ORIGINAL ARTICLE

Role of Electrocardiographic Manifestations in Admission Decision in Patients with Chronic Obstructive Pulmonary Disease Exacerbation

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ABSTRACT

Objective: To determine the ECG manifestations of COPD exacerbations and their roles in the decision making process in admission.

Study Design: A descriptive cross-sectional study.

Place and Duration of Study: Emergency Department (ED) of Kocaeli University, Turkey, from November 2016 to December 2017.

Methodology: All COPD patients who presented with exacerbation symptoms and agreed to participate in the study were enrolled, and the exacerbation characteristics were recorded in the standardised charts. Patients were excluded if they refused to participate in the study, if they presented repetitively to the ED with the same presentation, and if the ECG strip at the presentation could not be obtained. A binary logistic regression model was constructed to assess the factors predicting hospital admission, including the ECG features.

Results: A total of 146 patients were included in the final analysis. Upon presentation, 122 patients (83.6%) exhibited sinus rhythm, 21 exhibited atrial fibrillation (14.4%), and 3 of them were multifocal atrial tachycardia and junctional rhythm. Thirty-four admitted patients (41.0%) and 22 of the discharged patients (34.9%) exhibited ST and T wave changes in their ECGs (p=0.457). No statistically significant differences were found regarding the rhythms, axes, P wave characteristics, PR interval durations, QRS interval durations, corrected QT(QTc) durations, and bundle branch block occurrences between the admitted and discharged patients. Although the QTc dispersion was more prominent in the admitted group in the univariate analysis (p=0.035), the multivariate analysis revealed that only hypoxemia, older age, increased dyspnea scores, and sputum purulence were independent predictors of hospital admission.

Conclusion: None of the ECG findings were determined to be successful in predicting the admission needs in COPD exacerbations.

Key Words: *Chronic obstructive pulmonary disease, Electrocardiography, Cardiac arrhythmia, Emergency department.*

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major public health problem worldwide, and it is ranked as the eighth cause of disease burden globally.[1] COPD exacerbations are commonly encountered in the emergency department (ED), and they lead to more than 1.5 million ED visits annually.[2] Although the Global Initiative for Chronic Obstructive Lung Disease (GOLD) releases yearly guidelines regarding the management of COPD exacerbations, the hospitalisation decisions have not been standardised. They are commonly interpreted according to the institutional regulations.[3]

According to the GOLD guidelines, an ECG may aid in the diagnosis of coexisting cardiac problems in exacerbation states. In addition, newly occurring cardiac arrhythmias have been recognised as potential indications of hospitalisation in these same guidelines.[3] The value of ECG findings in COPD patients has been previously determined in many studies; however, the results differed due to the different study outcomes.[4-8]

Various pathophysiological mechanisms may play roles in the ECG changes in COPD patients, including an increased right ventricular afterload, right ventricular hypertrophy, and structural changes due to emphysema.[4] Ischemic ECG changes are common in patients with COPD,[5] and they may be associated with an increased risk of death.[6] Cardiac arrhythmias, including ventricular or supraventricular premature beats, supraventricular tachycardia, and atrial fibrillation, have also been detected frequently in the Holter recordings of COPD patients.[7] In addition, conduction abnormalities are common in COPD patients, and these patients tend to

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be more tachycardic when compared with healthy individuals.[8]

Many of these effects overlap with the increased risk of coexisting cardiac abnormalities, and they prevent the manifestation of specific ECG abnormalities in COPD patients.[4] Although an increasing body of evidence has become available on the ECG changes in COPD patients, the value of the ECG findings in exacerbation states in an ED setting is largely unknown. Therefore, the objective of the present study was to investigate the ECG manifestations of COPD exacerbations and their roles in the ED decision making processes.

METHODOLOGY

A descriptive cross-sectional study was carried out among individuals who presented to the ED with acute COPD exacerbations between November 2016 and December 2017. The two study sites were the EDs in one academic hospital (Kocaeli University) and one rural hospital (Bitlis State Hospital, Bitlis, Turkey). Institutional review board approval was obtained for this research, and the patients were asked to sign an informed consent form before they were enrolled in the study.

All the COPD patients who presented to the EDs with exacerbation symptoms were included in this study. GOLD definition was used to select the patients: "An exacerbation of COPD is an acute event characterised by a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication".[3] The COPD patients who met this definition and agreed to participate in the study were included. The patients were excluded if they refused to participate in the study at the initial presentation, if they presented repetitively to the ED with the same presentation during the study period, and if the ECG strip at the presentation could not be obtained. The primary outcome measure was admission rates of the patients with COPD exacerbations evaluated with the main ECG characteristics at the initial presentation. Other causes of ECG changes were not excluded from the study population.

The COPD patients were consecutively enrolled in the study, and each patient was evaluated for exacerbation characteristics by a senior emergency medicine resident or physician. After the signed informed consent was obtained, the patient received standard care for the COPD exacerbation, including oxygen, inhaled short-acting beta-2 agonists, and corticosteroids. Before the treatment was administered, an ECG was obtained in the ED. The COPD characteristics, including previous and active tobacco use, the number of previous exacerbation episodes, and the need for mechanical ventilation (invasive or noninvasive) over the last year, were recorded on the standard data charts. The dyspnea severity was specified using the Medical Research Council (MRC) breathlessness scale.[9] In addition, the presenting complaints, comorbid diseases, and arterial blood gas analysis results were also recorded. Increased sputum volume and increased sputum purulence were evaluated with subjective patient opinions about his/her general reflection about condition.

After the first bronchodilator treatment was administered and the laboratory and radiographic results were obtained, the physicians were asked to determine the hospitalisation needs of the patient. The physicians were not restricted to the use of only the GOLD guidelines[3] in the admission decision; they were free to make a decision using their clinical sense, regardless of the congestion of the hospital and/or intensive care unit beds.

ECG of each patient was photographed 40 cm away from an iPhone 7 Plus (Apple Inc., Cupertino, CA, USA). Then, the images were transferred to a PDF document in high resolution, and the measurements were made after 1,000% magnification in Adobe Acrobat Reader DC (Adobe Systems Software Ireland Ltd., Dublin, Ireland). The corrected QT intervals (QTc) were calculated using an online calculator (www.mdcalc.com) with Bazett's formula (QTc=QT/RR). The QT intervals were measured in 12 leads, and the QTc dispersion was defined as the difference between the maximum QTc length (QTc max) and the minimum QTc length (QTc min) in the ECG leads. The QT intervals for the patients with atrial fibrillation were not calculated because they would cause an error in the QT calculation.

All the statistical analyses were performed using the Statistical Package for the Social Sciences version 15.0 for Windows (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to test the normal distribution, and the continuous variables that were non-normally distributed were presented with the median and interquartile range (IQR). The continuous variables were tested with the Mann-Whitney U-test, and the categorical variables were tested with the Chi-squared test. A p-value of <0.05 was accepted as the nominal level of statistical significance.

The predictors of hospital admission in COPD exacerbations, including the ECG characteristics, were investigated using a multivariate logistic regression model. Each variable was tested in the univariate model, and those that were significant at an alpha level of 0.2 were then tested in the multivariate model. In addition, to include the variables into the multivariate model, a multicollinearity analysis was performed. Only one of the two variables was included in the multivariate analysis, if a correlation was found ($r>0.5$ level) between them in the Spearman correlation test. In the final analysis, the adjusted odds ratios (ORs) were presented with 95% confidence intervals (CIs).

RESULTS

A total of 151 patients were assessed for eligibility, and 146 of them were included in the final analysis; 80 were from the academic ED and 66 were from the rural ED (Figure 1). Among them, 83 patients were admitted to the hospital and 63 patients were discharged. In addition, 18 patients had admission indications for the intensive care unit. The most common patient complaints were increased dyspnea (96.6%) and cough (76.7%). The median MRC breathlessness scale (dyspnea) score was 4 (IQR=3-5).

The main demographic characteristics of the patients are shown in Table I. When the patients who were hospitalised and discharged were compared, the hospitalised patients presented with an increased sputum volume (p=0.019), increased sputum purulence (p=0.002), decreased oxygen saturation (p<0.001), and increased bicarbonate level (p=0.013). In addition, the MRC dyspnea scores and noninvasive mechanical ventilation needs were higher in the hospitalised patients when compared with the discharged patients (p<0.001 and p=0.031, respectively).

With regard to the ECG characteristics, 126 patients (83.6%) had sinus rhythms. The ECG manifestations and their associations with the admission status are

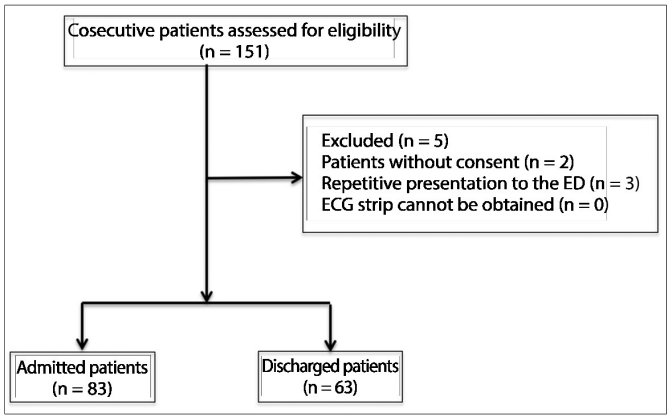

Figure 1: Patient flow chart.

Table I: Main demographical and clinical characteristics of patients.

	All patients (n=146)	Admitted patients (n=83)	Discharged patients (n=63)	p-value
Age (years)	68.1 ±10.4	69.3 ±10.9	66.6 ±9.5	0.120
Sex (male)	107 (73.3%)	64 (77.1%)	43 (68.3%)	0.231
Medical history				
Diabetes mellitus	28 (19.2%)	18 (21.7%)	10 (15.9%)	0.377
Hypertension	82 (56.2%)	44 (53.0%)	38 (60.3%)	0.378
Coronary artery disease	51 (34.9%)	32 (38.6%)	19 (30.2%)	0.292
Previous arrhytmia	29 (19.9%)	17 (20.5%)	12 (19.0%)	0.830
Exacerbation characteristics				
Dyspnea	141 (96.6%)	82 (98.8%)	59 (93.7%)	0.166
Increase in sputum volume	81 (55.5%)	53 (63.9%)	28 (44.4%)	0.019
Increase in sputum purulence	61 (41.8%)	44 (53.0%)	17 (27.0%)	0.002
Coughing	112 (76.7%)	66 (79.5%)	46 (73.0%)	0.357
Chest pain	54 (37.0%)	35 (42.2%)	19 (30.2%)	0.137
Altered mental status	3 (2.1%)	3 (3.6%)	0 (0.0%)	0.259
Continue smoking	25 (17.1%)	15 (18.1%)	10 (15.9%)	0.727
Cigarette (pack/year)	48 (25-63)	50 (26-64)	45 (23-63)	0.696
Number of presentations to the ED related to COPD within one year	6 (4-10)	6 (4-10)	5 (3-10)	0.222
Implementation of invasive mechanical ventilation within one year	0 (0-0)	0 (0-0)	0 (0-0)	0.254
Implementation of non-invasive mechanical ventilation within one year	0 (0-1)	0 (0-0)	0 (0-0)	0.031
Dyspnea score (MRC)	4 (3-5)	4 (4-5)	3 (2-4)	<0.001
Vital signs				
Temperature (°C)	36.6 (36.4-37.0)	36.7 (36.5-37.1)	36.6 (36.3-36.9)	0.064
Heart rate (beats/min)	103 (90-116)	104 (94-119)	102 (88-114)	0.132
Respiratory rate (breaths/min)	30 (26-34)	32 (26-34)	29 (24-32)	0.188
SpO_2 (%)	90 (82-94)	86 (79-92)	92 (90-95)	<0.001
Systolic blood pressure (mm Hg)	140 (120-157)	138 (120-151)	140 (122-160)	0.185
Arterial blood gas results				
pH	7.41 (7.37-7.44)	7.41 (7.36-7.44)	7.41 (7.38-7.44)	0.716
pO_2 (mm Hg)	59.8 (50.5-72.3)	56.9 (48.0-74.0)	62.7 (53.2-89.5)	0.133
pCO_2 (mm Hg)	41.5 (35.7-47.9)	42.4 (36.3-52.0)	38.2 (35.1-45.4)	0.051
Bicarbonate (mEq/L)	25.2 (23.3-27.3)	25.8 (24.0-27.8)	24.5 (22.5-26.3)	0.013
Lactate (mg/dL)	13.0 (9.9-17.7)	13.2 (10.2-17.6)	12.2 (9.0-19.0)	0.367

Table II: Electrocardiographic characteristics of the patients.

	Admitted patients (n=83)	Discharged patients (n=63)	p-value
Rhythm			
Sinus rhythm	69 (83.1%)	53 (84.1%)	0.972
Atrial fibrillation	12 (14.5%)	9 (14.3%)	
Multifocal atrial tachycardia	2 (2.4%)	0 (0.0%)	
Junctional rhythm	0 (0.0%)	1 (1.6%)	
Axis			
Normal axis	60 (72.3%)	49 (77.8%)	0.450
Left axis deviation	13 (15.7%)	9 (14.3%)	
Right axis deviation	5 (6.0%)	2 (3.2%)	
Undetermined axis	5 (6.0%)	3 (4.8%)	
P pulmonale	6 (8.3%)	2 (3.7%)	0.465
PR-segment depression	2 (2.8%)	3 (5.6%)	0.651
ST-segment deviation (any)	34 (41.0%)	22 (34.9%)	0.457
Septal leads	6 (7.2%)	3 (4.8%)	0.732
Lateral leads	16 (19.3%)	12 (19.0%)	0.972
Inferior leads	13 (15.7%)	10 (15.9%)	0.972
High lateral leads	12 (14.5%)	6 (9.5%)	0.369
S1Q3T3	1 (1.2%)	3 (4.8%)	0.315
Bundle branch block (any)	14 (16.9%)	10 (15.9%)	0.872
Right bundle branch block	3 (3.6%)	3 (4.8%)	1.000
Left bundle branch block	2 (2.4%)	0 (0.0%)	0.506
Premature ventricular contraction	5 (6.0%)	4 (6.3%)	1.000
PR interval (msec)	154 (138-172)	162 (145-179)	0.285
QRS interval (msec)	88 (80-100)	90 (82-97)	0.412
QTc min* (msec)	420 (400-439)	420 (397-448)	0.767
QTc max* (msec)	498 (472-532)	488 (462-514)	0.147
QTc dispersion* (msec)	77 (60-100)	69 (53-83)	0.035

** This variables were calculated after the patients with atrial fibrillation excluded.*

shown in Table II. Regarding the ischemic changes, 34 of the admitted patients (41.0%) and 22 of the discharged patients (34.9%) had ST-T wave changes in their ECGs (p=0.457). However, no statistically significant differences were found in the rhythms, axes, P wave characteristics, ST segment characteristics, PR interval durations, QRS interval durations, minimum QTc durations, maximum QTc durations, and bundle branch block occurrences between the admitted and discharged patients. In addition, the admitted patients exhibited an increased QTc dispersion, with a median of 77 msec (IQR=60-100), when compared with the discharged patients, with a median of 69 msec (IQR=53-83) (p=0.035).

A multivariate model was constructed to assess the hospitalisation needs in the COPD exacerbations (Table III). The Hosmer-Lemeshow test results confirmed that the model was fit (p=0.290). The increased sputum volumes and bicarbonate levels were excluded from the analysis, because they correlated with the increased sputum purulence and pCO_2 levels at the r >0.5 level. With regard to the results, an increased sputum purulence (OR=3.09, 95%CI=1.19 to 8.07), increased MRC dyspnea score (OR=3.33, 95% CI=1.97 to 5.60), increased age (OR=1.05, 95% CI=1.01 to 1.10), and

Table III: Multivariable logistic regression analysis to predict hospital admission in COPD exacerbations.

	Wald	p-value	Adjusted odds ratio (95% CI)
Increase in sputum purulence	5.31	0.021	3.09 (1.19 to 8.07)
Implementation of non-invasive mechanical ventilation within one year	0.15	0.699	1.03 (0.90 to 1.16)
SpO_2 (%)	1.22	0.269	0.97 (0.93 to 1.02)
Dyspnea score (MRC)	20.4	<0.001	3.33 (1.97 to 5.60)
QTc dispersion	0.01	0.913	1.00 (0.99 to 1.01)
Age (yr)	5.11	0.024	1.05 (1.01 to 1.10)
Dyspnea	1.24	0.266	4.99 (0.29 to 84.68)
Chest pain	1.89	0.169	1.90 (0.76 to 4.73)
Temperature	1.48	0.224	1.51 (0.78 to 2.92)
Heart rate	0.63	0.426	0.99 (0.97 to 1.01)
Systolic blood pressure	3.01	0.083	0.99 (0.97 to 1.01)
Respiratory rate	0.37	0.543	1.02 (0.96 to 1.07)
pO_2	4.45	0.035	0.98 (0.96 to 0.99)
pCO_2	0.07	0.796	1.01 (0.96 to 1.06)
QTc max	2.44	0.118	1.01 (0.99 to 1.02)

decreased pO_2 levels (OR=0.98, 95% CI=0.96 to 0.99) were found to be independent predictors of hospital admission in the COPD exacerbations. None of the ECG parameters, including the QTc dispersion, reached statistical significance in the multivariate model.

DISCUSSION

Like other patients with cardiopulmonary disease, various ECG changes are encountered in COPD patients. These changes are related to complex mechanisms, including prolonged hypoxic episodes and right ventricular strain. The results of the present study revealed that a cross-sectional ECG evaluation in an ED setting has very few contributions to the hospitalisation decision in patients with COPD exacerbations. It was observed that some of the ECG features that were frequently encountered in COPD patients in previous studies did not influence the physicians' hospitalisation decisions in the present study.

Patients with impaired pulmonary function have increased risks for cardiovascular conditions.[10,11] Moreover, patients with more severe COPD have higher cardiovascular morbidity and mortality than patients with less severe COPD.[12] According to Warnier *et al*., electrocardiographic manifestations of stable COPD included, but are not limited to, premature ventricular contractions (11%), ST segment depressions (10%), intraventricular blocks (10%), prolonged QTc intervals (9%), right bundle branch blocks (7%), and atrial fibrillation (7%).[8] However, the current study was carried out in exacerbation states, and the findings differed from those of stable COPD patients. In the exacerbation state, more ST segment deviations in both the admitted group (41%) and discharged group (34.9%) were found.

In the present study, the patients seemed to be more tachycardic, their QTc intervals and QTc dispersions were more prolonged, and the atrial fibrillation frequencies were fewer than in the individuals with stable COPD.

QT dispersion is an electrocardiographic marker of myocardial ischemia due to non-homogeneous ventricular repolarisation.[13] Increased QT dispersion is a negative prognostic finding in COPD patients, and this was investigated in one study involving a 5-year follow-up of mortality.[14] One recent study carried out on patients with acute COPD exacerbations argued that a QTc dispersion of about 48 msec may be a useful indicator for predicting mortality in acute COPD exacerbations.[15] The results of the present study confirmed that the admitted patients had a median QTc dispersion of 77 msec when compared with 69 msec in the patients who were discharged. However, the QTc dispersion was not found to be a predictor of hospitalisation.

Although newly occurring arrhythmias are accepted as a parameter indicating the need for admission in the GOLD guidelines, it is very difficult to recognise an arrhythmia during an ED visit. However, some studies dealing with 24-hour Holter monitoring concluded that COPD and its severity were independently associated with the occurrence of atrial fibrillation and non-sustained ventricular tachycardia.[16,17] The risk of atrial fibrillation is probably higher in hypercapnic patients with lower FEV1 values.[18] Although atrial fibrillation was a frequent arrhythmia in the present study, it was not found to be a predictor for hospitalisation in the present study. Other arrhythmias, including multifocal atrial tachycardia and junctional rhythms, were encountered extremely rarely.

COPD patients are more susceptible to the development of the premature atrial or ventricular complexes encountered in ECG strips.[8,19] Holtzman *et al*. argued that the frequency of premature contractions increased in accordance with the disease severity (19% in severe COPD *versus* 7% in mild or moderate COPD). In the present study, it was found that 6% of the admitted patients had premature ectopic contractions that were identified incidentally in the ECGs. One study conducted in patients admitted to the intensive care unit after COPD exacerbations revealed that some ECG abnormalities, including supraventricular ectopic beats and right and/or left ventricular hypertrophy, were independent predictors of cardiovascular complications.[20] The importance of these ectopic beats may be understood, if continuous monitoring is performed in COPD exacerbations.

The present study had two major limitations. First, the number of COPD exacerbations was limited, although the study was carried out in two centres. Second, the ECGs only present an instant image; therefore, they may not catch transient conditions, including atrial or ventricular arrhythmias. However, like the present study, emergency physicians usually make decisions using only one ECG strip in real EDs.

CONCLUSION

COPD patients can exhibit several pathological ECG findings, and those effects can be observed in ECGs in exacerbation cases. Contrary to the GOLD guidelines, a short-term ECG assessment in the ED is not suitable for determining a hospitalisation requirement. Moreover, the present study revealed that the detected pathological changes cannot be used in admission decisions in exacerbation states in the ED. Therefore, future studies should focus on the continuous monitoring of severe COPD patients after the ED presentation and its effects on the hospitalisation decision.

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