Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality worldwide \[1\]; it has been estimated that in 2030 it will become the third leading cause of death in the world \[2\]. Acute exacerbations of COPD (AECOPD) are unfavourable events interrupting the stable phase of disease \[3\]; an increase \[4\] and specific \[5\] activity of systemic inflammation and a deterioration of respiratory signs and symptoms are characteristics of AECOPD \[6\].

Usually, it’s common to observe and consider AECOPD as an acute event that progressively and repetitively influences the chronic natural history of COPD and causes a “loss of something”; several studies have in fact evaluated, related to AECOPD, the clinical evolution of COPD through the progressive decline in lung impairment \[7\] or through the reduced quality of life \[8\]. However, often COPD patients due to AECOPD require hospital admission and this aspect may have an influence on general prognosis during hospitalization and for a short period after discharge.

The close link between AECOPD and all-cause mortality was demonstrated some years ago \[9\]; severe AECOPD, in fact, have been considered to have an independent negative impact on the prognosis of COPD patients \[9\]. Although the frequency of AECOPD and the number of events have an important role in the mortality risk \[9\], also in a long-term period of evaluation \[10\], the risk of mortality does not appear to be strictly related to the level of pulmonary impairment \[11\].

Clearly, the impact of AECOPD on patients is the result of the combined effects of the previous conditions of the patient, the severity of the acute event and the therapeutic decisions made by physicians. Although the international Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines \[11\] have taught us all...
about the diagnosis and management of AECOPD[15] and several studies published over the last decade have investigated and founded clinical factors that potentially could be determinants of mortality for hospitalized patients with AECOPD, nothing has been reported on specific and useful recommendations for patients at risk of death. In fact, the possibility of having reliable screening criteria capable of identifying early on patients at a higher risk of death in the “critical period” of hospitalization and in the early post-discharge period could be useful to physicians in the management of these patients at risk. This aspect may in fact, be true especially when defining the prognosis of patients and then, adjusting levels of care and treatments, or optimizing timing of discharge and planning a follow-up visit.

With regards to variables influencing survival and related to the general characteristics of patients, age at admission[9,12-15], particularly in older patients[12,13,14], has been seen to be an important indicator of poor prognosis during hospitalization[9,12-17] and in the post-discharge period[12,15]. Moreover, the presence of associated comorbidities to COPD[9,12,15], may worsen the prognosis of AECOPD patients; in this context, cardiovascular disease plays a special role[13,14].

Related to the severity of COPD, several factors have been defined as risk factors. In particular, is has been demonstrated that patients with chronic respiratory failure and previous need for long-term home oxygen therapy (LTOT)[15,18] or non-invasive mechanical ventilation[17], patients with high values at admission of dyspnocia perception[13,15,17,19], and patients with very severe airflow obstruction (forced expiratory volume in the 1st second, FEV1 ≤ 30 % of predicted)[16,18] have increased an risk of death related to AECOPD.

With regards to clinical signs of AECOPD severity, the use of accessory inspiratory[13,15,17] or expiratory muscles[11], paradoxical breathing[13,17], cyanosis[11], lower limb oedema[13], and impaired neurological status[13,17], especially with a Glasgow score < 15[19], were found to be important factors related to mortality of AECOPD patients at and during hospitalization. Moreover, general blood gas alterations[12,14,16,18-19], in particular hypercapnia[12,14,19] or hypoxaemia[18,19], have been found to be strong predictors of mortality. Notably, a very recent study[12] demonstrates that the severity of respiratory acidosis in AECOPD increases progressively the risk of death during hospitalization (pH = 7.25-7.35 versus pH > 7.35 Odds Ratio-OR = 1.58 with a 95% Confidence Interval-CI 1.28-1.94; pH < 7.25 versus pH > 7.35 OR = 2.31, 95% CI 1.72-3.10). The need for ventilatory support, moreover, increases significantly the risk of death during hospitalization (OR = 3.66, 95% CI 2.99-4.48, p < 0.0001)[12].

In the context of post-discharge mortality, early hospital readmission for a new event of AECOPD (for example, in a period within 30 days from discharge) is a variable that “per se” influences prognosis of patients. Although several variables have been found to be predictors of early readmission[20-22], in fact, is has been demonstrated that readmission of patients to hospital in this period have a higher subsequent and progressive risk of death until in long follow-up period of 3-year[23]. Starting from the concept that a predictor of a 30-day readmission is the variable ≥ 2 previous exacerbation in a period of 1-year prior to index hospitalization (Hazard Ratio-HR = 2.47, 95% CI 1.51-4.05, p < 0.001)[23], the relationship in the events of AECOPD between the past and the prognosis is very close. Moreover, a study published in 2012 reported the presence of at least one previous exacerbation of COPD in the previous year [OR = 3.9, 95% CI 1.6-9.9, p = 0.004][19] as an independent predictor of adverse outcome defined by death during hospitalisation or the 1-month follow-up.

Finally, in order to define a specific score evaluating the prognosis of hospitalized AECOPD, an English prospective study[26] involving more than 900 patients has found the five strongest independent predictors of death during hospitalization (extended MRC Dyspnoea Score, coexistent pneumonia, consolidation, acidemia, and atrial fibrillation), then combined into a clinical prediction score (DECAF, Dyspnoea, Eosinopenia, Consolidation, Acidemia and atrial Fibrillation). Supported by an internal bootstrap validation, the DECAF score[26] demonstrates excellent ability in the discrimination of patient deaths during hospitalization (area under the receiver operator characteristic curve-AUC = 0.86, 95% CI 0.82 to 0.89). Moreover, in the subgroup of patients with coexistent pneumonia, DECAF exhibit a strong and significant prediction of in-hospital mortality power better than CURB-65 (Confusion, Urea, Respiratory Rate, Blood pressure, Age > 65) score[25] (AUC = 0.77 vs 0.66, p = 0.003)[26].

In conclusion, several clinical factors may be defined as risk factors for mortality at admission, during hospitalization and for a short period after discharge. In this context of looking for predictors of death in AECOPD, the possibility to have specific clinical prediction tools may help physicians to accurately predict prognosis and therefore, behave differently in the clinical management of patients. Now, a very interesting question that remains to be answered is: are there any clinical factors that are potentially modifiable by specific physician intervention?

**CONFLICT OF INTERESTS**

The authors declare that they do not have conflict of interests.

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