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**Title:** Pneumonic and non-pneumonic exacerbations of COPD: Systemic inflammatory response and clinical characteristics

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**Body:** Background: Community-acquired pneumonia (CAP) is a frequent event in patients with chronic obstructive pulmonary disease (COPD), although it is not currently considered an acute exacerbation (AECOPD). No studies have compared the inflammatory response of COPD patients who develop CAP or AECOPD. Aim was to characterize the systemic inflammatory response and the clinical and evolutive manifestations. Methods: Prospective data were collected from 253 COPD consecutively hospitalized patients. Comparative analyses were performed in AECOPD (n=137) and CAP+COPD patients (n=116). Clinical severity, blood biomarkers and mortality/re-hospitalization were respectively recorded on admission, at day 1/day 3/day 30, and in a follow-up period of 30/90 days/1 year. Results: COPD patients with CAP had higher FEV1 compared to COPD patients without pneumonia. In hospital and long-term outcomes (1 yr) were similar for both populations. However, AECOPD patients had more readmissions. At day 1 and day 3 CAP+COPD patients had significantly (p<0.001) higher serum levels of C-reactive protein (CRP), procalcitonin (PCT), tumour necrosis factor-alpha (TNF- $\alpha$ ) and interleukin (IL) 6. Repetition of the analyses after stratifying patients based on severity of disease, current inhaled pharmacotherapy and noninfectious AECOPD etiology confirmed higher levels of the same biomarkers in patients with CAP+COPD. CRP levels at day 1 resulted significant in a multivariate analysis to predict pneumonia. Conclusions: Our study confirms that there are two specific inflammatory profiles in hospitalized COPD patients in response to CAP (stronger response) and AECOPD with similar short and long term outcomes.