Heart & Lung 45 (2016) 359–362

Contents lists available at ScienceDirect

Heart & Lung

journal homepage: www.heartandlung.org

Care of Patients With Respiratory Disorders

# Identification of electrocardiographic values that indicate chronic obstructive pulmonary disease

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ARTICLE INFO

*Article history:*
Received 13 November 2015
Received in revised form
20 April 2016
Accepted 21 April 2016
Available online 10 May 2016

*Keywords:*
Electrocardiogram
Chronic obstructive pulmonary disease
Respiratory function test
QRS amplitude
Low voltage

ABSTRACT

*Background:* The purpose of this study was to investigate the association between respiratory function and electrocardiogram (ECG) characteristics in patients with chronic obstructive pulmonary disease (COPD), and to identify the ECG results that indicate possible COPD.
*Methods:* The association between respiratory function and ECG results was retrospectively analyzed in 45 patients with COPD and 100 patients without COPD (controls).
*Results:* Multiple logistic regression analysis revealed that QRS amplitude in lead I was a significant predictor of COPD (partial regression coefficient = −4.208, $p = 0.002$). Receiver operating characteristic curve analysis showed that a QRS amplitude less than 0.54 mV in lead I indicated possible COPD (sensitivity: 71%, specificity: 76%, area under the curve: 0.78 [95% confidence interval: 0.69–0.86], $p < 0.001$).
*Conclusion:* Low voltage in lead I (QRS less than 0.54 mV) is an important criterion in detecting COPD.


## Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by an airflow limitation that is not fully reversible. COPD is one of the leading causes of morbidity and mortality in both industrialized and developing countries because it significantly affects the lungs and the heart. Because COPD is related to the rate of cigarette smoking and length of history of smoking, symptoms of COPD usually manifest after the disease is in a progressive stage.[1–5] Thus, early detection of COPD is clinically important.[6,7] Previous studies reported characteristic electrocardiogram (ECG) changes such as a low QRS amplitude in lead I or a pulmonary P wave in patients with COPD,[8–10] but little is known about the clinical utility of ECG in detecting COPD. Because of this, we investigated the relationship between respiratory function and ECG values, and we identified those results that could be used to detect COPD.

## Methods

We retrospectively studied 45 patients diagnosed with COPD and 100 patients without COPD (controls) who were referred for respiratory function tests from October 2009 to March 2014 at the Kochi Medical School Hospital in Kochi, Japan. A standard 12-lead ECG was recorded within 6 months (median 14 days, range 0–155 days) of the respiratory function test. COPD was defined according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria: forced expiratory volume in 1 s/forced vital capacity ($FEV_1/FVC$) < 0.70 after bronchodilator use and exclusion of other causes.[11] All patients with COPD were in normal sinus rhythm and free of heart diseases and lungs diseases other than COPD. Patients in sinus rhythm and with normal respiratory function (vital capacity > 80%, $FEV_1/FVC > 0.70$) and neither heart nor lung diseases were selected as control subjects. Patients aged less than 45-years were excluded because a vertical P axis is a normal finding in healthy children and in many young adults.[12,13] This study complied with the Declaration of Helsinki. The Ethical Review Board of the Kochi Medical School reviewed the study design and protocol. Approval was waived in accordance with the Ethical Guidelines for Clinical Research issued by the Ministry of Health,

Conflicts of interest: The authors have no conflicts of interest.

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http://dx.doi.org/10.1016/j.hrtlng.2016.04.004

Labour and Welfare in Japan. Informed consent for the use of their data was obtained from all patients during their consultations. During the study period, 10 patients were excluded from this study because of invalid spirometry tests (lack of collaboration).

The Electrocardiograph FCP-7541 (Fukuda Denshi Co., Ltd, Japan), which was approved by Japan's Ministry of Health, Labour and Welfare was used to record ECGs. The respiratory function test was performed by using the respiratory function test system C-8800 (CHEST M.I., Inc., Japan) in accordance with the Japanese Respiratory Society (JRS) criteria.[14] The P axis, P interval, P amplitude, QRS axis, QRS interval, QRS amplitude in $V_1$, QRS amplitude in lead I, R amplitude in $V_1$, R amplitude in $V_5$, and QTc interval were measured by the ECG device, which was calibrated before each recording. The ECG findings were analyzed visually and manually. The respiratory function test measurements included $FEV_1/FVC$ and percent predicted value of $FEV_1$ (%$FEV_1$) (prediction equation specified by the JRS criteria[15]) after bronchodilator inhalation. The severity of airflow limitation in patients with COPD was classified according to the current GOLD criteria,[11] and ECG characteristics and respiratory function test characteristics of the patients in each COPD stage were compared and analyzed.

*Statistical analysis*

Categorical variables are presented as total number and percentage of patients. Continuous variables are presented as mean ± standard deviation. Differences between the groups were analyzed with the chi-square test for categorical variables and the Mann–Whitney *U*-test for continuous variables. Differences between characteristics of patients in each COPD stage were analyzed with the Kruskal–Wallis test for continuous variables. Correlations between $FEV_1/FVC$ and QRS amplitude in lead I and between %$FEV_1$ and QRS amplitude in lead I were assessed by using Pearson's correlation coefficient. Multiple logistic regression analysis was performed to determine the ECG characteristics independently related to COPD. The Akaike Information Criterion was used to select the top 3 parameters (P axis, QRS amplitude in lead I, and R amplitude in $V_5$) from significant differences by univariate analysis. Age and body mass index were also used as confounding factors. ROC curve analysis was used to determine the cut-off value for screening for COPD. A $p$ value $< 0.05$ was considered statistically significant. Data were analyzed with statistical analysis software R (Version 3.1.1.).

## Results

Clinical characteristics of patients with COPD and of controls are shown in Table 1. The patients with COPD had lower body weight and body mass index than the controls. Differences in ECG characteristics between the patients with COPD and the controls are shown in Table 2. There were significant differences between the groups for 6 of the 10 ECG parameters. All patients with COPD had positive amplitude in lead I. The patients with COPD had significantly greater P axis and QRS axis, longer P interval, higher P amplitude, lower QRS amplitude in lead I, and lower R amplitude in $V_5$ than the controls. To determine the important ECG characteristics of patients with COPD, 5 variables (P axis, QRS amplitude in lead I, R amplitude in $V_5$, age, and body mass index) were used in multiple logistic regression analysis. From the analysis, QRS amplitude in lead I emerged as a significant ECG parameter related to COPD (partial regression coefficient = −4.208, $p = 0.002$) (Table 3). QRS amplitude in lead I correlated significantly with $FEV_1/FVC$ ($r = 0.44$, $p < 0.001$) (Fig. 1) and %$FEV_1$ ($r = 0.30$, $p < 0.001$). The ROC curve analysis showed that a QRS amplitude in lead I less than 0.54 mV indicated possible COPD (sensitivity: 71%, specificity: 76%, area under the curve: 0.78 [95% confidence interval: 0.69–0.86], $p < 0.001$) (Fig. 2). When all patients with COPD were classified according to GOLD criteria (stage I, stage II, and stage III), significant differences in QRS amplitude in lead I were not found between 3 GOLD stages (Table 4).

**Table 1**
Clinical characteristics.

| Variables | COPD ($n = 45$) | Control ($n = 100$) | $p$ value |
|---|---|---|---|
| Men, $n$ (%) | 41 (91) | 93 (93) | 0.953 |
| Age (years) | 74 ± 8 | 72 ± 7 | 0.226 |
| Height (cm) | 162.7 ± 7.8 | 162.4 ± 6.7 | 0.909 |
| Body weight (kg) | 58.4 ± 10.7 | 62.1 ± 9.5 | 0.042 |
| Body mass index (kg/m$^2$) | 22.0 ± 3.4 | 23.5 ± 3.1 | 0.014 |
| $FEV_1/FVC$ | 0.52 ± 0.10 | 0.79 ± 0.04 | <0.001 |
| %$FEV_1$ (%) | 69 ± 21 | 101 ± 14 | <0.001 |

COPD = chronic obstructive pulmonary disease; $FEV_1$ = forced expiratory volume in 1 s, FVC = forced vital capacity.
Data are represented as $n$ (%) or mean ± standard deviation.

**Table 2**
ECG indices.

| Variables | COPD ($n = 45$) | Control ($n = 100$) | $p$ value |
|---|---|---|---|
| P axis (°) | 64 ± 32 | 53 ± 24 | <0.001 |
| P interval (sec) | 115 ± 22 | 110 ± 16 | 0.019 |
| P amplitude (mV) | 0.11 ± 0.06 | 0.09 ± 0.04 | 0.027 |
| QRS axis (°) | 53 ± 33 | 45 ± 23 | 0.007 |
| QRS interval (sec) | 104 ± 18 | 99 ± 10 | 0.316 |
| QRS amplitude in $V_1$ (mV) | 1.01 ± 0.37 | 1.04 ± 0.36 | 0.554 |
| QRS amplitude in lead I (mV) | 0.50 ± 0.24 | 0.75 ± 0.26 | <0.001 |
| R amplitude in $V_1$ (mV) | 0.31 ± 0.33 | 0.22 ± 0.15 | 0.789 |
| R amplitude in $V_5$ (mV) | 1.44 ± 0.58 | 1.77 ± 0.49 | <0.001 |
| QTc interval (sec) | 0.43 ± 0.03 | 0.42 ± 0.02 | 0.089 |

ECG = electrocardiogram; COPD = chronic obstructive pulmonary disease.
Data are represented as mean ± standard deviation.

## Discussion

These were the major findings of this study: (1) QRS amplitude in lead I correlated significantly with airflow limitation determined by $FEV_1/FVC$ and (2) QRS amplitude in lead I emerged as an independent variable related to COPD according to the multivariate analysis.

According to a previous meta-analysis, low $FEV_1$ was associated with cardiovascular mortality.[16] Several studies have shown characteristic changes in ECG in patients with COPD.[17–22] Previous studies demonstrated the usefulness of the P axis for the detection of COPD, and P wave verticalization has been shown to correlate with COPD.[17] Bajaj et al reported that a P wave greater in lead III than in lead I was a screening marker for emphysema.[22] Recently, Spodick et al reported that a vertical P axis more than 60° is a useful marker for COPD.[19,20] However, the present study did not show the usefulness of a vertical P axis, possibly because 39% of control subjects showed a P axis more than 60° and the number of patients with COPD demonstrating severe airflow limitation was insignificant.

In patients with COPD, a low QRS voltage is frequently seen in lead I.[18] A "lead I sign" is a QRS amplitude in lead I less than 0.15 mV

**Table 3**
Multiple logistic regression analysis.

| Coefficients | Partial regression coefficient | Std. error | $z$ value | $p$ value |
|---|---|---|---|---|
| (Intercept) | −1.073 | 2.847 | −0.377 | 0.706 |
| Age | 0.027 | 0.027 | 1.004 | 0.315 |
| Body mass index | 0.055 | 0.077 | 0.714 | 0.476 |
| P axis | 0.002 | 0.008 | 0.225 | 0.822 |
| QRS amplitude in lead I | −4.208 | 1.351 | −3.114 | 0.002 |
| R amplitude in $V_5$ | −0.287 | 0.476 | −0.604 | 0.546 |