



# Clinical Features of Smokers With Radiological Emphysema But Without Airway Limitation

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**BACKGROUND:** The clinical characteristics of patients with emphysema but without airway limitations remain unknown. The goal of this study was to compare the clinical features of current and former smokers without airflow limitation who have radiologic emphysema on chest CT scans vs a control group of current and ex-smokers without emphysema.

**METHODS:** Subjects enrolled had anthropometric characteristics recorded, provided a medical history, and underwent low-dose chest CT scanning. The following parameters were also evaluated: pulmonary function tests including diffusion capacity for carbon monoxide (DLCO), the modified Medical Research Council dyspnea score, COPD assessment test (CAT), and 6-min walk test (6MWT). A comparison was conducted between those with and without CT-confirmed emphysema.

**RESULTS:** Of the 203 subjects, 154 had emphysema, and 49 did not. Adjusted group comparisons revealed that a higher proportion of patients with emphysema according to low-dose chest CT scanning had an abnormal DLCO value ( $< 80\%$ ) (46% vs 19%;  $P = .02$ ), a decrease in percentage of oxygen saturation  $> 4\%$  during the 6MWT (8.5% vs 0;  $P = .04$ ), and an altered quality of life (CAT score  $\geq 10$ ) (32% vs 14%;  $P = .01$ ). A detailed analysis of the CAT questionnaire items revealed that more patients with emphysema had a score  $\geq 1$  in the “chest tightness” ( $P = .05$ ) and “limitation when doing activities at home” ( $P < .01$ ) items compared with those with no emphysema. They also experienced significantly more exacerbations in the previous year (0.19 vs 0.04;  $P = .02$ ).

**CONCLUSIONS:** A significant proportion of smokers with emphysema according to low-dose chest CT scanning but without airway limitation had alterations in their quality of life, number of exacerbations, DLCO values, and oxygen saturation during the 6MWT test.

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**KEY WORDS:** clinical; emphysema; smokers

**ABBREVIATIONS:** 6MWT = 6-min walk test; CAT = COPD assessment test; DLCO = diffusion capacity for carbon monoxide; SpO<sub>2</sub>% = percentage of oxygen saturation

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Drs Zulueta and de-Torres contributed equally to this work.

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COPD is characterized by airflow limitation on spirometry testing caused by the combination of small airway inflammation and destruction of lung parenchyma (emphysema), mainly due to tobacco exposure.<sup>1,2</sup> Emphysema itself is defined as an abnormal and permanent enlargement of the air spaces distal to the terminal bronchioles that is accompanied by destruction of the air space walls, with no obvious fibrosis (ie, there is no fibrosis visible to the naked eye).<sup>3</sup>

The advent of CT scanning has allowed the in vivo identification of emphysema in individuals, and its

presence has been noted in subjects without airflow limitation.<sup>4-6</sup> However, there is limited information regarding the clinical characteristics, if any, of individuals with emphysema but no airflow limitations. Until now, the information regarding the clinical presentation of smokers without airflow limitation in the studied population barely acknowledge the contribution of radiologic emphysema.<sup>7-11</sup>

The present study comprised a comprehensive assessment of the clinical and physiologic impact of visually detected radiologic emphysema in current and former smokers without airflow limitation.

## Methods

Current and former smokers were recruited between 2011 and 2015 at our pulmonary clinic; the participants were part of a lung cancer screening program.<sup>12</sup> Only individuals with normal postbronchodilator spirometric findings and a low-dose CT scan were included. We first consecutively included subjects with emphysema visually detected on CT scanning. We then selected from a group of control subjects (ie, subjects with normal spirometric findings without CT-detected emphysema) with similar age, sex, and pack-year history (Fig 1). Subjects with spirometry-confirmed COPD or those who had a history of asthma, TB, or other confounding diseases were excluded.

Our institution's ethics committee approved the study (institutional review board approval number 28/2012), and all patients provided written informed consent.

### Clinical and Physiologic Evaluation

Age, sex, presence of significant comorbidities, smoking status, pack-year history, and number of exacerbations in the last year (defined according to the presence of cough, sputum production, and dyspnea that required the use of antibiotics, systemic glucocorticoids,

bronchodilators, medical consultation, hospitalization, or an emergency department visit) were recorded. Lung function measurements (Vmax 2) were determined.<sup>13</sup> The 6-min walk test (6MWT) was performed according to American Thoracic Society guidelines.<sup>14</sup> A drop in percentage of oxygen saturation (SPO<sub>2</sub>) ≥ 4% during the test was considered a significant desaturation.<sup>15</sup> Dyspnea was assessed by using the modified Medical Research Council scale; scores range from 0 to 4.<sup>16,17</sup>

Patients were asked to self-administer the COPD assessment test (CAT),<sup>18</sup> which includes eight items with scores ranging from 0 to 5 (0 = no impairment). An overall score is calculated by adding the score from each item, with total scores ranging from 0 to 40; higher scores indicate a more severe health impairment. In patients with COPD, a CAT score > 10 is considered clinically relevant.<sup>19</sup> Serum levels of glucose, cholesterol, hemoglobin, creatinine, urea, and alpha<sub>1</sub>-antitrypsin were also determined.

### Low-Dose CT Scanning

Low-dose chest CT scanning examinations were performed in a single breath-hold at end-inspiration with a multidetector CT scanner (Somatom Sensation 64) at low-radiation-dose settings (120 kVp, 20-40 mAs). All CT scans were reconstructed with 1.25-mm slice thickness and 1-mm intervals using a high spatial frequency reconstruction algorithm. Images were displayed at window settings appropriate for viewing the lung parenchyma/window width of 1,500 HU and window center of -650 HU.

All images were read by two expert chest radiologists for visual assessment of the presence and extent of emphysema, using validated criteria to define the percentage of lung parenchyma affected: mild, 0 to 25%; moderate, 26% to 50%; severe, 51% to 75%; and very severe, > 75%.<sup>20</sup> Both radiologists were blinded to the clinical information of the participants. A previous study found that the concordance between readers for the presence and degree of emphysema was excellent (kappa coefficient: 0.9).<sup>21</sup> For the purpose of the present study, patients were classified according to whether they had emphysema. One potential drawback of our study may be the use of low radiation doses to assess the extent of pulmonary emphysema, but studies comparing low vs standard radiation doses have shown minimal differences between these two approaches.<sup>22</sup>

### Data Analysis

Quantitative data are represented as mean ± SD or median (interquartile range), depending on data distribution; qualitative data are represented by using relative frequencies. Comparison of qualitative variables between ≥ 2 groups was performed by using the

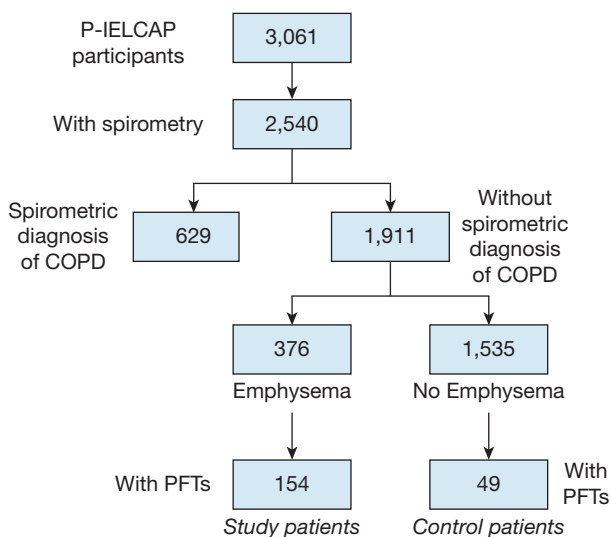


Figure 1 – Flowchart explaining how the patients were recruited to participate in the study. PFT, pulmonary function tests; P-IELCAP = Pamplona site of International Early Lung Cancer Program.

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