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Title: Stability of COPD phenotypes over time

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Body: Three phenotypes (severe respiratory, moderate respiratory, and systemic COPD) were previously identified by cluster analysis in COPD patients, which differed in clinical expression and outcomes (Garcia-Aymerich 2011, Thorax). Aim: To study the stability of these phenotypes over time. Methods: 251 COPD patients from the PAC-COPD study participated in a follow-up visit a mean of 1.7 years after their baseline assessment. Symptoms, lifestyle, comorbidities, quality of life, body mass and composition, complete lung function, muscle function, 6-min walking test, and serum inflammatory biomarkers were measured. Patients were grouped according to the distribution of 104 variables (phenotypic traits) using partitioning cluster analysis (kmeans). Results: Two or three groups were suggested as the best clustering statistical alternatives, and three groups were clinically more meaningful. Group 1 (n=116 (46%), 69 y) included patients with worse airflow limitation, hyperinflation, and impaired gas exchange; patients in Group 2 (n=108 (43%), 70 y) exhibited better health in all domains; Group 3 (n=27 (8%), 74 y) had a higher prevalence of respiratory symptoms, worse quality of life, impaired exercise capacity and muscle strength, and a higher proportion of co-morbidities. The baseline "severe respiratory" group mostly fell (91%) in follow-up Group 1; 25% and 70% of patients in baseline "moderate respiratory" belonged to follow-up Group 1 and 2, respectively; patients in baseline "systemic" phenotype were distributed across all phenotypes but represented 70% of follow-up Group 3. Conclusion: The three phenotypes identified in the follow-up visit exhibit very similar clinical characteristics than the baseline ones. Most patients remain in the same group.