COPD exacerbations in the emergency department: Epidemiology and related costs. A retrospective cohort multicentre study from the Italian Society of Emergency Medicine (SIMEU)

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A R T I C L E I N F O

A B S T R A C T

Acute exacerbations of chronic obstructive pulmonary disease (AECOPDs) frequently cause patients with COPD to access the emergency department and have a negative impact on the course of the disease. The objectives of our study were: 1) describing the socio-demographic and clinical characteristics, and the clinical management, of patients with AECOPD, when they present to the emergency department; and 2) estimating the costs related to the management of these patients. We conducted a retrospective cohort study in Italy, collecting data on 4396 patients, from 34 centres. Patients had a mean (SD) age of 76,6 (10.6) years, and 61.2% of them where males. > 70% of the patients had a moderate to very high comorbidity burden, and heart failure was present in 26.4% of the cohort. The 64.6% of patients were admitted to hospital wards, with a mean (SD) length of stay of 10.8 (9.8) days. The estimated cost per patient was 2617 €. Conclusions: Patients attending the ED for an AECOPD are old and present important comorbidities. The rate of admission is high, and costs are remarkable.

1. Introduction

1.1. Background

Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) are one of the most frequent reasons for patients with COPD to access the emergency department (ED) and be hospitalized. Moreover, AECOPD may require invasive mechanical ventilation (IMV), and are associated with increased in-hospital mortality [1]. In Italy, COPD has a prevalence of between 2 and 11% [2,3]. The care of these patients requires a remarkable amount of health resources, largely because of acute exacerbations [4]. Despite the burden of the disease, little is known about the demographic and clinical characteristics of patients with AECOPD when thy present to the ED, and about how they are managed in the first hours. Understanding the characteristic of patients attending the ED for an AECOPD and how they are managed in that setting can help improving the quality of their care.

1.2. Objectives

The present study aimed to describe the socio-demographic characteristics of patients presenting to the ED for an AECOPD, and their clinical management in the ED. Moreover, an estimation of the costs of resources utilization in relation to ED patients with AECOPD has been performed.

2. Material and methods

2.1. Study design

This was a retrospective cohort, multicentre study. The present manuscript has been prepared according to the RECORD [5] statement.

2.2. Study population and data collection

Patients accessing the ED for an AECOPD were eligible to the study. People aged < 40 years were excluded from the study, to omit those likely to have asthma rather than COPD [6]. Patients were recruited in 34 teaching and non-teaching hospitals, in different areas of Italy, from January the 1st to December the 31th, 2014. Fig. 1 shows the geographical distribution of the participating centres. The ED databases were used for the selection of patients and for data extraction.

Patients with an either primary or secondary ED discharge diagnosis of "AECOPD" (code 491.21), according to the International Classification of Diseases, 9th Revision, were identified. Moreover, the term "BPCO" (COPD in Italian) was searched in the textual diagnosis (if a free space for written diagnosis was provided by the ED management software of the participating centres). Since this was a broad search strategy, two authors (FG and GV) performed a first selection of retrieved cases to exclude those cases for which the primary diagnosis was unrelated to AECOPD (e.g. atrial fibrillation in patient with COPD). This selection process was performed independently by the two authors for the first 1503 cases (data from the first 5 centres). Disagreements were solved via discussion, in order to increase accuracy and consistency between reviewers for case selection in the remaining retrieved cases, which were screened only by one author. To further enhance specificity, an additional selection of retrieved cases was performed, after a training, by centre-level study contributors. This selection was based on the clinical chart data, to ensure that the ED access was actually due to an AECOPD.

Data collected for epidemiological purposes were as follows: patient

Fig. 1. Geographical distribution of the participating centres.

demographic characteristics, home treatment for COPD, comorbidities, use of ambulance for ED access, ED treatment for COPD, ED disposition (i.e. discharge, short term observation, or admission), the occurrence of in-hospital death, the need for invasive mechanical ventilation, and, in case of admission, duration of the hospital stay and ward of admittance. Information regarding sex, blood pressure at presentation, the presence of pneumonia or respiratory failure, and the variables included in the Charlson Comorbidity Index (CCI) [7] was recorded. Respiratory failure was considered present if explicitly reported among the diagnosis or in case of SpO2 < 90%.

2.2.1. Costs

For the estimation of resources consumption, in addition to the use of ambulance for ED access and the ED disposition, the diagnosis related group (DRG) and relative costs have been recorded.

2.3. Ethical considerations

The Research Ethics Committee approved the study, and the research was conducted according to the principles of the Declaration of Helsinki. In consideration of the retrospective nature of the study and

the fact that data were anonymized before being entered the general database, no informed consent was required.

2.4. Analysis

To assess agreement between authors for cases selection, we used the k statistic, which measures agreement beyond chance [8]. Quantitative variables were reported as mean and standard deviation, qualitative variables as frequencies.

Costs were estimated as follow: €118 in case of ambulance call, plus €242 per ED visit followed by discharge [9], or the mean of recorded costs according to the DRG in case of admittance.

3. Results

Data on 4396 patients presenting to the ED for an AECOPD from January the 1st, 2014 to December the 31th, 2014 were obtained from 34 centres. Agreement for patient selection among authors was substantial (k = 0.78). Table 1 shows the baseline characteristic and Table 2 the ED management and outcome of included patients. The mean (SD) age was 76.6 (10.6) years, and 38.8% were female. The comorbidity burden according to the CCI was low (CCI 0) in 1242 (28.3%) cases, moderate (CCI 1–2) in 1890 (43.0%), high (CCI 3–4) in 833 (19.0%), and very high in 431 (9.8%). The most common comorbidities were heart failure (26.4%) and coronary artery disease (22.6%). A diagnosis of respiratory failure was associated to AECOPD in 1241 (30.4%) patients, and a diagnosis of pneumonia in 448 patients (11.0%). Treatments mainly adopted in EDs were oxygen therapy (59.9%), bronchodilators (60.8%), inhaled steroids (57.8%), steroids (71.0%), and antibiotics (22.8%). Systemic steroids where used in 2302 (53.1%) patients, and inhaled steroids in 2467 (56.9%), with an overlap between systemic and inhaled steroids in 1700 (39.2%) patients. Following the ED visit, 1192 patients (27.1%) were discharged; 115 (2.6%) received a short-term observation; 2839 (64.6%) were admitted to hospital wards. The main wards of admission were Internal Medicine/Geriatrics (64.6%), and Pulmonology (18.1%), while forty-two patients (1.7%) were admitted to Critical Care. In-hospital death occurred in 159 patients (3.6%), IMV was deemed necessary in 83 (2.0%) cases. The mean (SD) length of stay for an admitted patient was 10.8 (9.8) days. AECOPD accounted for 0.5% of overall ED access, and 36.6% of cases occurred in the first 3 months of the year.

The mean (SD) reported cost for an admitted patient was €3820 (3437). Given that 1) 54.7% of patients reached the ED by ambulance (estimated cost €118), 2) 64.6% of patients were admitted to the hospital, and 3) the rest of them received an ED visit (estimated cost €242), we calculated an average cost of 2617 € per patient attending the ED for an AECOPD.

4. Discussion

In our study, patients attending the ED for an AECOPD were on average older than 75, mainly males, and they often presented comorbidities, commonly heart failure. The therapy administered in the ED diverged from guidelines on the use of bronchodilators and steroids [10] in one third of cases, with bronchodilators being used in 60.8% of patients, steroids in 71.0%, and with an overlap of inhaled and systemic steroids in 39.2%. The rate of admissions was high, and costs were remarkable.

To our knowledge, the characteristics of patients with AECOPD have never been described using data directly from the ED in Italy. The large number of contributing centres (34) corroborates our confidence in the study results. Despite these strengths, our study had some limitations. First, the retrospective nature of the study and the fact that we relied on administrative data, could have disturbed the correct identification of patients with AECOPD. In an effort to address this problem, we combined two search strategies, one based on ICD-9 classification and one

based on descriptive diagnosis. Moreover, we carefully selected cases through a 2-step process. Also, the retrospective nature of the study could have affected the quality of some data, in particular those relating to medical history and medications [11]. Unfortunately, no data on the smoking habits and the results of arterial blood gas analysis were available. Furthermore, the in-hospital follow-up period could have been too short, especially for patients not admitted to the hospital (35.4%). For these patients, an adverse outcome was less probable, but still possible. Unfortunately, despite our efforts, we had no chance to retrieve reliable data on follow-up after hospital discharge.

Eleven percent of the included patients had a concomitant diagnosis of pneumonia. It is indeed true that some studies excluded pneumonia when defining a COPD exacerbation [12], and the GOLD 2017 guidelines adhere to this definition: "As comorbidities are common in COPD patients, exacerbations must be differentiated clinically from other events such as […] pneumonia" [13]. However, at the time we planned the study and started the data collection, this was still matter of discussion [14], and in GOLD 2014 it is stated that: "Other conditions (pneumonia […]) may mimic or aggravate an exacerbation of COPD." [10] For this reason, and to be consistent with our inclusion criteria and the everyday clinical practice, we decided not to exclude these patients.

Our estimate of the costs related to the emergency care of patients with AECOPD is limited by the fact that the distribution of the reported costs for admitted patients is wide, and by the use of a general cost of the ED visit of discharged patients, not specific to AECOPD. It is reasonable to assert that the ED management of a patient with an AECOPD requires more resources than the average of ED patients, in terms of diagnostic efforts, monitoring, and therapeutic measures. Still, we think

Table 1
Baseline characteristics of patients with exacerbation of chronic obstructive pulmonary disease seen in the emergency department.

Characteristic	Overall (n = 4396, 34 centres) N. (%)/mean(SD)
Demographics	
Female	1706 (38.8)
Age, years	76.6 (10.6)
Medical history	
Heart failure	1162 (26.4)
Coronary artery disease	995 (22.6)
Peripheral vascular disease	502 (11.4)
Cerebrovascular disease	634 (14.4)
Diabetes without end organ damage	774 (17.6)
Diabetes with end organ damage	228 (5.2)
Moderate or severe renal disease	531 (12.1)
Connective tissue disease	97 (2.2)
Dementia	490 (11.2)
Peptic ulcer disease	245 (5.6)
Mild liver disease	177 (4.0)
Moderate or severe liver disease	25 (0.6)
Cancer	578 (13.2)
Metastatic cancer	88 (2.0)
CMI	
Class 1 (CMI 0)	1242 (28.3)
Class 2 (CMI 1–2)	1890 (43.0)
Class 3 (CMI 3–4)	833 (19.0)
Class 4 (CMI ≥ 5)	431 (9.8)
Current respiratory medications	
Oxygen therapy	1048 (24.8)
Inhaled beta agonists	2080 (49.9)
Inhaled anticholinergic	1454 (34.9)
Inhaled steroid	1844 (44.2)
Systemic steroids	718 (17.2)
Theophylline	312 (7.5)
Antibiotics	662 (15.8)
Non invasive ventilation	115 (2.7)
CPAP	86 (2.0)

SD: standard deviation, CMI: Charlson comorbidity index, CPAP: Continuous Positive Airway Pressure.

Table 2

ED management and outcome of patients with exacerbation of chronic obstructive pulmonary disease.

Characteristic	Overall (n = 4396, 34 centres) N. (%)/mean(SD)
Arrival status	
Ambulance call	2395 (54.7)
Tachycardia (> 109 bpm)	771 (18.5)
Tachypnea (> 20)	1779 (51.2)
Systolic blood pressure < 90 mm Hg	58 (1.4)
Sat02 < 90%	1116 (26.2)
ED therapy	
Oxygen therapy	2570 (59.9)
Bronchodilators	2636 (60.8)
Inhaled beta agonists	2581 (59.6)
Inhaled anticholinergic	1877 (43.3)
Steroids	3079 (71.0)
Inhaled steroids	2467 (56.9)
Systemic steroids	2302 (53.1)
Both inhaled and systemic	1700 (39.2)
Systemic beta agonists	19 (0.4)
Theophylline	186 (4.3)
Antibiotics	991 (22.8)
Non invasive ventilation	274 (6.3)
CPAP	102 (2.3)
Associated conditions	
Respiratory failure	1241 (30.4)
Pneumonia	448 (11.0)
Altered mental status	316 (7.9)
ED disposition	
Discharged	1192 (27.1)
Short-term observation	115 (2.6)
Admitted to hospital	2839 (64.6)
Others	249 (5.7)
Department of admittance	
Critical care	42 (1.7)
Internal Medicine & Geriatrics	1944 (78.6)
Pulmonology	448 (18.1)
Others	41 (1.5)
Outcomes	220 (5.0)
Invasive mechanical ventilation	83 (2.0)
In hospital death	159 (3.6)

SD: standard deviation, ED: Emergency Department, CPAP: Continuous Positive Airway Pressure.

that our approximation can be useful to have an idea of the costs of the resources used in this setting.

The low adherence to treatment guidelines, in terms of bronchodilators and steroids, confirms the results of a previous study conducted in 29 EDs in North America [15]. In particular, in this study, a median of 1 short-acting beta-agonist treatment was received across the cohort, only 1 patient was treated with anticholinergic aerosol, and only 62% of patients received systemic corticosteroids. Notably, even if this was a study on elderly patients, and age > 55 years was an inclusion criteria, the mean age of the population was 71 years, well below the mean of 76.6 found in our population. This difference might be due to the fact that the study described was conducted in a different setting and was prospective. It is known that retrospective studies, despite limitations like the lower quality of data and a higher proportion of missing data, can better represent the usual clinical practice [16]. The time lag in translational research is about 17 years [17], but this does not justify the low adherence to guidelines for the management of a disease which remained unchanged in > 25 years [18]. A previous survey among Italian outpatients with respiratory diseases (15% of which had COPD) revealed the poor patients' disease awareness and adherence to therapy, associated with a lack of diagnostic and follow up efficacy (< 2% of patients had performed a blood gas analysis in the previous year) [19]. This, together with the results of our study, reflects the need for a "call for alignment" with the current recommendations and guidelines. The present study might represent the occasion to work on the

implementation of available evidences in the management of AECOPD. Finally, we believe that our study succeeded in representing the complex picture composed by the so called real life patients and their real life physicians, and the difficulties faced daily in our EDs.

5. Conclusions

AECOPDs accounts for 0.5% of ED visits and are economically onerous. Patients with AECOPD attending the EDs are old, frequently affected by several comorbidities, and are burdened by a high prevalence of an adverse outcome.

References

[1] Soler-Cataluna JJ, Martinez-Garcia MA, Roman Sanchez P, Salcedo E, Navarro M, Ochando R. Severe acute exacerbations and mortality in patients with chronic obstructive pulmonary disease. Thorax 2005;60(11):925–31. http://dx.doi.org/10.1136/thx.2005.040527.

[2] Cazzola M, Puxeddu E, Bettoncelli G, Novelli L, Segreti A, Cricelli C, et al. The prevalence of asthma and COPD in Italy: a practice-based study. Respir Med 2011;105(3):386–91. http://dx.doi.org/10.1016/j.rmed.2010.09.022.

[3] Rycroft CE, Heyes A, Lanza L, Becker K. Epidemiology of chronic obstructive pulmonary disease: a literature review. Int J Chron Obstruct Pulmon Dis 2012;7:457–94. http://dx.doi.org/10.2147/COPD.S32330.

[4] Dal Negro R, Rossi A, Cerveri I. The burden of COPD in Italy: results from the confronting COPD survey. Respir. Med. 2003;97(Suppl. C):S43–50.

[5] Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, et al. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. PLoS Med 2015;12(10):e1001885http://dx.doi.org/10.1371/journal.pmed.1001885.

[6] Shorr AF, Sun X, Johannes RS, Derby KG, Tabak YP. Predicting the need for mechanical ventilation in acute exacerbations of chronic obstructive pulmonary disease: comparing the CURB-65 and BAP-65 scores. J Crit Care 2012;27(6):564–70. http://dx.doi.org/10.1016/j.jcrc.2012.02.015.

[7] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40(5):373–83.

[8] McGinn T, Wyer PC, Newman TB, Keitz S, Leipzig R, For GG, et al. Tips for learners of evidence-based medicine: 3. Measures of observer variability (kappa statistic). CMAJ 2004;171(11):1369–73. http://dx.doi.org/10.1503/cmaj.1031981.

[9] Proposta metodologica per la valutazione dei costi dell'emergenza. Ministero della Salute. 2007 (Accessed 09/14/2017 2017).

[10] Decramer M. Global Strategy for the Diagnosis,Management, and Prevention of Chronic Obstructive Lung Disease (GOLD) 2014. http://goldcopd.org/; 2014 (Accessed 01/20/2015).

[11] Kern LM, Malhotra S, Barron Y, Quaresimo J, Dhopeshwarkar R, Pichardo M, et al. Accuracy of electronically reported "meaningful use" clinical quality measures: a cross-sectional study. Ann Intern Med 2013;158(2):77–83. http://dx.doi.org/10.7326/0003-4819-158-2-201301150-00001.

[12] Sethi S, Evans N, Grant BJ, Murphy TF. New strains of bacteria and exacerbations of chronic obstructive pulmonary disease. N Engl J Med 2002;347(7):465–71. http://dx.doi.org/10.1056/NEJMoa012561.

[13] From the Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017. (2017). http://goldcopd.org/gold-2017-global-strategy-diagnosis-management-prevention-copd/.

[14] Evensen AE. Management of COPD exacerbations. Am Fam Physician 2010;81(5):607–13.

[15] Cydulka RK, Rowe BH, Clark S, Emerman CL, Camargo Jr. CA, Investigators M. Emergency department management of acute exacerbations of chronic obstructive pulmonary disease in the elderly: the Multicenter Airway Research Collaboration. J Am Geriatr Soc 2003;51(7):908–16.

[16] Sorensen HT, Sabroe S, Olsen J. A framework for evaluation of secondary data

sources for epidemiological research. Int J Epidemiol 1996;25(2):435–42.

[17] Morris ZS, Wooding S, Grant J. The answer is 17 years, what is the question: understanding time lags in translational research. J R Soc Med 2011;104(12):510–20. http://dx.doi.org/10.1258/jrsm.2011.110180.

[18] Aaron SD. Management and prevention of exacerbations of COPD. BMJ 2014;349:g5237http://dx.doi.org/10.1136/bmj.g5237.

[19] Santus P, Picciolo S, Proietto A, Falcone F, Mangiacavallo A, Pellegrino G, et al. Doctor-patient relationship: a resource to improve respiratory diseases management. Eur J Intern Med 2012;23(5):442–6. http://dx.doi.org/10.1016/j.ejim.2012.04.004.