Chronic Obstructive Pulmonary Disease Exacerbations: Better Standards – Better Prognosis?

Sylvia Hartl

Ludwig Boltzmann Institute of COPD and Respiratory Epidemiology, Otto Wagner Hospital, Vienna, Austria

Chronic obstructive pulmonary disease (COPD) is one of the most important noncommunicable chronic respiratory diseases [1]. In recent years, acute exacerbations of COPD (AECOPD) have been identified as major modifiers of the course of the disease [2–4]. Exacerbations requiring admission to hospital, which might occur in moderate to severe COPD, are the major threats of poor survival [5, 6]. Both the number and severity of exacerbations determine poor outcome. In addition, the severity of an exacerbation increases the risk of relapse and readmission to hospital [3]. Although the need for hospital admission is high in severe COPD (70% of all exacerbations), patients with moderate COPD also require hospital admission.

COPD management recommendations therefore focus on the reduction of AECOPD via prevention and treatment strategies. In clinical practice, the diagnosis of exacerbations relies on the spirometry-proven diagnosis of COPD and the increase of symptoms of dyspnea, sputum color and quantity, and cough. The assessment of the severity of an exacerbation needs a thorough medical history and additional diagnostic tests like blood gas analysis and X-ray [7].

In this issue of *Respiration*, the paper of Myint et al. [8] shows that concomitant infiltrates in AECOPD, suspected as pneumonia, worsen various important outcome pa-

rameters: the length of stay (LOS) in hospital, the need for noninvasive or invasive ventilation, the level of disability after discharge, and death. The authors were able to demonstrate that the diagnosis of pneumonia was unexpected, based on clinical grounds, and would easily have been missed if not detected by chest X-ray. In this study, 16% of the patients with AECOPD showed pulmonary infiltrates consistent with pneumonia on chest X-rays even though patients with predominant clinical signs of pneumonia upon admission were excluded. Consistent with these findings, a recent overview of hospitalizations of COPD patients in the USA showed that pneumonia was a frequent second diagnosis (22%) in AECOPD patients upon admission [9]. In this survey, 822,500 hospital-admitted patients with COPD exacerbations had on average a hospital stay of 4.3 days. In the study of Myint et al. [8], the LOS was markedly increased to 7–14 days in AECOPD patients with concomitant radiological findings of pneumonia. Although patients with concomitant infiltrates were more likely to suffer from comorbidities and a higher level of disability, radiological detection of pneumonia was still an independent risk factor for a longer hospital stay. This is in accordance with a Finnish registry cohort [10] where a secondary diagnosis of pneumonia in elderly COPD patients increased the LOS to up to 14.7 days. LOS is an important risk factor for hospi-

tal mortality and for increasing the costs of treatment. Therefore, risk stratification is one of the important issues of hospital admissions.

The outcome of pneumonia relates to prognostic scores like the CURB-65, which offers guidance to clinicians on the management of such patients [11]. In the study of Myint et al. [8], patients without the predominant clinical findings of pneumonia, presenting with severe symptoms of AECOPD, are not likely to be scored for pneumonia risk stratification and therefore might not receive adequate treatment. This is the first study looking at the impact of the X-ray findings on the prognosis of AECOPD. The strength of this study is its statistical power due to the high number of cases. Taking into account that in a recent review of in-hospital management of AECOPD [12] up to 13% of COPD patients did not receive any X-ray upon admission, the study by Myint et al. [8] in this journal might call for stricter management programs in the future.

Moreover, in this study, 16% of patients with AECOPD and concomitant infiltrates had need of mechanical ventilation. This is a substantially higher rate than the overall rate of 2.9% in a population of hospital-admitted AECOPD patients in the study of Roberts et al. [13] and of 9.8% in the study of Bratzler et al. [14].

Connors et al. [15] showed a high in-hospital mortality rate of 11% and Seneff et al. [16] showed an even worse mortality rate of 24% in COPD patients with acute respiratory failure. The increased in-hospital mortality rate of 7.5% of severe AECOPD with minor secondary pneumonia in the study of Myint et al. [8] is likely to be associated with the high proportion of mechanically ventilated patients.

This does not explain the increased 90-day mortality rate of 17% after discharge of the AECOPD patients, as only amongst those with persisting hypercapnia after respiratory failure has there been a proven increase in mortality after discharge [17]. Other concomitant diseases like cardiac failure and coronary artery disease (elevated BNP and/or troponin T) effect hospital mortality dramatically (up to 28%), but cardiac failure does not impact mortality after discharge [18]. Therefore it seems that the authors of this study have identified an independent risk factor for mortality in hospital-admitted AECOPD patients.

Another aspect of hospital-admitted AECOPD cases is the high readmission rate. Readmission rates in various studies differ from 11% within 14 days to 43% after 6 months [12, 14, 19]. Soler-Cataluña et al. [3], some years ago, were the first to demonstrate that mortality is in-

creased 3-fold by a higher frequency of exacerbations in hospital-admitted AECOPD patients. They identified specific risk factors like age, baseline lung function and blood gases on admission. In the study of Myint et al. [8], a higher age and severe hypoxemia were recorded, but no difference in baseline FEV₁ – when available on admission – was seen. However, pneumonia added an independent risk to all the other risk factors mentioned.

Aiming for a reduction of readmissions, recently published studies have addressed treatment models (e.g. early discharge, integrated care models) for COPD patients after hospitalization. These complex treatment programs include rehabilitation, education, psychological counseling and medication adherence surveillance. In practice, such programs are often available only as pilot projects and resources for them are still scarce [20, 21]. The definition of additional risk factors for bad outcome, like pulmonary infiltrates in COPD exacerbation, might support more comprehensive selection criteria for such discharge models.

The UK National COPD Resources and Outcome Project 2008 [8] identified unrevealed risk factors as outcome predictors and it therefore supports more standardization of COPD care, inducing better predictable treatment for well-defined groups of COPD patients.

Financial Disclosure and Conflicts of Interest

The author does not have any conflicts of interest regarding the topic of the editorial.

References

- 1 Bousquet J, Kiley J, Bateman ED, Viegi G, Cruz AA, Khaltayev N, Ait Khaled N, Baena-Cagnani CE, Barreto ML, Billo N, Canonica GW, Carlsen K-H, Chavannes N, Chuchalin A, Drazen J, Fabbri LM, Gerbase MW, Humbert M, Joos G, Masjedi MR, Makino S, Rabe K, To T, Zhi L: Prioritised research agenda for prevention and control of chronic respiratory diseases. *Eur Respir J* 2010;36:995–1001.
- 2 Donaldson GC, Seemungal TAR, Bhowmik A, Wedzicha JA: Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease. *Thorax* 2002;57:847–852.
- 3 Soler-Cataluña JJ, Martínez-García MA, Román Sánchez P, Salcedo E, Navarro M, Ochando R: Severe acute exacerbations and mortality in patients with chronic obstructive pulmonary disease. *Thorax* 2005;60:925–931.

- 4 Wedzicha JA, Seemungal TA: COPD exacerbations: defining their cause and prevention. *Lancet* 2007;370:786–796.
- 5 Hurst JR, Vestbo J, Anzueto A, et al: Susceptibility to exacerbation in chronic obstructive pulmonary disease. *N Engl J Med* 2010; 363:1128–1138.
- 6 Garcia-Aymerich J, Farrero E, Felez MA, et al: Risk factors of readmission to hospital for a COPD exacerbation: a prospective study. *Thorax* 2003;58:100–105.
- 7 Global Initiative for Chronic Obstructive Lung Disease: Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: 2009 update. <http://www.goldcopd.com>.
- 8 Myint PK, Lowe D, Stone RA, Buckingham RJ, Roberts CM: UK National COPD Resources and Outcome Project 2008: patients with chronic obstructive pulmonary disease exacerbations who present with radiological pneumonia have worse outcome compared to those with non-pneumonic chronic obstructive pulmonary disease exacerbations. *Respiration* 2011;82:320–327.
- 9 Wier LM, Elixhauser A, Pfuntner A, Au DH: Overview of Hospitalizations among Patients with COPD, 2008: Statistical Brief #106. Rockville, Agency for Health Care Policy and Research (US), 2006–2011.
- 10 Kinnunen T, Säynäjäkangas O, Tuuponen T, Keistinen T: Impact of comorbidities on the duration of COPD patients' hospital episodes. *Respir Med* 2003;97:143–146.
- 11 Chen JH, Chang SS, Liu JJ, Chan RC, Wu JY, Wang WC, Lee SH, Lee CC: Comparison of clinical characteristics and performance of pneumonia severity score and CURB-65 among younger adults, elderly and very old subjects. *Thorax* 2010;65:971–977.
- 12 Lodewijckx C, Sermeus W, Vanhaecht K, Panella M, Deneckere S, Leigheb F, Decramer M: Inhospital management of COPD exacerbations: a systematic review of the literature with regard to adherence to international guidelines. *J Eval Clin Pract* 2009;15: 1101–1110.
- 13 Roberts CM, Ryland I, Lowe D, Kelly Y, Bucknall CE, Pearson MG: Audit of acute admissions of COPD: standards of care and management in the hospital setting. *Eur Respir J* 2001;17:343–347.
- 14 Bratzler DW, Oehlert WH, McAdams LM, Leon J, Jiang H, Piatt D: Management of acute exacerbations of chronic obstructive pulmonary disease in the elderly: physician practices in the community hospital setting. *J Okla State Med Assoc* 2004;97:227–232.
- 15 Connors AF Jr, Dawson NV, Thomas C, Harrell FE Jr, Desbiens N, Fulkerson WJ, Kussin P, Bellamy P, Goldman L, Knaus WA: Outcomes following acute exacerbation of severe chronic obstructive lung disease. *Am J Respir Crit Care Med* 1996;154:959–967.
- 16 Seneff MG, Wagner DP, Wagner RP, Zimmerman JE, Knaus WA: Hospital and 1-year survival of patients admitted to intensive care units with acute exacerbation of chronic obstructive pulmonary disease. *JAMA* 1995;274:1852–1857.
- 17 Chu CM, Chan VL, Lin AW, Wong IW, Leung WS, Lai CK: Readmission rates and life threatening events in COPD survivors treated with non-invasive ventilation for acute hypercapnic respiratory failure. *Thorax* 2004;59:1020–1025.
- 18 Chang CL, Robinson SC, Mills GD, Sullivan GD, Karalus NC, McLachlan JD, Hancox RJ: Biochemical markers of cardiac dysfunction predict mortality in acute exacerbations of COPD. *Thorax* 2011, E-pub ahead of print.
- 19 Lindenauer PK, Pekow P, Gao S, Crawford AS, Gutierrez B, Benjamin EM: Quality of care for patients hospitalized for acute exacerbations of chronic obstructive pulmonary disease. *Ann Intern Med* 2006;144:894–903.
- 20 Kruis AL, van Adrichem J, Erkelens MR, Scheepers H, In't Veen H, Jean WM, Niels M, Chavannes H: Sustained effects of integrated COPD management on health status and exercise capacity in primary care patients. *Int J Chron Obstruct Pulm Dis* 2010;5:407–413.
- 21 Chavannes NH, Grijzen M, van den Akker M, Scheepers H, Nijdam M, Tiep B, Muris J: Integrated disease management improves one-year quality of life in primary care COPD patients: a controlled clinical trial. *Prim Care Respir J* 2009;18:171–176.