doi • 10.5578/tt.20229901
Tuberk Toraks 2022;70(1):1-7
Received/Geliş Tarihi: 07.04.2020 • Accepted/Kabul Ediliş Tarihi: 28.12.2021

RESEARCH ARTICLE
KLİNİK ÇALIŞMA

Electrocardiogram parameters for predicting future arrhythmia in patients with stable chronic obstructive pulmonary disease

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ABSTRACT

Electrocardiogram parameters for predicting future arrhythmia in patients with stable chronic obstructive pulmonary disease

Introduction: *Arrhythmia is one of the common comorbidities in chronic obstructive pulmonary disease (COPD). The aim of this study was to evaluate arrhythmia predictors by using ECG in non-hypoxemic patients with stable COPD in outpatient clinics.*

Materials and Methods: *Fifty patients with COPD and 21 age-sex matched healthy controls were enrolled. Exclusion criteria were having history of exacerbation in the last two months, any cardiac symptoms, comorbidities, hypoxemia for COPD patients, and additionally, history of smoking for healthy controls. Twelve-lead ECGs were obtained from all patients.*

Results: *Mean was 55 ± 4 year in all participants. Median Medical Research Council (MRC) score of COPD patients was 2 and median value of FEV_1 was 49%. Median heart rate of COPD patients was 77/min with normal sinus rhythm, significantly faster than healthy controls. P-min, QTcmin, Tp-edisp, Tp-e/QT were significantly different from the control group. In patients with COPD, whilst significant correlations between pulmonary functions and Qtc-min, Qtc-max, p-min were found, there were no significant differences between groups of spirometric stages. Smoking and mMRC dyspnea scale were not correlated with ECG findings.*

Conclusion: *This study showed that non-hypoxemic COPD patients with decreased pulmonary functions, without cardiac symptoms and comorbidities, could have risks for atrial, ventricular arrhythmias regardless of dyspnea, smoking.*

Key words: *Arrhythmia; COPD; outpatient clinic; pulmonary function tests*

Cite this article as: *Candemir İ, Baskovski E, Candemir B, Kaymaz D. Electrocardiogram parameters for predicting future arrhythmia in patients with stable chronic obstructive pulmonary disease. Tuberk Toraks 2022;70(1):1-7.*

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ÖZ

Stabil kronik obstrüktif akciğer hastalığı olan hastalarda gelecekteki aritmi tahmininde elektrokardiyogram parametreleri

Giriş: *Aritmi, kronik obstrüktif akciğer hastalığında (KOAH) sık görülen komorbiditelerden biridir. Bu çalışmada amacımız polikliniklerde stabil KOAH'lı hipoksemik olmayan hastalarda EKG kullanılarak aritmi belirleyicilerini değerlendirmekti.*

Materyal ve Metod: *Çalışmaya 50 KOAH tanılı hasta, kontrol grubu olarak benzer cinsiyet ve yaşta olan 21 sağlıklı birey alındı. Dışlama kriterleri, KOAH hastaları için son iki aydır alevlenme öyküsü, kardiyak semptomlar, komorbiditeler, hipoksemi, ek olarak, sağlıklı kontroller için sigara öyküsüydü. Tüm hastalara on iki derivasyonlu EKG çekildi.*

Bulgular: *Tüm katılımcıların yaş ortalamaları 55 ± 4 yıl idi. KOAH'lılarda medyan mMRC skoru 2, FEV_1'in medyan değeri %49'du. KOAH hastalarının medyan kalp atım hızı normal sinüs ritmi ile 77/dakikaydı, sağlıklı kontrollerden anlamlı derecede daha hızlıydı. P-min, QTcmin, Tp-edisp, Tp-e/QT kontrol grubundan anlamlı olarak farklıydı. KOAHlı hastalarda, solunum fonksiyonları ile Qtc-min, Qtc-max, p-min arasında anlamlı korelasyonlar bulunurken, spirometrik evre grupları arasında anlamlı fark bulunmadı. Sigara kullanımı, mMRC dispne skalası EKG bulguları ile korele değildi.*

Sonuç: *Bu çalışma, solunum fonksiyonları azalmış, kardiyak semptomları, komorbiditeleri olmayan non-hipoksemik KOAH hastalarında; nefes darlığı, sigara içiminden bağımsız olarak atriyal, ventriküler aritmi riski bulunabileceğini göstermiştir.*

Anahtar kelimeler: *Aritmi; KOAH; poliklinik; solunum fonksiyon testleri*

INTRODUCTION

Chronic obstructive pulmonary disease (COPD), as a progressive disease, is ranked as the third cause of death all around the world (1) and characterized by airflow limitation with accompanying several co-morbidities. A common and mortal comorbidity of COPD is cardiovascular disease (2). Cardiovascular disorders have been found to be more common and more mortal risk factors than respiratory failure in mild COPD (3). Furthermore, FEV_1 predicted % has been found be an independent risk factor for myocardial infarction regardless of smoking history (4,5). Due to close settlement of the heart and lungs, disorders both notably influence each other. Systemic inflammation, oxidative stress, autonomous dysfunction, beta mimetic bronchodilators, pulmonary hyperinflation, hypoxemia, hypercapnia, acidemia are potential risk factors for cardiovascular disorders. The long-term effects of hypoxic pulmonary vasoconstriction upon the right side of the heart, causing pulmonary hypertension and subsequent right atrial and right ventricular hypertrophy eventually results in cor pulmonale. Lung hyperexpansion, another risk factor, causes external compression of the heart and lowering of the diaphragms, with consequent elongation and vertical orientation of the heart. Due to its fixed attachments to the great vessels, the heart undergoes clockwise rotation in the transverse plane, with movement of the right ventricle anteriorly and displacement of the left ventricle posteriorly. The presence of increased air between the heart and recording electrodes has a dampening effect, leading to reduced amplitude of the QRS complexes.

Electrocardiography is a reliable, simple and cost-effective screening device. It is also easy to perform in outpatient clinics and a practical tool for predicting atrial and/or ventricular dysfunction. Chronic obstructive pulmonary diseases influences the electrical events of the heart in many aspects. It produces various anatomic changes that effect the ECG in unique ways. The most common ECG abnormalities in COPD patients are bundle branch blocks and axis deviations (6).

The aim of this study was to evaluate arrhythmia predictors by using ECG in patients with stable COPD who did not have cardiac symptoms, comorbidities, cor pulmonale and had oxygen saturation over 90% with pulse oximeter in room air in outpatient clinic.

MATERIALS and METHODS

Patients Characteristics

The patients with diagnosis of COPD for at least a year who were stable, have oxygen saturation over 90% in room air with pulse oximeter, and did not have a history of exacerbation in last two months, any cardiac symptoms such as chest pain, syncope, presyncope, tachycardia, any comorbidities such as hypertension, heart failure, history of arrhythmia, diabetes mellitus, cerebrovascular disease, depression, sleep disorders, cor-pulmonale and without pretibial edema, cardiac arrhythmia, systolic murmur, bibasilar crackles in physical examination were included to the study.

Healthy Control

Age and sex matched healthy control without history of any disease, symptoms and smoking. All of the

patients' written consent and institutional review board approvals had been taken before the enrollment to the study.

Electrocardiogram

Twelve-lead ECGs (Nihon Kohden Corporation, model ECG-1350 K, Tokyo, Japan) at a speed of 25 mm/s were obtained from all patients while resting in supine position. All ECGs were scanned using high DPI scanners and imported into electronical ECG analysis application (EP Callipers). All measurements involving ECG were performed electronically using high magnification in the aforementioned application (Figure 1). Heart rates were calculated by averaging three consecutive RR intervals on DII derivation. All measurements on ECG were evaluated by the same cardiologist. Shortest and longest P wave length (Pmin and Pmax, respectively, marked by black annotations), shortest and longest QT (QTmin and QTmax, respectively, marked by blue annotations) interval, shortest and longest Tpe segment (Tpe min and Tpe max, respectively, marked by red annotations) were calculated from 12-lead surface ECG. P wave dispersion (PWD) was defined as Pmax-Pmin. The QT intervals were calculated for each derivation by measuring from the beginning of the QRS complex to the end of the T wave off-set, as defined by the return of the terminal T wave to isoelectric TP baseline and QT was corrected for heart rate using the Bazzett's formula (7). Corrected QT (QTc) dispersion was calculated by substracting shortest QTc (QTcmin) from longest QTc (QTcmax) interval. TPe dispersions was defined as TPemax-TPemin. The Tp-e interval was measured as the averages of all leads from the peak of T wave to the end (8). The Tp-e/QT ratio was also calculated by dividing Tp-e by QT (Figure 1).

Other Measurements

Spirometry was performed to determine the forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and FEV_1/FVC using a spirometer (AS-507, Minato Medical Science, Tokyo, Japan) in accordance with the ATS-ERS guidelines (9). FVC and FEV_1 were measured for three times and the greatest value was recorded. The patients were allocated into the post-bronchodilator spirometric stage (10). Dyspnea was assessed using the modified Medical Research Council (mMRC) scale.

RESULTS

Fifty patients with COPD and 21 age-sex matched healthy controls were enrolled to the study. Mean age was 55 ± 4 year in all participants. Median mMRC score of COPD patients was 2 (0:4) and median value of FEV_1 was 49% (23:84), FVC was 56% (30:94), FEV_1/FVC 66% (39:70) and FEF_{25-75} was 34% (13:100). Distributions of patients with COPD according to spirometric stage included 3 (6%) patients with stage 1, 22 (44%) patients with stage 2, 18 (36%) patients with stage 3, 7 (14%) patients with stage 4. Median value of the mounts of cigarette smoking was 35 (0:120) pack/years.

Median heart rate of COPD patients was 77/min (54:106) with normal sinus rhythm and significantly faster than healthy controls (p= 0.012). P wave dispersion was found statistically similar to the controls with value of 50 msec in patients with COPD.

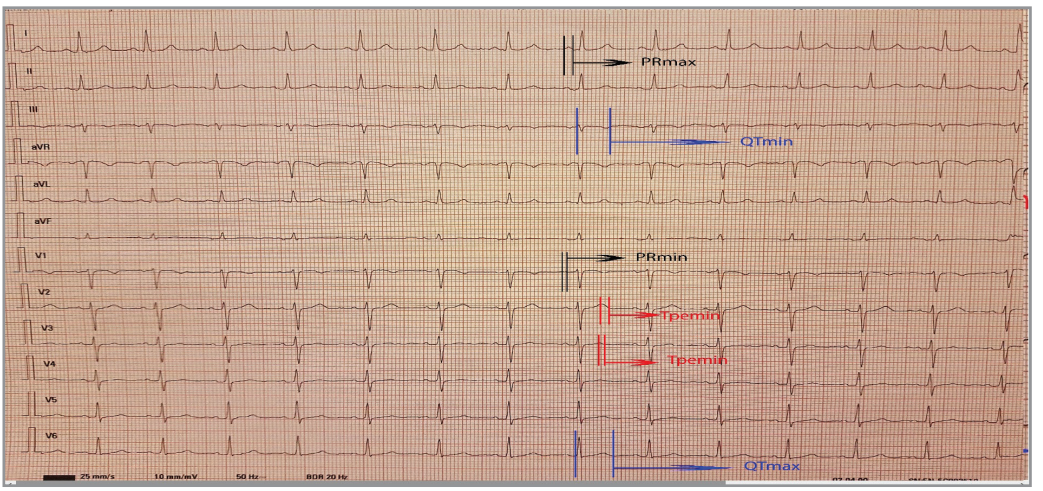


Figure 1. Methods of ECG measurements.

Table 1. ECG findings of both groups

	Patients with COPD	Healthy Controls	p
Sex (male/female)	43/7	18/3	0.972
rate	76 ± 12 77 (54:106)	70 ± 8 72 (57:89)	0.012
p-max	96 ± 20 100 (40:140)	103 ± 18 100 (80:140)	0.119
p-min	47 ± 11 40 (20:80)	61 ± 15 60(40:90)	**0.001**
pwd	50 ± 20 50 (10:100)	43 ± 21 40 (10:80)	0.205
Qtc-min	363 ± 26 361 (321:455)	378 ± 21 375 (341:428)	**0.012**
Qtc-max	409 ± 27 409 (353:506)	418 ± 19 416 (386:460)	0.145
Qtc-Disp	47 ± 17 46 (21:94)	41 ± 16 41 (20:78)	0.086
Tpe-min	52 ± 17 60 (20:100)	56±10 60 (40:70)	0.253
Tpe-max	95 ± 17 95 (60:140)	89 ± 14 80 (60:120)	0.228
Tpe-disp	42 ± 17 40 (20:100)	33 ± 15 30 (0:70)	**0.042**
Tpe/Qt	0.23 ± 0.03 0.23 (0.15:0.34)	0.21 ± 0.03 0.20 (0.14:0.29)	**0.043**

P-min: p wave minimum, p-max: p wave maximum, PWD: P wave dispersion, QTc: Corrected QT, Qtc-Disp: QTc dispersion, Tpe min: Tpe minimum, Tpe max: Tpe maximum, Tpe-disp: Tpe dipersion.

Additionally, p-min, QTc min, Tp-e disp, Tp-e/QT ratio were significantly different from the control group in COPD patients (Table 1). In patients with COPD, whilst significant correlations between pulmonary functions and ECG findings [FEV1% and Qtc-min (p= 0.013, r= 0.355, Figure 2), Qtc-max (p= 0.003, r= 0.414, Figure-3); FVC % and Qtc-min (p= 0.010, r= 0.369, Figure 2), Qtc-max (p= 0.004, r= -0.408, Figure-3); FEF_{25-75}% and p-min (p= 0.039, r= 0.300), Qtc-min (p= 0.023, r= 0.328, Figure 2), Qtc-max (p= 0.014, r= 0.351, Figure 3)] were found, there were no significant differences in ECG findings between groups according to spirometric stage. There was also no significant correlation between smoking, mMRC dyspnea scale and ECG findings.

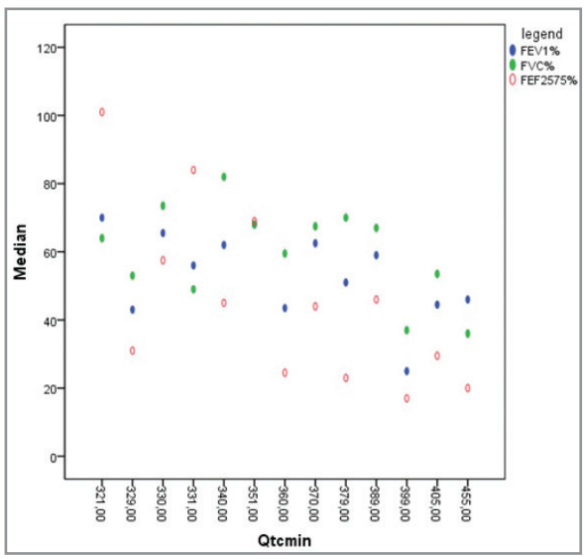


Figure 2. Correlation between pulmonary function tests and QTc min.

DISCUSSION

This study showed that patients with stable COPD could have risks for atrial and ventricular arrhythmias even they have no cardiac symptoms or disorders,

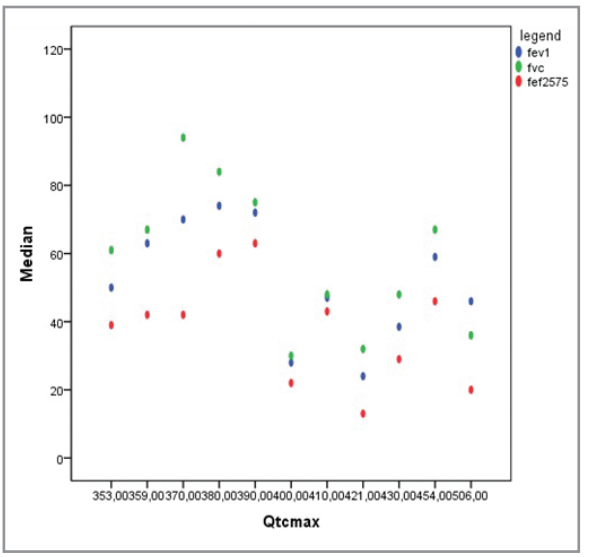


Figure 3. Correlation between pulmonary function tests and QTc max.

comorbidities, desaturation regardless of dyspnea sensation, and smoking and decreased pulmonary functions could be a predictor for arrhythmias in these patients.

There are several abnormal ECG findings in patients with COPD. It has been shown that reduced heart rate variability is present in patients with COPD (11-13). A reduced heart rate variability is the result of sensitive sympathetic activity and reduced vagal tone, which have been thought to be a potential risk factor for sudden cardiac death (14). In our study, heart rate was found to be higher in patients with COPD than that of controls.

P-wave dispersion (PWD) has been proposed for the prediction of atrial fibrillation (AF). Increased p-max and PWD duration is known to increase the risk of atrial fibrillation (15). In a study performed by Dilaveris et al. (16), a cutoff value is recommended as 110 msec for p-max and as 40 msec for PWD in order to distinguish the healthy controls from the patients. PWD ≥40 ms indicates the presence of heterogeneous electrical activity in different regions of the atrium that might cause atrial tachyarrhythmias (ATAs). Thus, PWD is a strong predictor of ATAs and especially AF. Although PWD was found statistically similar to the control group, value of PWD was over 40 msec with value of 50 msec in patients with COPD in our study.

Another important predictor of life-threatening ventricular arrhythmias, the dispersion of QT interval, is a marker of alterations in ventricular repolarization and defined as the difference between the maximum (QTmax) and minimum QT (QTmin) intervals on ECG. QTc prolongation was associated with an increased mortality risk in a cohort of 246 COPD patients (17), and there are conflicting data about QTC interval. Besides significantly longer QTc interval has been observed in COPD patients than healthy controls in some studies (12,13), in others, no significant difference has been observed between COPD patients and healthy controls (18,19) similar to our study. An abnormally short QT interval (≤300 msec) has also been associated with sudden cardiac dead (20) and has been shown to be related with COPD (21). In our study while QTc min was over 300 msec in COPD patients, it was statistically shorter than the control group. Tp-e interval, an another arrhythmogenesis predictor, is measured as the distance from the peak of the T-wave to the end point and Tp-e/QT ratios are reported to be associated with increased ventricular arrhythmogenesis (12,13,17). In recent studies performed in different groups of patients with diseases such as left ventricular hypertrophy, hypertrophic cardiomyopathy and implantable cardioverter defibrillator, Tp-e/QT ratio has been suggested to be more beneficial in the evaluation of ventricular repolarization and arrhythmogenesis, compared to Tp-e interval and QTc (22,23). In our study, Tpe disp and Tp-e/QT ratio were found to be lower than healthy controls. While the shortening in QT may mask repolarization disturbances, the fact that the comparison of Tp-Te (being a more sensitive parameter) with QT is significantly higher that control group may support the theory that the last portion of the repolarization still does not change despite a relatively shortened QT.

Influencing factors for ECG abnormality in patients with COPD have been investigated. A significant univariate association between QT dispersion with FEV_1% and FVC% predicted respectively was found in COPD patients. However, in a multivariate analysis corrected for covariates (17), this association did not remain statistically significant. In another study which compared 30 COPD patients with and without increased QT dispersion regarding possible factors influencing QT dispersion, there were no independently associated factors (24). In our study, QTc

minimum and maximum was associated with pulmonary function, and FEF_{25-75}% was also found to be correlated with P-min. It was suggested that small airway obstruction could be more sensitive to both atrial and ventricular arrhythmias. However, ECG findings were not found to correlate with spirometric stage. Additionally, dyspnea sensation and smoking were not found to be associated with ECG findings.

Other contributing factors for arrhythmias in patients with COPD are bronchodilators. Particularly short-acting beta-agonists (SABAs) have been shown to be associated with mortal arrhythmias (25). Most of our patients were under medication of long-acting anticholinergics, beta-agonists ± inhaled corticosteroids and usually did not have need of using SABA. Conversely, drugs that are known to influence serum electrolytes and therefore ECG parameters, such as antihypertensive drugs, and drugs that may directly influence ECG parameters, such as antidepressants were not included in the medical therapy of any participants since comorbid conditions were included in the exclusion criteria. Additionally, as patients with COPD were not in exacerbation period, they were not using antibiotics when they were enrolled to the study.

There are several studies about ECG abnormalities in COPD patients, but there are only few patients with stable COPD who were non-hypoxemic and had no symptoms and comorbidities in outpatient clinics. As a prospective study, ECG findings were compared with healthy controls but the limitation of the study was one single center and it could not be generalized.

CONCLUSION

Routine ECG should be performed in patients with COPD in outpatient clinics due to the fact that ECG in patients with stable COPD (oxygen saturation over 90% in room air) especially with impaired pulmonary functions who do not have cardiac symptoms or any comorbidities such as hypertension, diabetes mellitus, cor-pulmonale may be helpful in predicting cardiac arrhythmic problems.

Ethical Committee Approval: This study approval was obtained from Ataturk Chest Diseases and Chest Surgery Education and Research Hospital Board (Decision No: 598, Date: 03.05.2018).

CONFLICT of INTEREST

The authors declare that they have no conflict of interest.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: All of authors

Analysis/Interpretation: İC, EB

Data acqusition: İC, DK

Writing: İC, EB, DK

Clinical Revision: EB, İC, BC

Final Approval: All of authors

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