ORIGINAL RESEARCH

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Susceptibility to frequent exacerbation in COPD patients: impact of the exacerbations history, vaccinations and comorbidities?

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Abbreviation list:

COPD = Chronic Obstructive Pulmonary Disease; **CNIL** = Commission nationale de l'informatique et des libertés National (Data Protection and Privacy Commission); **CCTIRS** = Advisory Committee for Data Procession in Health Research; **FEV_1** = Forced Expiratory Volume in 1 second; **FVC** = Forced vital capacity; **RV** = Residual Volume; **TLC** = Total Lung Capacity; **EELV** = The end-expiratory lung volume; **VC** = Vital Capacity; **IC** = Inspiratory Capacity; **FRC** = Functional residual Capacity; **BMI** = Body Mass Index; **GOLD** = Global Initiative for Chronic Obstructive Lung Disease; **mMRC** = modified Medical Research Council; **CAT** = COPD Assessment Test; **ATS** = the American Thoracic Society; **ERS =** the European Respiratory Society; **PFT**= pulmonary function test; **LABA =** long-acting β-agonist; **LAMA =** long-acting muscarinic antagonist; **ICS =** inhaled corticosteroid; **SABA =** short-acting β-agonist; **RNIPP =** Répertoire national d'Identification des personnes physiques (National identification register of private individuals). **ROC =** receiver operating characteristic.

ABSTRACT

INTRODUCTION: Exacerbations are key events in the natural history of COPD, but our understanding of their longitudinal determinants remains unclear. We used data from a large observational study to test the hypothesis that vaccination status and comorbidities could be associated with the occurrence of exacerbations profile.

METHODS: Diagnosed COPD patients have been included by their pulmonologists, with up to 3 years of follow-up. Data were analyzed using the KmL method designed to cluster longitudinal data and receiver operating characteristic curve analysis to determine the best threshold to allocate patients to identified clusters.

RESULTS: 932 COPD patients were included since January 2014, 446 patients (65.68% males, 35.59% current smokers) were followed over a period of 3 years with complete data. 239(28.15%) patients reported two or more exacerbations in the year before enrolment (frequent exacerbations). Among them 142(16.68%) also had frequent exacerbations in the first year of the study, and 69(8.10%) who remained frequent exacerbators in the second year. Based on our hypothesis, we were able to determine four phenotypes: A (infrequent), B (frequent in underweight patients), C (transient), and D (frequent in obese patients). Frequent exacerbators had more airflow limitation and symptoms. Irrespective of cut-offs set to define the optimal number of clusters, a history of exacerbations OR: 3.72[2.53-5.49], presence of anxiety OR: 2.03[1.24-3.31] and absence of the annual influenza vaccination OR: 1.97[1.20-3.24] remained associated with the frequent exacerbator phenotypes.

CONCLUSIONS: The most important determinants of frequent exacerbations are a history of exacerbations, anxiety and unvaccinated against influenza.

KEY WORDS: COPD Phenotypes, Frequent Exacerbator, Cluster analysis, longitudinal analysis.