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Predictors of outcomes in COPD exacerbation cases presenting to the emergency department

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ABSTRACT: The aim of the present prospective multicentric study was to develop a simple rule for the prediction of poor outcome in patients presenting to emergency departments with initially non-life threatening-chronic obstructive pulmonary disease (COPD) exacerbations in a real-life setting.

All patients with an acute exacerbation of COPD visiting the emergency departments of 103 hospitals during a 3-month period were included, except those who immediately required intensive care unit admission and/or ventilatory support. The data collected included patient characteristics, in-hospital outcomes (mortality and length of stay) and mode of discharge (unsupported or need for post-hospital assistance).

The in-hospital mortality rate was 7.4% (59 out of 794). Independent prognostic factors were age, number of clinical signs of severity (among cyanosis, impaired neurological status, lower limb oedema, asterixis and use of accessory inspiratory or expiratory muscles) and dyspnoea grade in the stable state. The need for post-hospital support was also predicted by female sex. In order to construct and validate a prediction score for mortality based on these items, patients were randomly allocated to a derivation and a validation cohort. The prediction score showed good discrimination, with a c-statistic of 0.79 in the derivation cohort and 0.83 in the validation cohort.

Thus simple purely clinical factors can reliably predict the risk of death and requirement for post-hospital support in an initially non-life threatening-acute exacerbation of chronic obstructive pulmonary disease. Their use needs to be prospectively validated.

KEYWORDS: Chronic obstructive pulmonary disease, emergency department, exacerbation, outcome, prognosis

Chronic obstructive pulmonary disease (COPD) is a major healthcare issue; its prevalence in the adult population ranges 4–10%, and World Health Organization projections predict that COPD-related mortality and disability will continue to increase worldwide until at least ~2030 [1]. Exacerbations are major events in the history of the disease, especially when hospitalisation is required. First, in-hospital mortality is high, although it varies markedly between studies (2.5–30%), depending upon the mode of recruitment and setting (medical ward *versus* intensive care unit (ICU)) [2–6]. Secondly, exacerbations markedly impair quality of life [7], and their repetition may affect the natural history of the disease, as assessed by the rate of lung function decline [8, 9] and mortality [10]. Finally, they have a societal impact; although only 10–15% of COPD patients are hospitalised, they are responsible for more than half of COPD-related healthcare expenses, and, among respiratory diseases, COPD is the leading cause of direct medical costs [11–15]. Exacerbation-related costs increase in the growing population of elderly subjects, who require post-hospital support more frequently [16].

Several studies have identified factors independently associated with in-hospital mortality due to COPD exacerbations, including nonrespiratory (especially cardiac) organ system dysfunction, duration of hospital stay, older age, comorbid conditions and nutritional status, arterial oxygen (P_{a,O_2}) and carbon dioxide tension at entry, and requirement for ICU admission [4, 5, 17–22]. However, independent prognostic factors are quite variable between studies, probably related

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to differences in patient populations, settings, duration of follow-up, variables collected and statistical methods. In addition, these studies did not specifically target patients visiting emergency departments (EDs), and, therefore, were not restricted to factors readily available in that environment. Thus it remains difficult to provide clinicians working in the emergency context with simple and reliable criteria for the identification of patients at risk of in-hospital death and help to decide whether or not the patient should be hospitalised and in which setting (medical ward or ICU).

Therefore, a real-life study was conducted in order to assess determinants of in-hospital outcomes in patients visiting EDs for COPD exacerbations. The outcomes considered were in-hospital mortality and requirement for post-hospital support (either convalescence or nursing home or domiciliary support). A prediction score was built using a randomly selected subgroup of the study participants (derivation cohort) and tested in the other half of the recruited sample (validation cohort).

MATERIALS AND METHODS

The study protocol and case report form have already been published [23], along with supplementary online data. All procedures were approved by the ethics committee of Versailles hospital (Versailles, France) and by the institutional review boards of the scientific societies involved (the Société de Pneumologie de Langue Française, SAMU de France and the Société Française de Médecine d'Urgence), and informed consent was obtained from all of the patients.

Study design

Following a feasibility study in three centres, the present prospective observational study was conducted in 113 centres representative of French hospitals. The centres were asked to include all consecutive patients visiting their EDs between November 2003 and February 2004 with a diagnosis of certain or probable exacerbation of COPD at entry. Included patients were followed until discharge from hospital.

Since this was meant to be a real-life study, there was no constraint or guideline regarding investigations, admission and discharge decisions or treatments. In each centre, an emergency physician and a respiratory physician were in charge of quality control.

Inclusion criteria

Patients were included if they presented with a probable or certain exacerbation of COPD, as defined by the appearance or increase of dyspnoea in a patient with known COPD or risk factors for COPD (age >40 yrs and current or past cumulative tobacco consumption of >10 pack-yrs). Patients meeting these criteria were not included when the investigator judged that the predominant diagnosis was or was likely to be pulmonary embolism, congestive heart failure, pneumothorax or pleurisy, or when the predominant underlying respiratory disease was asthma, bronchiectasis, heart failure, thromboembolic disease or restrictive respiratory insufficiency. All of these exclusion criteria were left to the clinician's discretion in order to ensure that the real-life nature of the study was respected. Patients requiring immediate ICU monitoring and/or noninvasive or invasive ventilation, as judged by the ED physician, were not included.

Data collected

The data collected were limited to observations and results that are readily available in all EDs, and addressed the following issues.

Baseline status

The data collected related to sociodemographic characteristics, occupation, smoking history, known diagnosis of COPD, chronic bronchitis or emphysema, age at first respiratory symptoms, usual severity of dyspnoea using a modified Medical Research Council scale (0: dyspnoea during intensive exercise only; 1: dyspnoea when climbing two or more flights of stairs; 2: dyspnoea when walking uphill or quickly on level ground; 3: dyspnoea when walking on level ground at the same pace as persons of the same age; 4: dyspnoea when walking at their own pace on level ground; 5: dyspnoea when eating, dressing or preventing the patient leaving home) [24], reported number of emergency visits and hospitalisations during the past 6 months, usual follow-up (general practitioner and/or respiratory physician) and maintenance treatments.

Exacerbation management in the ED

Data were collected regarding the duration of the exacerbation, treatments and medical visits before arrival in the ED, origin of referral, dyspnoea grade at entry, clinical signs of severity, auscultatory findings, arterial blood gas variables, diagnostic procedures and treatments, and length of stay in the ED.

Exacerbation management following discharge from the ED

The data collected related to hospitalisation and its setting(s) (general medical ward, respiratory medicine department and ICU) and duration, diagnostic procedures and treatments.

Discharge from hospital

Data were collected regarding vital status, final diagnosis (confirmed exacerbation of COPD or alternative diagnosis), certain or probable aetiology of the exacerbation, mode of discharge (to home with or without support or to convalescence or nursing home), treatment and planned medical appointments. The diagnosis of COPD exacerbation was considered as confirmed (or rejected) after review by the local coordinating respiratory physician.

Statistical analysis

Data are presented as mean ± SD or percentage. The in-hospital outcomes of interest were death and requirement for post-hospital support (either convalescence, nursing home or domiciliary support). A two-step analytical plan was applied.

The first step was the exploratory assessment of predictors of death and the need for post-hospital support in the whole population in order to ensure maximal statistical power. Univariate analyses (Chi-squared test for categorical variables and an unpaired t-test or ANOVA for continuous variables) were first performed in order to determine which variables were associated with these outcomes. Then, initial symptoms and signs associated with an increased risk of in-hospital death on univariate analysis were aggregated in a clinical severity index, which was integrated into the subsequent analysis.

Finally, multivariate analyses were performed; a backward stepwise procedure using a logistic regression model was applied, including the variables that were significant at a p-value of <0.20 in the univariate analyses. Variables were eliminated one at a time from the model based on likelihood ratio tests. Variables were eligible for inclusion into the final model if they were significantly associated with in-hospital outcomes, with a p-value of <0.05.

The second step aimed to confirm the performance of the proposed group of items as predictors of risk of death. The population sample was randomly split into two groups, a derivation cohort (n=353) and a validation cohort (n=334). In the derivation cohort, a backward stepwise logistic regression procedure was performed as described previously, and used to develop a point-based risk scoring system; the number of points assigned to each risk factor was obtained by dividing each β coefficient by the smallest β coefficient significantly different from 0 and rounding to the nearest integer. A risk score was assigned to each participant in both the derivation and the validation cohorts by summing the number of points corresponding to each risk factor. Model discrimination was assessed using the c-statistic, which is analogous to the area under the receiver operating characteristic curve [25]. In both the derivation and the validation cohorts, subjects were divided into three groups depending upon the tertile of the score, and mortality rates were compared between groups.

TABLE 1 Characteristics of patients with available data

	Patients n	Data
Age yrs	780	72.5±11.8
Male sex	784	70.0
Pre-hospital care	794	21.5
Self-referral	781	20.5
Current/ex-smokers	734	30.8/ 49.9
Cumulative tobacco smoking pack-yrs	734	46.4±30.0
Occupational exposure to gas, fumes, dusts	721	28.3
Known COPD#	721	84.6
Age at beginning of exertional dyspnoea yrs	652	53.3±17.8
Baseline dyspnoea grade	701	
0–1		22.5
2–3		46.2
4–5		31.3
Previous lung function test	748	69.9
Usual follow-up	763	
Respiratory physician		40.8
General practitioner		34.3
Both		16.5
None		8.4
Usual maintenance treatment	767	
β_2-agonists		69.6
Anticholinergic agents		37.5
Inhaled corticosteroids		43.8
Oral corticosteroids		13.8
Long-term oxygen therapy		23.2

Data are presented as mean±SD or percentage. Total number of recruited patients, n=794. COPD: chronic obstructive pulmonary disease. #: including chronic bronchitis and emphysema.

RESULTS

Among the 113 centres that agreed to participate, 103 (91%) were active and recruited 794 patients.

Patient characteristics

Table 1 describes the demographic characteristics of the population and gives details of risk factors and medical history. The proportion of retired patients was 78.6%. In addition, 9.0% did not work any more due to disability. Among the whole population, 27.1% received home support and 8.4% lived in an institution. At least one emergency visit during the previous 6 months was reported by 68.2% and at least one hospitalisation by 37.6%. Initial clinical presentation, severity index, diagnostic procedures and treatments in the ED

TABLE 2 Initial presentation, diagnostic procedures and treatments

	Patients n	Data
Increased/recent symptoms	791	
Dyspnoea		99.2
Cough		78.1
Expectoration		59.7
Sputum purulence		42.6
mMRC dyspnoea grade at entry	741	4.2±1.1
0–1		2.8
2–3		19.6
4–5		77.6
Signs of severity	793	
Cyanosis		29.0
Neurological impairment		11.0
Lower limb oedema		23.3
Asterixis		7.8
Use of accessory inspiratory muscles		50.9
Expiratory use of abdominal muscles		37.8
Signs from clinical severity index	793	
0		27.6
1–2		47.7
⩾3		24.7
Cardiac frequency beats·min^{-1}	785	98.5±19.8
Respiratory frequency breaths·min^{-1}	706	26.9±7.2
Arterial blood pressure mmHg	752	144±28/78±16
Peak expiratory flow rate	767	
Measurement		16.9
Result L·min^{-1}		185.1±84.9
Treatments	789	
β_2-agonists		89.2
Anticholinergic agents		80.1
Inhaled corticosteroids		6.7
Systemic corticosteroids		45.5
Oxygen therapy		82.8
Length of stay in the ED h	667	11.8±14.1

Data are presented as mean±SD or percentage. mMRC: modified UK Medical Research Council; ED: emergency department. 1 mmHg=0.133 kPa.

are detailed in table 2. Wheezing was recorded in 69.3% and focal crackles in 28.9%. The vast majority (72.4%) of patients presented with at least one severity criterion.

Only 84 (10.5%) patients were discharged home from the ED, whereas 533 (67.1%) were hospitalised in a medical ward, 95 (11.9%) in an ICU and 62 (7.8%) in another hospital.

Compared to those hospitalised in a medical ward or an ICU, patients discharged home from the ED were younger and less often referred by a doctor; in addition, they showed fewer signs of severity and lower cardiac and respiratory frequencies (data not shown).

At discharge from hospital, the diagnosis of COPD exacerbation was considered as confirmed in 723 (91.6%) patients. Alternative diagnoses were another respiratory disease in 37 patients, a cardiovascular disease in 19 and another illness in six. When the final diagnosis was a COPD exacerbation, the two main reported aetiologies were bronchial infection in 68.1% and pneumonia in 14.5%. In 4.7% of cases, investigators reported that no aetiology was found.

Factors associated with in-hospital death, need for post-hospital support and length of stay

The in-hospital mortality rate was 7.4% (59 deaths). At the end of hospital stay, discharge to home without any particular support was possible in 472 (59.5%) patients, whereas 214 (26.9%) required home support or were transferred to convalescence or nursing homes. Since it was not planned to follow patients transferred to other hospitals, 49 (6.2%) patients were excluded from the analysis. Table 3 shows factors associated with death and need for post-hospital support (at home or in convalescence or nursing homes) on univariate analysis, and table 4 presents the results of multivariate logistic regression analysis when all clinical signs of severity (cyanosis, impaired neurological status, lower limb oedema, asterixis, use of inspiratory accessory muscles and expiratory use of abdominal muscles) were individually integrated into the model. Cardiac and respiratory frequencies did not differ between patients who died and survivors (98.3±23.9 *versus* 98.5±19.5 beats·min^{-1} and 28.2±8.2 *versus* 26.7±7.1 breaths·min^{-1}, respectively). As mentioned in the Statistical analysis section, a three-grade clinical severity index (no severity criteria, one or two severity criteria, and at least thee severity criteria) was constructed on the basis of the number of clinical signs of severity at entry. Using this score, independent prognostic factors on multivariate analysis were age, clinical severity index at entry and baseline dyspnoea grade (table 5). Determinants of the need for post-hospital support on multivariate analysis were sex and risk factors for death (tables 4 and 5).

The need for post-hospital support increased length of stay on univariate analysis (17.3±13.9 *versus* 10.5±7.1 days; $p<0.0001$), but this effect interacted with the clinical severity index, which was more powerfully associated with length of stay on multivariate analysis (data not shown).

Derivation and validation of the prediction score

In the derivation cohort, the variables independently associated with risk of death were the same as in the whole population (age, clinical severity index at entry and baseline dyspnoea grade; table 5). The points assigned to each of these three predictors using β coefficients were as follows: 1) 0: age <70 yrs; 1: age ⩾70 yrs; 2) 0: no severity signs; 2: 1–2 signs; 3: ⩾3 signs; and 3) 0: baseline dyspnoea grades 0–1; 1: grades 2–3; 2: grades 4–5.

TABLE 3 Factors associated with death and need for post-hospital support at discharge on univariate analysis

	Death		Supported discharge	
	Present	Absent	Present	Absent
Age yrs	78.6±8.1	72.0±12.0*	78.4±9.6	68.9±11.9*
Self-referral	5.1	21.8*	15.8	23.9*
Previous home support/institutionalisation	56.9	33.8*	60.4	21.0*
Body mass index kg·m^{-2}	24.1±5.3	25.5±5.8	24.8±6.0	25.8±5.7
Dyspnoea grade	4.6±0.6	4.1±1.1*	4.4±1.0	4.0±1.2*
Cyanosis	50.9	27.3*	37.1	23.6*
Neurological impairment	37.3	8.9*	16.9	5.3*
Lower limb oedema	33.9	22.5*	27.7	20.0*
Asterixis	17.0	7.1*	7.0	7.0
Use of inspiratory accessory muscles	72.9	49.2*	60.6	42.3*
Expiratory use of abdominal muscles	52.5	36.7*	44.6	32.9*
Clinical severity index	1.5±0.6	0.9±0.7*	1.1±0.7	0.8±0.7*
Respiratory frequency breaths·min^{-1}	28.2±8.2	26.7±7.1	27.6±7.2	26.1±7.0*
Cardiac frequency beats·min^{-1}	98.3±23.9	98.5±19.5	98.2±20.0	98.3±19.2
Hospitalisation during past 6 months	53.2	36.6*	44.9	33.4*
Maintenance oral corticosteroids	22.2	13.2	14.8	12.1
Long-term oxygen therapy	50.0	21.2*	29.1	17.4*

Data are presented as mean±SD or percentage. *: $p<0.05$ *versus* death/supported discharge.

TABLE 4 Odds ratio for death and need for post-hospital support at discharge on multivariate logistic regression analysis[#]

	Risk of death	Post-hospital support need
Females *versus* males		2.2 (1.4–3.4)
Age ⩾70 yrs	4.5 (1.6–12.1)	3.4 (2.1–5.5)
Clinical signs of severity at entry		
Cyanosis	1.5 (0.7–3.0)	1.6 (1.0–2.6)
Neurological impairment	5.1 (2.4–10.8)	3.3 (1.6–6.7)
Lower limb oedema	1.0 (0.4–2.0)	1.0 (0.5–1.5)
Asterixis	1.7 (0.6–4.3)	0.7 (0.3–1.7)
Use of inspiratory accessory muscles	2.6 (1.1–6.2)	1.6 (1.0–2.7)
Expiratory use of abdominal muscles	0.9 (0.4–1.9)	1.2 (0.7–2.0)
Baseline dyspnoea grade		
0–1	1.0	1.0
2–3	3.6 (0.7–16.5)	1.3 (0.7–2.2)
4–5	6.5 (1.4–29.3)	2.0 (1.1–3.6)

Data are presented as odds ratio (95% confidence interval). [#]: when all clinical signs of severity are individually integrated into the model.

Table 6 shows the risk of death in the derivation and validation cohorts dependent upon this score. The prediction characteristics are depicted using the c-statistic and sensitivity and specificity.

Mortality strongly increased with increasing prediction score in both the derivation and the validation cohort. The prediction score showed good discrimination for mortality, with a c-statistic of 0.79 in the derivation cohort and 0.83 in the validation cohort.

DISCUSSION

The main result of the present real-life study is the identification of simple, immediately accessible and strong predictors of in-hospital death and the need for post-hospital support in COPD patients visiting the ED due to an exacerbation. In addition, the study permitted the derivation and validation of a prediction score based on these items. To the present authors' knowledge, this is the first prospective study to determine outcomes and prognostic factors in patients with COPD exacerbations presenting to the ED. These factors should help in determining: 1) where patients need to be oriented, and 2) for which patients post-hospital support should be prepared early in order to facilitate and hasten discharge; this last point is illustrated by the increased length of stay when post-hospital support was required.

TABLE 5 Independent prognostic factors for death and need for post-hospital support at discharge on multivariate logistic regression analysis[#]

	Risk of death	Post-hospital support need
Females *versus* males		2.3 (1.5–3.6)
Age ⩾70 yrs	3.7 (1.3–9.8)	3.4 (2.1–5.3)
Severity index signs at entry		
0	1.0	1.0
1–2	5.1 (1.1–22.7)	1.6 (0.9–2.6)
⩾3	13.1 (2.9–57.7)	2.9 (1.7–5.1)
Baseline dyspnoea grade		
0–1	1.0	1.0
2–3	3.3 (0.7–14.9)	1.3 (0.7–2.2)
4–5	5.5 (1.2–24.6)	2.1 (1.2–3.6)

Data are presented as odds ratio (95% confidence interval). For both clinical severity index and dyspnoea grade, a dose–effect relationship is observed. [#]: when clinical signs of severity are aggregated in a clinical severity index based on the number of signs present at entry.

Patient characteristics

Despite the recruitment through EDs, a relatively high proportion (41%) of the patients were followed by a respiratory physician, and 70% received treatment for COPD. Although 70% reported undergoing lung function testing or peak expiratory flow rate measurement during past years, only very few of them were able to provide the results of such measurements. In line with these figures, a high proportion (85%) of subjects reported knowing that they had COPD,

TABLE 6 In-hospital mortality in the derivation and validation cohorts by prediction score tertile

	Derivation	Validation
Subjects n	353	334
Tertile 1 (0–1 points)	1.7 (2)	0.0 (0)
Tertile 2 (2–3 points)	4.6 (5)	4.8 (5)
Tertile 3 (>4 points)	15.5 (19)	12.3 (14)
c-statistic	0.79	0.83
Sensitivity[#,¶]	19/26=0.73	14/19=0.74
Specificity[#,+]	223/327=0.68	215/315=0.68

Data are presented as % (n), unless otherwise stated. [#]: tertile 3 *versus* tertiles 1 plus 2; [¶]: sensitivity (true positive/true positive plus false negative); [+]: specificity (true negative/true negative plus false positive).

emphysema or chronic bronchitis. This is probably related to the mode of recruitment used in the present study; physicians were asked to include patients with increased dyspnoea (this criterion was indeed satisfied in almost all of the patients) and a diagnosis of certain or probable COPD exacerbation, with no other dominant respiratory disease or cause of acute respiratory failure (*e.g.* left heart failure or pulmonary embolism). Thus they probably tended to include mainly patients with known COPD, omitting most of the unknown proportion of patients in whom the disease is discovered when the first exacerbation occurs. This would also explain the relatively high level of baseline dyspnoea in most patients and their frequent recourse to healthcare resources in the months preceding the study.

Despite this, the results of lung function tests were known for only a few of the patients, which suggests the need for improving the education of both doctors and patients. Such information could be of interest for the evaluation of the prognosis of an exacerbation and in the decision as to whether and where admission should be considered, but, at present, lung function test results are too infrequently available to be included in a prediction rule, at least in the setting of French hospitals.

Similarly, peak expiratory flow rate was seldom measured, which makes it difficult to interpret its lack of predictive potential. Finally, the conditions of measurement of arterial blood gas levels (*i.e.* with or without supplemental oxygen) were too heterogeneous to permit any conclusion as to their prognostic value in the real-life ED setting.

Risk factors for in-hospital death

Although all guidelines list clinical and biological signs of severity that should lead to hospitalisation or admission to the ICU [26–28], only a few studies have addressed this important issue. These studies were reviewed in 2001 in an evidence-based process conducted jointly by the American College of Physicians and the American Society of Internal Medicine [29]. At that time, only 11 studies had been conducted to identify predictors of in-patient mortality, and eight had identified such factors in populations ranging 74–3,050 subjects, recruited with markedly variable inclusion criteria. Of these studies, only five performed multivariate analysis and four were performed in ICU patients alone. The internal validity scores were fairly good but external validity and degree of validation were poor. In the five largest studies with multivariate analysis (n=322–3,050), the independent predictors of in-hospital death were age, acute physiology score, body mass index, functional status before the exacerbation, P_{a,O_2}/inspiratory oxygen fraction ratio, need for mechanical ventilation, serum albumin and sodium levels, and cardiac comorbid conditions. None of these studies provides physicians with a simple prediction rule to aid in the decision as to where a given patient should be managed. In the present study, it was found that three simple clinical criteria were potent predictors of mortality, suggesting that they should be systematically assessed at entry in COPD exacerbations and used to decide where patients should be oriented. These criteria were age, number of clinical signs of severity at entry and baseline dyspnoea grade. Among individual clinical signs of severity, neurological impairment and use of inspiratory accessory muscles were the only factors independently associated with an increased risk of death; however, adding other signs of severity through the aggregated clinical severity index increased the predictive value of the model.

One strength of the present study is that, following identification of predictors of death in the whole study population, two subgroups were randomly constituted to construct a prediction score and assess its validity. As mentioned in the Results section, this score was very easy to calculate, and, when the derivation and validation populations were classified according to score tertile, marked differences in mortality were observed between the two subgroups. In addition, prediction characteristics depicted by the c-statistic, sensitivity and specificity were satisfactory, especially considering the simplicity of the score and particularly the lack of requirement for nonclinical data. Indeed, the c-statistic was higher than that reported by Celli *et al.* [30] for the BODE (body mass index, airflow obstruction, dyspnoea and exercise capacity index).

Whether or not such a prediction score might improve patient outcome remains to be determined in a prospective validation study.

Predictors of need for post-hospital support

Although the need for post-hospital support is clearly an increasingly important clinical and economic issue, the present authors are not aware of any previous studies aimed at identifying the corresponding clinical predictors.

In the present study, factors associated with an increased risk of death were also predictors of the need for post-hospital support, at home or in intermediate care facilities or institutions. This finding is not surprising; if they survive, the most severe patients show an increased level of dependence when they are discharged. Identification of these factors may be useful in helping to reduce length of stay, since patients who need post-hospital support as a consequence of increased severity stay longer, which probably relates to two different causes; first, the time taken to recover a health status compatible with discharge may be longer; and, secondly, hospitalisation may be prolonged by difficulties in organising adequate post-hospital support. Such difficulties are likely to become increasingly frequent, considering the increasing age of the population [16]. This will have not only clinical consequences through the increased hospital-related morbidity, quality-of-life impairment and mortality, but also economic consequences since hospital stays account for approximately half of all COPD-related healthcare expenses, with COPD representing the second leading respiratory cause of direct and indirect healthcare costs in the USA and 3.5% of all healthcare expenses in France [8, 11].

Interestingly, the need for post-hospital support was not independently related to any kind of pre-hospital support (home support or residence in a nursing home); the most likely explanation of this is that, in most cases, pre-hospital support was also determined by dyspnoea severity (data not shown).

Limitations of the present study

As mentioned previously, one main limitation was the lack of lung function and relevant arterial blood gas data, making it impossible to include them in the prediction rule. However, this has to be considered as corresponding to what occurs in

the real-life setting; thus it does not decrease the value of the identified prognostic factors.

Another limitation is the lack of post-hospital mortality data, which would be mandatory for: 1) validation of the prognostic factors found in the present study and their transformation into admission/discharge criteria; and 2) assessment of the validity of decisions of immediate discharge from the ED. In order to achieve these goals, a large ongoing prospective study includes detailed follow-up at 3 months and assessment of vital status at 3 yrs [31].

Recruitment bias also has to be considered. Indeed, the mean number of patients recruited per centre per month was quite small (approximately three), far lower than that expected during the winter period. As mentioned previously, recruitment was obviously limited to patients with a fairly certain diagnosis of COPD exacerbation at entry. In addition, most centres were active only during short periods of time (1–4 weeks), and local coordinators checked that cases obviously corresponding to inclusion criteria were not omitted, suggesting that the recruitment was not far from exhaustive during active inclusion periods. Limiting the recruitment period to one winter season ensured that, if some kind of seasonal bias might influence predictors of outcomes, it was homogenously distributed throughout the study period and centres. In addition, since such a bias exists, it corresponds to what happens in real life, and does not compromise the applicability of the results to the period when COPD exacerbations are the greatest cause of concern for clinicians and hospitals.

Finally, the present findings do not apply to COPD cases discovered at the occasion of their first exacerbation since the disease had already been diagnosed in most patients. They also do not apply to patients who require immediate ventilatory support and/or ICU admission when presenting to the ED; inclusion was indeed limited to patients who did not require immediate ventilatory support, as decided by the attending emergency physician. The purpose of this restriction was to limit the heterogeneity of the population and to avoid biasing the results by including a subgroup of patients with very severe exacerbation, which could have induced the identification of factors that might not be applicable to exacerbations of lesser severity.

Conclusions

The present study provides simple prognostic factors for use in patients with chronic obstructive pulmonary disease exacerbations presenting to the emergency department. The corresponding variables are exclusively clinical and very easy to measure at entry in the real-life context, and represent powerful predictors of the risk of both death and need for post-hospital support. Thus, following prospective validation, they may be useful for clinicians in helping them with: 1) admission and orientation decisions; 2) anticipation of the need for intermediate care facilities or home support; and 3) informing patients and relatives on exacerbation-related short-term risks.

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