The molecular and clinical diseasome of comorbid diseases in chronic obstructive pulmonary disease

Authors
Rosa Faner, Alba Gutiérrez-Sacristán, Ady Castro-Acosta, Solène Grosdidier, Milagros Sánchez-Mayor, Jose Luis Lopez-Campos, Francisco Pozo-Rodríguez, Ferran Sanz, Laura I. Furlong, Alvar Agustí

a Fundació Hospital Clinic-IDIBAPS, CIBERES, Barcelona, Spain
b Integrative Biomedical Informatics Group-IMIM-UPF, Barcelona, Spain
c Instituto de Investigación, Hospital 12 de Octubre, Madrid, Spain
d Unidad Médico-Quirúrgica de Enfermedades Respiratorias. Instituto de Biomedicina de Sevilla. Sevilla, Spain
e Servicio de Neumología, Instituto del Torax, Hospital Clínico, Universitat de Barcelona. Barcelona, Spain

Correspondence
Rosa Faner
Fundació Hospital Clínic-IDIBAPS
Rosselló, 149. 08036 Barcelona, Spain
Tel.: +34 93 227 57 07. E-mail: rfaner@clinic.ub.es

The molecular and clinical relationships of comorbidities in patients with Chronic Obstructive Pulmonary Disease (COPD) are unclear.

The objectives of this work are: (1) to describe and compare the Molecular (MD) and Clinical Diseasome (CD) in COPD patients; and, (2) to investigate the relationship of airflow limitation severity, age, smoking and mortality with the CD.

We analyzed 5,447 patients hospitalized because of an exacerbation of COPD, and determined the prevalence of 11 diseases listed in the Charlson Comorbidity Index. In the MD, two of these diseases were linked if they share disease-associated genes and/or if the proteins encoded by these genes are connected in the interactome. In the CD, two diseases were linked if their co-occurrence was higher than expected by chance (p<0.05) and have a Relative Risk>1 and a Phi (ϕ)-correlation>0. From the 11 diseases considered in the analysis, a maximum of 55 disease pairs can occur. We observed that 25 of them (46%) were included in the MD and 23 (42%) in the CD; 11 of these disease pairs were identified both in the MD and CD. The CD was not significantly influenced by the severity of airflow limitation, age and/or smoking exposure, but mortality was associated with a more strongly connected CD.

In conclusion, comorbidities in COPD form a network both at the clinical and molecular levels. About half of the disease pairs identified clinically share molecular mechanisms. In this particular cohort, the CD appears independent of airflow limitation severity, age or cumulative smoking exposure.