Identification of COPD Patients at High Risk for Lung Cancer Mortality Using the COPD-LUCSS-DLCO

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BACKGROUND: The COPD-Lung Cancer Screening Score (COPD-LUCSS) is a tool designed to help identify patients with COPD with the highest risk of developing lung cancer (LC). The COPD-LUCSS includes the determination of radiological emphysema, a potential limitation for its implementation in clinical practice. The diffusing capacity for carbon monoxide (DLCO) is a surrogate marker of emphysema and correlates well with CT-determined emphysema.

OBJECTIVE: To explore the use of the COPD-LUCSS using the DLCO instead of radiological emphysema, as a tool to identify patients with COPD at higher risk of LC death.

METHODS: The Body Mass Index, Airflow Obstruction, Dyspnea, Exercise Performance international cohort database was analyzed. By logistic regression analysis, we confirmed that the other parameters included in the COPD-LUCSS (age > 60, pack-years > 60, BMI < 25) were independently associated with LC death. We selected the best cutoff value for DLCO that independently predicted LC death. We then integrated the new COPD-LUCSS-DLCO assigning points to each parameter according to its hazard ratio value in the Cox regression model. The score ranges from 0 to 8 points.

RESULTS: By regression analysis, age > 60, BMI <25 kg/m², pack-year history > 60, and DLCO < 60% were independently associated with LC diagnosis. Two COPD-LUCSS-DLCO risk categories were identified: low risk (scores 0-3) and high risk (scores 3.5-8). In comparison to patients at low risk, risk of death from LC increased 2.4-fold (95% CI, 2.0-2.7) in the high-risk category.

CONCLUSIONS: The COPD-LUCSS using DLCO instead of CT-determined emphysema is a useful tool to identify patients with COPD at risk of LC death and may help in its implementation in clinical practice. CHEST 2016; 149(4):936-942

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Lung cancer (LC) is one of the most frequent causes of death in patients with COPD,[1] and strategies to identify patients at high risk of developing LC are urgently needed. The National Lung Screening Trial demonstrated that performing a low-dose CT (LDCT) scan of the chest in a selected sample of active or former smokers decreases LC mortality by at least 20%.[2] This has led the US Preventive Services Task Force and several professional organizations to recommend screening for higher risk individuals.[3-6]

Because of their high risk, patients with COPD may be good targets for LC screening programs.[7] The recently developed COPD-Lung Cancer Screening Score (LUCSS) has been tested and validated in two different populations of patients with COPD participating in LC screening programs in the United States and Spain.[8] The score ranges from 0 to 10 points and includes four parameters: age > 60 years (3 points), pack-year history > 60 (2 points), BMI < 25 kg/m^2 (1 point), and the presence of radiological emphysema (4 points). The need for visual assessment of the presence or absence of radiological emphysema could potentially limit the implementation of this score because it requires a chest CT. However, the diffusing capacity for carbon monoxide (DLCO), which is widely available in most pulmonary medicine services, has been shown to correlate with the degree of emphysema[9-12] and could be used as a surrogate marker.

The aim of this study is to validate the use of the COPD-LUCSS-DLCO (using the DLCO instead of radiological emphysema) as a tool to identify patients with the highest risk of dying from LC in a large and well-characterized population of patients with COPD. Using DLCO instead of CT-determined emphysema may help to introduce LUCSS into clinical practice.

Methods

Patients with COPD participating in this study were part of the Body Mass Index, Airflow Obstruction, Dyspnea, Exercise Performance (BODE) international cohort that was recruited and followed between January 1997 and December 2013.[13] For the purpose of the present study, the outcomes of LC diagnosis and death were specifically targeted in an effort to provide novel information on the important interaction between COPD and LC. All patients were prospectively recruited in pulmonary clinics in one hospital in the United States (Bay Pines VA Medical Healthcare System, Bay Pines, FL) and three in Spain (Hospital Miguel Servet, Zaragoza; Clinica Universidad de Navarra, Pamplona; and Hospital Nuestra Sra de La Candelaria, Tenerife). All patients regularly seen in the pulmonary clinics were invited to participate in the study regardless of disease severity.

COPD was defined by a history of smoking at least 10 pack-years and an FEV$_1$/FVC ratio of less than 0.70 after 400 μg of inhaled albuterol.[14] Patients were excluded if they had a history of asthma, bronchiectasis, tuberculosis, or other confounding diseases such as severe congestive heart failure (stage III-IV New York Heart Association), obliterative bronchiolitis, or diffuse panbronchiolitis. At entry time, none of the patients had symptoms (hemoptysis, cough, recent weight loss, or chest pain) or chest radiograph findings suggestive of LC. All COPD participants were clinically stable (free of exacerbation for at least 8 weeks) and were receiving standard medical treatment according to the American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines.[14]

The human-research review board at each institution approved the study, and all patients signed an informed consent (Comité de Etica de la Investigación, Universidad de Navarra Institutional Review Board No.: 043/2006).

Clinical and Physiological Parameters Measurements

Trained personnel obtained the following information at the time of recruitment: age, sex, and body mass index (BMI), calculated as the weight in kilograms divided by height in square meters. A specific questionnaire was used to determine smoking status (current or former) and smoking history (age at initiation and discontinuation as well as intensity). From this information we calculated the total smoking exposure and expressed it as pack-years.

Pulmonary function tests (spirometry, lung volumes, and diffusing capacity) were performed following ATS/ERS guidelines[14] on all patients at study entry, and those values were used in the present study. Patients were classified using the grades of airway limitation proposed by the new Global Initiative for COPD (GOLD) strategy.[15] The inspiratory capacity was measured as previously described. The DLCO was determined by the single breath technique following the ATS/ERS guidelines.[16] We used the following formula to adjust for hemoglobin levels: DLCO predicted corrected = DLCO predicted × [1.7 × Hgb/(age-sex-factor + Hgb)],[17] where Hgb indicates hemoglobin.

The presence of comorbidities was evaluated using the Charlson comorbidity index.[18]

LC Diagnosis and Histological Type

The time between enrollment and either diagnosis of or death from LC was expressed in months.

Cause of Death

The cause of death was investigated in all of the patients, as previously published in the BODE study protocol.[13] Patients were evaluated after enrollment and seen every 6 months for at least 10 years or until death. The patient and family were contacted if the patient failed to return for appointments. Death from any cause was recorded. The investigators at each site determined the cause of death after reviewing the medical record and death certificate.

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