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Title: Emphysema distribution determines distinct pulmonary function features

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Body: Lung emphysema has distinct clinical features that can be independent of airflow obstruction severity. The aim of this study was to evaluate the impact of emphysema distribution on patients' clinical and functional features. Eighty-six patients (mean age 65.2±12.2 years, 62.7±38.4 smoking pack-year) underwent clinical and lung CT scan evaluation. They were classified according to a lung CT 5-point visual scoring system for emphysema distribution. Groups were compared according to this stratification. Patients had mild airflow limitation in 28.2%, moderate in 22.4%, severe in 29.4% and very severe in 20%. Upper lung (UL) predominant emphysema was present in 36% patients, 25.6% cases had moderately UL predominance, 22.1% had moderately lower lung (LL) predominance and 16.3% had homogeneous distribution. Moderately LL predominant emphysema was associated to lower paO₂/fiO₂ ratio, FEV₁, FVC, FEV₁/FVC, DLCO and DLCO/VA (r= -0.456 to r= -0.603, p<0.0005). Patients with moderate LL predominance are more probable to have FEV₁<65% than patients with UL predominant emphysema (OR 4.55, 95%CI 1.23-16.88; p=0.023) and paO₂/fiO₂ ratio <285 (OR 30.38, 95%CI 3.33-277.31; p= 0.002). Patients with homogeneous emphysema had lower 6-minute walk distance (F=5.007, p=0.003) and higher desaturation (H=11.860, p=0.008). They had also higher RV/TLC, although without achieving significance (p=0.064). Moderately predominant emphysema in LL was related to more severe disease than UL predominance. Patients with homogeneous emphysema had greater hyperinflation and worse exercise performance. Distribution of emphysema has an important impact on functional parameters and should be considered in disease evaluation.