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Airflow obstruction and left ventricular filling pressure in suspected chronic obstructive pulmonary disease

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ABSTRACT

Left ventricular (LV) filling impairment is present in patients with chronic obstructive pulmonary disease (COPD). Airflow obstruction is related to reduced LV end-diastolic volume, stroke volume, and cardiac output. The ratio of peak early diastolic filling velocity of the mitral inflow to peak early diastolic velocity of the mitral annulus (E/e'), an echocardiographic parameter, can be applied as a surrogate marker of LV filling pressures. Forty-seven individuals with suspected COPD underwent pulmonary function tests and echocardiography. The ratio of forced expiratory volume in 1 s to forced vital capacity (FEV1/FVC) and the E/e' ratio were determined. Multivariate linear regression analysis showed that the FEV1/FVC ratio ($\beta = 0.01$; 95% confidence interval, 0.001–0.019; $p = 0.036$) independently predicted the log transformed E/e' ratio. An increase of FEV1/FVC ratio (in percentage) by 1 unit was associated with an increase of the E/e' ratio multiplied by 1.01. Airflow obstruction inversely predicts LV filling pressure in suspected COPD cases.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is defined as airflow obstruction that is not fully reversible, according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2007 guideline (Rabe et al., 2007). Among individuals without very severe lung disease, Barr et al. (2010) found that airflow obstruction is inversely related to left ventricular (LV) end-diastolic volume, stroke volume, and cardiac output. The LV diastolic dysfunction is present in patients with COPD (Funk et al., 2008).

Therefore, the changes of LV diastolic pressure are important in individuals with airflow obstruction. The LV diastolic pressure is a common surrogate for preload which is one of the major determinants for cardiac output. With the help of echocardiography, Ommen et al. (2000) demonstrated that the ratio of peak early diastolic filling velocity of mitral inflow to peak early diastolic velocity of mitral annulus (E/e') was correlated with the mean LV diastolic pressure and $E/e' < 8$ accurately predicted normal (not increased) LV filling pressure. The E/e' ratio can be applied for the prediction of LV filling pressures (Nagueh et al., 2009).

We hypothesized that LV filling pressure is inversely correlated with airflow obstruction in patients with COPD. The E/e' ratio was used to represent LV diastolic pressure/filling pressure. Therefore, the purpose of the present study was to estimate LV filling pressure (by E/e' ratio) and verify the relationship between LV filling pressure and airflow obstruction in individuals with suspected COPD.

2. Methods

2.1. Study population

Data were obtained from the results of another study that was approved by the Medical Ethics and Institution Review Board of En Chu Kong Hospital (ECKIRB99003) and designed for exercise-related arrhythmia in patients with COPD. Informed consent was

Abbreviations: A, peak late diastolic filling velocities of the mitral inflow; COPD, chronic obstructive pulmonary disease; E, peak early diastolic filling velocities of the mitral inflow; E/A, ratio of early to late peak diastolic filling velocities of the mitral inflow; E/e', the ratio of peak early diastolic filling velocity of the mitral inflow to peak early diastolic velocity of the mitral annulus; e', peak early diastolic velocity of the septal mitral annulus; FEV1, forced expiratory volume in 1 s; FEV1/FVC, ratio of forced expiratory volume in 1 s to forced vital capacity; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; $\ln E/e'$, the log transformed ratio of peak early diastolic filling velocity of the mitral inflow to peak early diastolic velocity of the mitral annulus; LV, left ventricular; LVEF, left ventricular ejection fraction; SpO2, arterial oxygen saturation by pulse oximetry.

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obtained. Subjects were enrolled from the chest outpatient clinic of En Chu Kong Hospital, a regional hospital in Taiwan, from July 2010 to June 2012. Patients with coronary artery disease, old myocardial infarction, atrial fibrillation, atrial flutter, history of heart failure, permanent pacemaker, very severe COPD, cor pulmonale, or acute exacerbation of COPD were excluded. The data from a total of 47 suspected COPD cases were analyzed. All subjects underwent pulmonary function testing and echocardiography. All subjects were divided into 4 groups for details. The subjects with normal spirometry were categorized as group 1. The subjects with GOLD stage I/II/III were categorized as groups 2, 3, and 4 respectively.

2.2. Pulmonary function testing

All subjects underwent pulmonary function testing (American Thoracic Society, 1995). The following parameters were analyzed: the forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), and the FEV1/FVC ratio. The arterial oxygen saturation (SpO2) was measured using pulse oximetry (M1020A SpO2 front-end module on the Hewlett-Packard Component Monitoring System, Hewlett-Packard, Boeblingen, Germany).

2.3. Echocardiography

In all subjects, M-mode, 2-dimensional, pulsed Doppler, and pulsed wave tissue Doppler imaging were performed using the iE33 echocardiographic imaging system (Philips Ultrasound, Bothell, WA, USA) with an S5-1 probe (1–5 MHz). Right ventricular, left atrial, and LV dimensions were measured from the M-mode images. The LVEF was determined using the formula of Teichholz et al. (1976). The LV mass was calculated (Devereux and Reichek, 1977) and the presence of LV hypertrophy was determined (Lin et al., 2007). The cut-off point for pulmonary hypertension was a tricuspid regurgitation peak value greater than 2.5 m/s that corresponded to a pulmonary arterial systolic pressure greater than 35 mmHg (Bossone et al., 1999; Chan et al., 1987; Yilmaz et al., 2005; Yock and Popp, 1984).

Pulsed wave Doppler recordings of the mitral inflow velocities were obtained using the apical 4-chamber view. The peak early (E) and late (A) filling velocities and the ratio of early to late peak diastolic filling velocities of the mitral inflow (E/A) were determined. The peak early diastolic velocity (e') of the septal mitral annulus was measured by pulsed wave tissue Doppler imaging. The E/e' ratio was calculated as a surrogate marker of the LV filling pressure (Nagueh et al., 2009).

2.4. Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 15.0 for Windows (SPSS, Chicago, IL, USA). Continuous variables are presented as mean and standard deviation. Categorical variables are expressed as frequency and percentage.

For comparisons between different groups, the analysis of variance or Kruskal–Wallis test was used for continuous variables as appropriate, and Pearson's χ^2 test or Fisher's exact test was used for categorical variables as appropriate.

The E/e' ratio data were log transformed to normalize their distributions ($\ln E/e'$) where appropriate for regression and correlation analyses. The relationships between $\ln E/e'$ and potential predictive factors were examined using Pearson's correlation coefficient for parametric data and Spearman's correlation coefficient for nonparametric data.

Univariate and multivariate linear regression analysis was performed to determine the predictors of $\ln E/e'$. The following variables were included as potential predictors: age, sex, body surface area, body height, body weight, body mass index, systolic blood pressure, diastolic blood pressure, heart rate, hypertension, diabetes mellitus, smoking, FEV1, FVC, FEV1/FVC, SpO2, right ventricular/left atrial/LV dimensions, LVEF, A, LV mass, LV hypertrophy, pulmonary artery systolic pressure, and pulmonary hypertension. A p value <0.05 was considered significant.

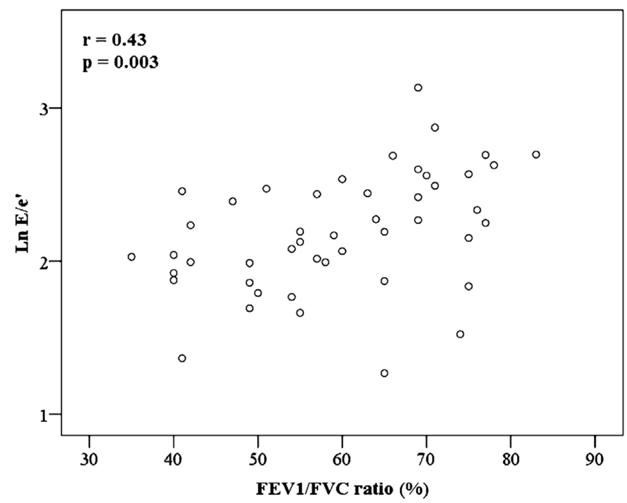

Fig. 1. Scatterplot showing the relationship between the ratio of forced expiratory volume in 1 s to forced vital capacity (FEV1/FVC) and the log transformed ratio of peak early diastolic filling velocity of the mitral inflow to peak early diastolic velocity of the mitral annulus ($\ln E/e'$).

3. Results

The mean age was 69.74 ± 9.19 years, and there were 43 men and 4 women. The mean body surface area was 1.66 ± 0.13 m^2 and body height was 162 ± 5 cm. The mean body mass index was 24.1 ± 3.5 kg/m^2. The mean systolic and diastolic blood pressure was 130.7 ± 21.2 and 79.3 ± 11.1 mmHg. The mean heart rate was 84.2 ± 16.5 bpm. There were 24 subjects with hypertension, 5 with diabetes mellitus, and 35 smokers.

The mean FEV1 was 71.7 ± 22.22% of the predicted value and the FVC was 86.98 ± 19.40% of the predicted value. The mean FEV1/FVC ratio was 59.7 ± 12.71%. The number of subjects with mild, moderate, and severe COPD was 11, 11 and 13, respectively, according to the GOLD 2007 guideline. The remaining subjects had normal spirometry. The mean and minimum SpO2 value was 96.7 ± 1.67% and 94% under room air conditions.

The right ventricular, left atrial, and LV dimensions were within normal limits and all subjects had preserved LV systolic function (mean LVEF (%) 69.74 ± 5.71). The mean E/A ratio was 0.711 ± 0.312, the mean e' value was 6.44 ± 2.17 cm/s, and the mean E/e' ratio was 9.60 ± 3.78. The mean LV mass was 210.5 ± 79.0 g and 21 subjects had LV hypertrophy. The mean estimated pulmonary artery systolic pressure was 29.66 ± 8.79 mmHg and 10 subjects had pulmonary hypertension.

The details of all characteristics among different groups are shown in Tables 1 and 2. The mean FEV1 and mean FEV1/FVC ratio are decreased from groups 1 to 4 (Table 1). The E/e' ratio is decreased from groups 1 to 4 (Table 2).

The $\ln E/e'$ was correlated with A (Pearson's correlation coefficient = 0.336; p = 0.021) and the FEV1/FVC ratio (Pearson's correlation coefficient = 0.43; p = 0.003; Fig. 1).

The results of the univariate and multivariate linear regression analyses for the predictors of $\ln E/e'$ are summarized in Table 3. Only the FEV1/FVC ratio (β = 0.01; 95% confidence interval, 0.001–0.019; p = 0.036) independently predicted $\ln E/e'$. An increase