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Longitudinal deteriorations in patient reported outcomes in patients with COPD

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Summary Goals of effective management of patients with chronic obstructive pulmonary disease (COPD) include relieving their symptoms and improving their health status. We examined how such patient reported outcomes would change longitudinally in comparison to physiological outcomes in COPD.

One hundred thirty-seven male outpatients with stable COPD were recruited for the study. The subjects health status was evaluated using the St. George's Respiratory Questionnaire (SGRQ) and the Chronic Respiratory Disease Questionnaire (CRQ). Their dyspnoea using the modified Medical Research Council (MRC) scale and their psychological status using the Hospital Anxiety and Depression Scale (HADS) were assessed upon entry and every 6 months thereafter over a 5-year period. Pulmonary function and exercise capacity as evaluated by peak oxygen uptake ($\dot{V}_{O_2}$) on progressive cycle ergometry were also followed over the same time.

Using mixed effects models to estimate the slopes for the changes, scores on the SGRQ, the CRQ, the MRC and the HADS worsened in a statistically significant manner over time. However, changes only weakly correlated with changes in forced expiratory volume in 1 s (FEV_1) and peak $\dot{V}_{O_2}$.

We demonstrated that although changes in pulmonary function and exercise capacity are well known in patients with COPD, patient reported outcomes such as health status, dyspnoea and psychological status also deteriorated significantly over time. In addition, deteriorations in patient reported outcomes only weakly correlated to changes in physiological indices. To capture the overall deterioration

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of COPD from the subjective viewpoints of the patients, patient reported outcomes should be followed separately from physiological outcomes.

Introduction

The goals of effective management of patients with stable chronic obstructive pulmonary disease (COPD) include relieving their symptoms and improving their health status, since none of the existing pharmacological medications for COPD has been shown to modify disease progression.[1] However, in comparison to physiological changes in pulmonary function, which is the hallmark of this disease, the progression of patient reported outcomes over time has been examined less frequently. Since the traditional test of pulmonary function as assessed by the forced expiratory volume in 1 s (FEV_1) does not necessarily correlate strongly with patient reported clinical outcomes such as health status, dyspnoea or psychological status,[2–4] a separate follow-up survey is important to capture the overall deterioration in COPD from the viewpoint of patients themselves.

Understanding the composition of patient reported outcomes versus physician centered physiological outcomes in COPD is indispensable, because patients and physicians do not always share viewpoints on what is important in this disease. As both types of outcomes reflect complementary aspects during the long-term follow-up of COPD, their assessments will enable clinicians to evaluate the overall effectiveness of the management of this disease.

In analyzing longitudinal data, how to deal with dropouts who withdraw from follow-up is a problem, because high numbers of dropouts are reported in COPD clinical trials. For example, in the Inhaled Steroids in Obstructive Lung Disease (ISOLDE) study, 46.5% of the patients dropped out at 3 years.[5] Calverley et al.[6] reported that losing these patients from the final analysis can reduce the power of the study to achieve its primary endpoint as discontinued subjects were those with the most rapidly deteriorating health status or pulmonary function. Therefore, we attempted to analyze longitudinal data in patients with COPD and asthma, including dropouts.[7–10]

We followed longitudinal changes in physiological outcomes and patient reported outcomes of health status, dyspnoea and psychological status over 5 years in patients with COPD, and partly elsewhere reported the physiological deteriorations in exercise capacity and pulmonary function.[7] We hypothesized that both types of outcomes would deteriorate over time, but that their correlations would be weak. Therefore, in the present observational study, we analyzed the 5–year longitudinal changes in patient reported outcomes in patients with COPD, and compared them with changes in physician centered physiological outcomes.

Methods

Subjects

We recruited 137 consecutive male outpatients with moderate to very severe COPD between September 1995 and April 1997, as previously reported.[7] Entry criteria included: (1) a smoking history of more than 20 pack-years; (2) maximal FEV_1/forced vital capacity ratio of less than 0.7 and postbronchodilator FEV_1 of less than 80% of the predicted normal; (3) regular attendance over 6 months; (4) no COPD exacerbations over the preceding 6 weeks; and (5) no uncontrolled comorbidities. Clinical measurements were evaluated on the same day. COPD patients meeting entry criteria were asked to have their clinical outcomes evaluated at entry and every 6 months thereafter over a 5–year period.[7] When an exacerbation of COPD requiring a change in treatment occurred within 4 weeks of a reassessment day, the evaluation was postponed for at least 4 weeks until the patient recovered. The present study was performed as part of our standard outpatient treatment and care, and verbal informed consent was obtained from all patients.

Patient reported outcomes

Health status was measured using the disease-specific measurements: the St. George's Respiratory Questionnaire (SGRQ)[11] and the Chronic Respiratory Disease Questionnaire (CRQ)[12]; their Japanese versions have been previously validated.[3] On the SGRQ, 3 components: symptoms, activity and impacts, and the total scores were calculated, ranging from 0 to 100. On the CRQ, the patients rated 20 items on a seven-point scale, and the 4 domains of dyspnoea,