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Distance and oxygen desaturation in 6-min walk test predict prognosis in COPD patients

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Summary
The aim of the present study was to predict the prognosis of Chronic obstructive pulmonary disease (COPD) patients who underwent comprehensive pulmonary rehabilitation (PR). A total of 144 patients who performed PR between 1992 and 1999 was assessed. After PR, 67 patients underwent lung volume reduction surgery (LVRS). Baseline data before PR consisted of body mass index, serum albumin levels, use of supplement oxygen at home, pulmonary function, arterial blood gas analysis, and distance and fall of hemoglobin oxygen saturation (ΔSpO_2) in 6-min walk test. In addition to pre-PR factors, treatment with LVRS was taken into the analysis. The prognostic significance of variables influencing survival was determined by univariate analysis with Log rank test or multivariate analysis using Cox's proportional hazard model. By a median follow-up time of 8.4 years, the median survival time was 8.1 years (95% confidence interval: 6.9–9.4 years). Albumin level, $PaCO_2$, distance and ΔSpO_2 were significant prognostic factors in univariate analysis. LVRS did not affect the prognosis. The multivariate analysis showed short distance and increase of ΔSpO_2 as significant independent predictors of the risk of death. 6-min walk test was very useful for predicting the prognosis of the COPD patients.

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Introduction

Chronic obstructive pulmonary disease (COPD) has become a common disease worldwide.[1] The prevalence of COPD in subjects aged $\geqslant$40 years increased 10.9% more than expected according to a Japanese epidemiology study conducted in 2000.[2] COPD is currently the fourth leading cause of death in the world, and further increases in the prevalence and mortality of the disease can be predicted in the coming decades.[3] Several factors including reduced expiratory volume in 1 s (FEV_1), hypoxia, hypercapnea, a short distance walked in a fixed time, a high degree of functional breathlessness, and a low body mass index (BMI) were associated with an increased risk of death.[3,4]

Pulmonary rehabilitation (PR) is an effective intervention in patients with COPD.[1,5] Troosters et al. reported that the current best estimate using 7 randomized studies (total 596 patients) was that PR reduced the short-term (1–1.5 year) risk of dying by 31% although this reduction was not statistically significant.[6] In addition, lung volume reduction surgery (LVRS) has been proposed as a palliative treatment for severe COPD patients.[3] Overall, LVRS offered no survival benefit; however, their subgroup analysis demonstrated that patients with predominantly upper-lobe emphysema and low base-line exercise capacity had an advantage in survival.[7] Accordingly, PR and LVRS may prolong survival for COPD patients.

We started our comprehensive PR program for COPD in 1992 at Minami-Okayama Medical Center and LVRS was performed in eligible patients after PR. The aim of this study was to predict the prognosis of COPD by evaluating prognostic factors in all patients participating in our PR program despite LVRS.

Methods

The diagnosis of COPD and classification of severity was defined according to the global strategy for the diagnosis, management, and prevention of COPD updated 2004.[3] The patients have symptoms of cough, sputum, or dyspnea, and/or a history of exposure to risk factors for the disease. The presence of a postbronchodilator $FEV_1 < 80\%$ of the predicted value in combination with an FEV_1/forced vital capacity (FVC) $< 70\%$ confirms the presence of airflow limitation that is not fully reversible. Reversibility was defined as an increase in FEV_1 greater than 12% and/or 200 mL after inhalation of β-agonist. Classification of severity was as follows: mild COPD (stage I), $FEV_1 > 80\%$ predicted; moderate COPD (stage II), $50\% \leqslant FEV_1 < 80\%$; severe COPD (stage III), $30\% \leqslant FEV_1 < 50\%$; very severe COPD (stage IV), $FEV_1 < 30\%$.[3] Inclusion criteria of this study were as follows: (1) the ability to walk for 6 min, (2) never having participated in a rehabilitation program before, (3) absence of a comorbid disease that would make it unlikely that the patient could participate in a PR program, for example, severe pulmonary hypertension with dizziness or syncope on exercise, severe congestive heart failure refractory to medical management, unstable coronary disease, and mental deterioration. The patients received optimal medical treatment including β-agonists, anticholinergic drugs, theophylline, and/or (inhaled or oral) steroids. A stable condition whilst receiving medical treatment was required before PR commenced. This study was performed as part of our standard inpatient treatment and care.

Baseline data before PR consists of height, body weight, BMI, serum albumin level, and use of supplement oxygen at home. Pulmonary function data such as FEV_1% predicted, FEV_1/FVC, and % vital capacity (VC) were assessed with spirometry (Chestac-25, Chest, Tokyo, Japan). Predicted FEV_1 values were obtained from the guidelines of the Japanese Respiratory Society[8]: FEV_1 (L) for men = 0.036 × height (cm) − 0.028 × age (yr) − 1.178; FEV_1 (L) for women = 0.022 × height (cm) − 0.022 × age (yr) − 0.055. Arterial blood gases were taken at rest. Patients with hypoxemia at rest (< 55 Torr) were prescribed oxygen therapy, so that PaO_2 and $PaCO_2$ were measured while they were receiving oxygen. The patients performed 6-min walk (6MW) tests. Six-min walk distance (6MWD) was defined as the longest distance possible in 6MW without encouragement. A practice walk was not included. They were allowed to stop and rest if necessary. They walked with hemoglobin oxygen saturation (SpO_2) monitors. ΔSpO_2 (SpO_2 level just before 6MW − minimum SpO_2 level during 6MW) was also assessed. All the data were before PR.

The comprehensive PR including exercise and educational activities, which are described elsewhere in detail,[9] were performed using a hospitalized program from 4 to 8 weeks. Briefly, patients attended the rehabilitation unit on 5 half-days per week. Exercise included cycle ergometer training, treadmill training, upper and lower extremity strength training, breathing therapies, and relaxation therapies. The education program was also given on weekdays. Inclusion criteria for LVRS were as follows: (1) marked restriction in the activity of daily life despite maximal medical therapy; (2) marked hyperinflation (% total lung capacity > 120%) by dilutional method; (3) diffuse but inhomogeneous emphysema (existence of target areas); (4) ability to participate in a vigorous PR program before and after LVRS; (5) smoking cessation for at least 3 months. Exclusion criteria for LVRS were as follows: (1) pulmonary hypertension (mean pulmonary artery pressure > 30 mmHg) measured by Swan-Ganz catheter; (2) active bronchopulmonary infection; (3) severe bronchial asthma; (4) severe pleural adhesion (for example, prior thoracotomy or chemical pleurodesis); (5) hypercapnea ($PaCO_2 > 60$ Torr).[10] The patients underwent PR for 4 weeks after LVRS.

Statistical analyses were performed with the SPSS Base System™ and Advanced Statistics™ programs (SPSS, Chicago, IL, USA). To compare categorized variables between two groups, Pearson χ^2 was used. The influence of variables on survival was studied by univariate and multivariate analyses. We categorized potential prognostic variables, which were dichotomized into normal and abnormal values based on standard norms ($PaCO_2$: 45 Torr, %VC: 80%); the usual baseline of the supplemental oxygen for hypoxemic patients (PaO_2: 60 Torr); the cutoff line in stage III and IV (FEV_1% of predicted: 30%), or median values for age, BMI, albumin, 6MWD and ΔSpO_2 in this study. All survival data have been updated to 13 December 2004. The overall survival time from the beginning of PR was calculated using the method of Kaplan-Meier. We determined the prognostic significance of variables by univariate analysis with Log rank test or multivariate analysis using Cox's proportional hazard model