received date: November 05, 2018; Accepted date: November 23, 2018; Published date: November 29, 2018

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### Abstract

**Background:** Chronic obstructive pulmonary disease (COPD) is associated with increased risk of cardiovascular morbidity and mortality. The aim of this study is to investigate the effect of effort test on corrected QT (QTc) and corrected QT dispersion (QTcd) in patients with newly diagnosed and untreated COPD patients.

**Patients and method:** Thirty-three patients who were referred to the chest diseases polyclinic between September and December 2018, who had no previous treatment, who had evidence of obstruction in the pulmonary function test were included in the study. As control group, 36 patients who were referred to the cardiology clinic with chest pain, who had no COPD, had an indication for effort test, were negative for effort test, were selected. The study group was initially subjected to pulmonary function test. Patients were then enrolled in the effort test according to the Bruce protocol. QTc and QTcd values were calculated for resting and peak exercise.

**Results:** The resting QTcd value of the study group was  $39.8333 \pm 3.6762$  msec, value of control group was  $38.0244 \pm 4.298$  msec ( $p=0.113113$ ,  $t=1.221961$ ). Peak exercise QTcd values in the study and control groups were  $63.356 \pm 5.408$  msec,  $44.475 \pm 5.0572$  ( $p<0.00001$ ,  $t=18.37567$ ), respectively.

**Conclusion:** There was a statistically significant difference in resting and peak exercise QTcd values in the study group. There was no statistically significant difference between two groups' resting QTcd values. There was a significant difference between peak exercise QTcd values in the study group and control group.

**Keywords:** COPD; Corrected QT dispersion; Stress testing

### Introduction

Chronic obstructive pulmonary disease (COPD) is associated with increased risk of cardiovascular morbidity and mortality [1-3]. Previous community-based studies have shown that the risk of sudden cardiac death (SCD) in patients with COPD is increased 2-3 times [4]. However, the mechanisms underlying the relationship between COPD and SCD are still unclear, and predictors of malignant cardiac arrhythmias and the predictors of SCD in COPD have not been identified. The change of cardiac repolarization is an important mechanism for the development of malignant arrhythmias and the occurrence of SCD [5-7]. The findings obtained by surface electrocardiography (ECG) represent the distribution of repolarization and electrical homogeneity of the ventricles [8]. Results of previous studies with heart failure [9], patients with long QT syndrome [10] and older individuals [11] have shown that there may be a relationship between malignant arrhythmia and SCD with alteration of cardiac repolarization findings such as QT interval and QT dispersion.

In acute exacerbations of COPD patients and in COPD, QT dispersion and ventricular electrical heterogeneity have been investigated and increased in some studies [12-14]. In addition, COPD patients may have a higher frequency of cardiac arrhythmias and the severity of airway obstruction is thought to be associated with arrhythmia formation [15-17]. It has been shown that QT dispersion

can be increased with stress test in hypertensive patients [18]. In addition, it was shown that QT dispersion may be increased by exercise test in healthy individuals [19]. Preliminary evidence from a small case-control study suggests that an increased maximal QT interval is associated with the development of ventricular arrhythmia in patients with COPD [20]. However, the effect of stress test on QT dispersion and ventricular electrical heterogeneity in COPD patients was not investigated. The aim of this study was to investigate the effect of stress test on QT in patients with newly diagnosed and untreated COPD patients and to investigate whether effort is associated with sudden cardiac death and malignant ventricular arrhythmias in COPD patients.

### Methodology

#### Patients

Thirty-three patients who were admitted to the chest diseases polyclinic between March-August 2018, who had not received prior treatment, had obstructive pulmonary function test, were included in the study. The mean age of the study group, consisted of 19 female and 17 male patients, was calculated as  $47.88 \pm 8.96$  (29-71). The control group consisted of 40 patients who presented to the cardiology polyclinic with chest pain, had no COPD, had exercise test indication, were found to be negative. The mean age of the control group, consisted of 22 female and 18 male patients, was calculated as  $48.64 \pm 7.33$  (30-72). Patients with a systemic disease such as liver, heart,

kidney, systemic hypertension and diabetes mellitus were excluded from the study. There was no statistically significant difference between the two groups' demographic information.

**Methods**

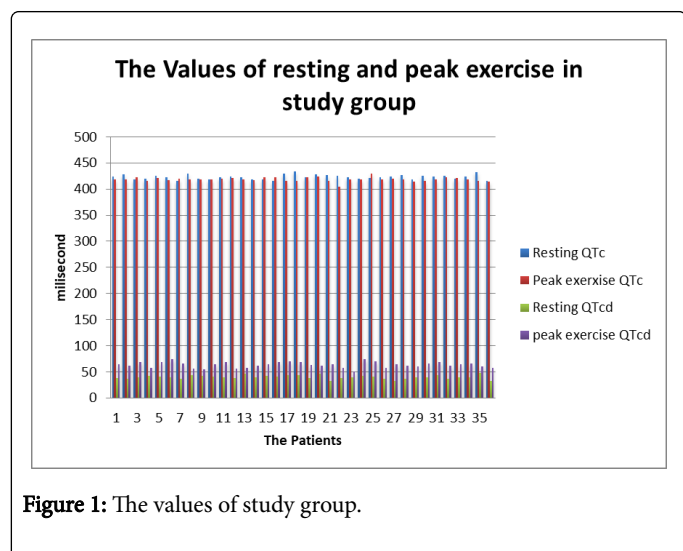
All participants underwent a standard pulmonary functional test according to the American Thoracic Society [21] to measure forced expiratory volume (FEV1) and forced vital capacity (FVC) within one second. In these patients, FEV1 / FVC <70% was considered as a sign of obstruction [22]. Then, patients underwent routine ECG's [23]. Resting QT values of the patients were measured in routine ECG. The mean of the corrected QT (QTc) interval of the three successive pulses in each lead was taken as the QTc interval of that derivation [24]. Patients whose QTc interval was calculated in at least 9 leads were included in the study. The QTc dispersion (QTcd) was measured by calculating the difference between the longest QTc interval and the shortest QTc interval. All of these evaluations were performed for both the study group and the control group. Patients were then subjected to stress test according to Bruce protocol [25]. When 88% of the maximal heart rate was reached, the test was terminated. Resting, peak exercise data of the patients were recorded. Thus, resting QTc and QTcd values as well as peak exercise values were calculated.

**Statistical analysis**

SPSS software for data collection and analysis (Version X; IBM, Armonk, NY) and analysis using t-test. If all tests are p<0.05, the differences are statistically significant.

**Results**

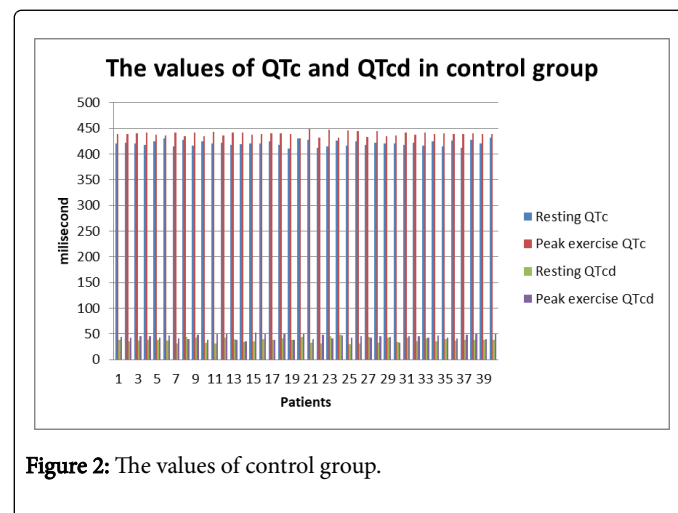
In the study group, the resting QTc value was  $421.1389 \pm 4.6115$  msec, and the peak exercise QTc value was  $419.6389 \pm 4.0225$  msec. There was a statistically significant difference between them ( $p=0.001229$ ,  $t=3.264$ ) (Figure 1).



**Figure 1:** The values of study group.

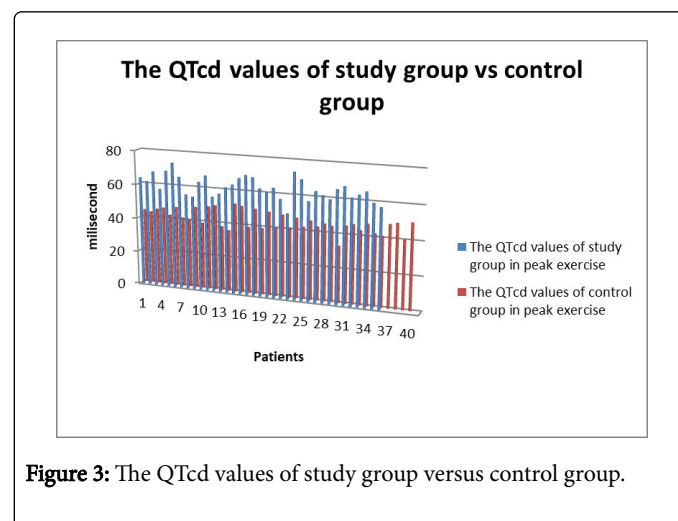
This data showed that QTc duration was shortened by exercise test in the study group. In the control group, the basal QTc value was  $420.424 \pm 4.9717$  msec, in the study group, the resting QTc value was  $421.1389 \pm 4.6115$  msec. No statistically significant difference was found between the control and the study group ( $p=0.140294$ ,

$t=1.088214$ ). Resting QTc values were similar in control group and study group. The peak exercise QTc value of the control group was  $438.925 \pm 4.0582$  msec while the study group was  $419.6389 \pm 4.0225$  msec and the difference was statistically significant ( $p<0.00001$ ,  $t=21.764$ ) (Figure 2).

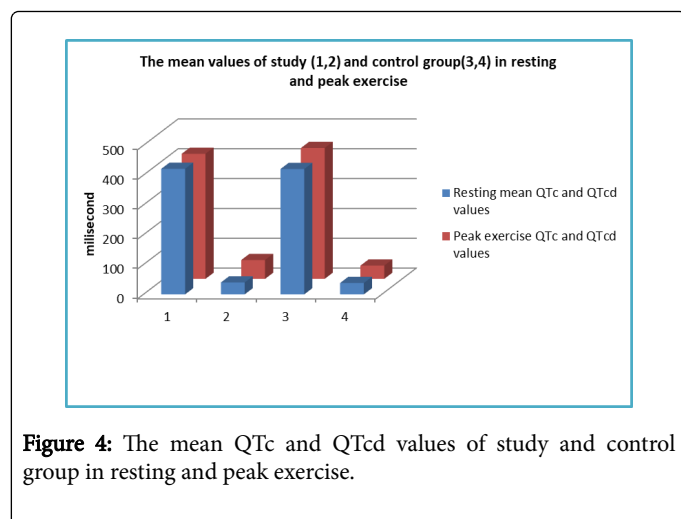


**Figure 2:** The values of control group.

It was observed that the QTc value was increased with the stress test in the control group more than the study group. While baseline QTcd was  $39.8333 \pm 3.6762$  msec in the study group, peak exercise QTcd value was  $63.356 \pm 5.408$  msec and the difference between the two values was statistically significant ( $p<0.00001$ ,  $t=24.6918$ ). In the study group, it was observed that QTcd duration was significantly increased with exercise test. The baseline and peak exercise QTcd values in the control group were  $38.0244 \pm 4.298$  msec and  $44.475 \pm 4.0572$  msec, respectively. The difference between the two values was statistically significant ( $p<0.0001$ ,  $t=6.708204$ ). Although QTcd was significantly prolonged in the control group with the exercise test, QTcd prolongation was in the normal range and the risk of ventricular arrhythmia was low. In the control group, QTcd time was significantly increased with exercise test. The peak exercise QTcd values of the study group and control group were  $63.356 \pm 5.408$  msec and  $44.475 \pm 4.0572$  msec, respectively. The difference between the two groups was statistically significant ( $p<0.00001$ ,  $t=18.37567$ ) (Figures 3 and 4).



**Figure 3:** The QTcd values of study group versus control group.



It was observed that QTcd periods were prolonged with exercise test in both control group and study group. However, the prolongation of QTcd in the control group was within normal limits, while the chances of ventricular arrhythmia were low in control group and in the study group, the risk of ventricular arrhythmias increased abnormally.

## Discussion

This study investigated the effect of exercise test according to Bruce protocol on QTc and QTcd in a heterogeneous group of patients who were diagnosed with COPD for the first time and had not received any treatment before. The main finding in this study was that the peak exercise value of the QTcd value of the study group was higher than both the control group and the resting QTcd of the study group and the difference was statistically significant.

A significant difference between the study group and the control group between resting and peak exercise QTcd values measured before and after the effort test was shown to be appropriate for study and control group study purposes. In our prospective study, the increase in QTcd, was statistically significant, a predictor of malignant arrhythmias with exertion in COPD patients diagnosed for the first time, is an important outcome to consider in patients with COPD.

Modified cardiac repolarization may expose these patients to an increased risk for malignant ventricular arrhythmias and SCD. Several pathologies have been reported to increase the risk of SCD, including coronary artery disease, cardiomyopathy, congenital heart disease, and long QT syndrome and electrophysiological abnormalities [26].

A prolonged QT interval and increased QT dispersion are increased markers of malignant cardiac arrhythmias and risk of SCD [9,27]. The prolongation of QTc to >450 ms was defined as a risk factor for malignant ventricular arrhythmias and SCD [28].

QT dispersion (QTd) reflects spatial differences at the time of myocardial recovery. Previous studies have shown that an increase in QT d>60 ms is associated with malignant ventricular arrhythmias [16] and development of SCD [20].

Again in one study, QTcd was found to be as high as our study in the group of patients with hypertensive response compared to healthy people by stress test [29]. Although many studies have previously shown that the hypoxia extends the QTcd to a pronounced extent [30],

QTc and QTcd have not been shown to be prolonged by the exercise test.

In another study, salbutamol given as a metered dose in children with acute asthma attack had a statistically non-significant prolongative effect on QT, QTc and QTd and QTcd [31]. In another study, the electrophysiological effects of salbutamol, a beta2-selective agonist, were investigated. Salbutamol had the most effective on atrioventricular node in the heart. Impaired effects of decelerating ventricular conduction were observed and the refractory duration of myocardium was shortened. QT dispersion was found to be prolonged [32].

In our study, a significant difference was found between the study and control groups in values of QTcd. In other words, the chances of ventricular arrhythmia in the study group were higher than the control group. In other words, the risk of ventricular arrhythmia induced by effort was higher in the study group than in the control group.

As a result, in patients with newly diagnosed COPD, it is thought that there may be a greater risk of ventricular arrhythmias with exertion.

## Conclusions

**Study limitations:** In our study, the number of cases is small, healthier data can be made with larger case studies. In addition, long-term studies should be made in order to observation the effect of medical therapy on the prolonged QTcd times and ventricular arrhythmias induced by the exercise test. More comprehensive and long-term follow-up studies should be performed to obtain healthier data.

## Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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