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OUTCOMES OF COPD IN PATIENTS ADMITTED IN ICU BY COMMUNITY-ACQUIRED PNEUMONIA

General Medicine

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ABSTRACT

The mortality rate of chronic obstructive pulmonary disease (COPD) patients with community-acquired pneumonia (CAP) is reported to be low. However, studies carried out to date have included <20% of critically ill patients. **Aims And Objectives** - To calculate mortality and risk of mechanical ventilation than other immunocompetent patients hospitalised in the ICU with SCAP without COPD. **Material And Methods** - The current authors performed a secondary analysis of a prospective study evaluating 108 immuno-competent patients admitted to the intensive care unit (ICU) for severe CAP. **Results -** In total, 44 COPD patients were compared with 64 non-COPD patients. In COPD patients, ICU mortality (odds ratio (OR) 1.58; 95% confidence interval (CI) 1.01–1.43) and mechanical ventilation (OR 2.78; 95% CI 1.63–4.74) rates were higher than in non- COPD patients. The ICU mortality was 39% for COPD patients initially intubated and 50% for those who failed noninvasive ventilation. The proportion of patients who were males, aged ≥70 yrs, smokers and who had chronic heart disease or *Pseudomonas aeruginosa* were higher in COPD patients. Inappropriate empirical antibiotic therapy was associated with higher mortality (OR 3.8; 95% CI 1.19–12.6). ICU mortality in COPD patients with adequate therapy was associated with bilateral pneumonia (OR 2.32; 95% CI 1.18–4.53) and shock (OR 3.53; 95% CI 1.31–9.71). **Conclusion** - chronic obstructive pulmonary disease patients hospitalised with community-acquired pneumonia in the intensive care unit had higher mortality and need of mechanical ventilation when compared with patients without chronic obstructive pulmonary disease.

KEYWORDS

chronic obstructive disease, intubation, critical ill.

INTRODUCTION

A strong association between chronic obstructive pulmonary disease (COPD) and severe community-acquired pneumonia (SCAP), mainly caused by Streptococcus pneumoniae or Haemophilus influenzae, has been suggested [1, 2]. For COPD in particular, this elevated incidence appears to be explained by altered pulmonary defence mechanisms [3]. Fekety et al.[4]reported a higher incidence of pneumococcal pneumonia in COPD patients than in control patients.

COPD is one of the most frequent comorbidities in patients admitted to hospital for CAP and respiratory failure [5]. In a prospective study of SCAP the specific goal was to examine if the presence of COPD was a predictor for increased mortality in ICU patients hospitalised for pneumonia. A secondary objective was to assess how the use of non-invasive ventilation (NIV) influenced outcome.

MATERIAL & METHODS

Between May 1, 2023 to 30th September , 2023, 108 consecutive patients with CAP admitted to ICUs were enrolled. Institutional review board approval was obtained in accordance with local requirements. Patients were observed until death or ICU discharges.

The enrolled patients were consecutive cases aged ≥18 yrs, with conclusive evidence of pneumonia as primary diagnosis, confirmed by chest radiography. The study focused on patients in the ICU and excluded patients with respiratory infections other than pneumonia (for example, exacerbated COPD patients), and those on home oxygen therapy. Immuno-compromised patients (i.e. patients with HIV infection, neoplasia, those taking cytotoxic drugs or long-term oral steroid therapy, such as daily doses of >20 mg of prednisolone or the equivalent for >2 weeks) were excluded, as well as patients with asthma, interstitial lung diseases or aspiration pneumonia.

Patients with COPD criteria were enrolled in this sub-study. Appropriate therapy was defined as the use of at least one antibiotic to which all isolates were susceptible in vitro or (for Pneumocystis jiroveci or Legionella pneumophila) were expected to be susceptible. Pre-existing COPD was defined as a disease state characterised by the presence of airflow limitation due to chronic bronchitis or emphysema. The airflow obstruction may be accompanied by airway hyper-reactivity and may be partially reversible. Details of other definitions, including pneumonia or shock, among others, have been reported elsewhere . A patient was considered to be a smoker if they had smoked more than one packet per day within the past 10 yrs . Mechanical ventilation included invasive ventilation and NIV.A wide range of demographic, clinical and laboratory measures were recorded in each patient, as described previously. In the current study, particular emphasis was placed on the age of the patients, history of smoking, presence of other co-morbidities, and severity of illness measured by the acute physiological score (APS) of Acute Physiology And Chronic Health Evaluation (APACHE) II score.

Patients in whom standard treatment or NIV was not successful underwent endotracheal intubation. Variables considered as indicating unsuccessful standard treatment or NIV have been reported previously and included: failure to maintain an arterial oxygen tension/inspiratory oxygen fraction of >85; need to protect the airways; inability to spontaneously clear tracheal secretions; agitation requiring sedation; inability to tolerate the face mask; an increase in the arterial carbon dioxide accompanied by a pH <7.20; or septic shock. Treatment decisions for all study participants, including determination of the need for intubation or mechanical ventilation, were made by the primary clinical teams.

An organism was considered to be a “definitive” aetiological agent only if it was isolated from blood or pleural fluid, or if serological tests revealed a four-fold increase in antibody levels. Isolation of P. jiroveci or culture of L. pneumophila or Mycobacterium tuberculosis was considered the basis of a “definitive” diagnosis, in accordance with current guidelines. Microorganisms isolated from other cultures, including bronchoscopic samples, or with a positive urinary antigen test were considered as “probable”.

Discrete variables were expressed as counts (%) and continuous variables as mean±sd, unless stated otherwise. All statistical tests were two-sided. Differences in categorical variables were calculated using a two-sided likelihood ratio Chi-squared test for nondichotomous categorical variables and a two-sided Fisher's exact test for dichotomous variables. The Kaplan–Meier estimate-of-survival curve was used to determine the probability of survival for COPD and non-COPD patients at 28 days. Survival curves were compared using the log-rank test. Cox proportional hazards regression was used to adjust for severity of the impact of independent variables on ICU mortality. Factors associated with increased mortality by bivariate analysis ($p \leq 0.05$) were entered into the model. A p- value <0.05 was considered as significant. In addition to p-values, odds ratios (OR) and 95% confidence intervals (CI) were calculated.

RESULTS

In total, 108 patients were recruited for the original study . Of these, 1.9% were excluded due to aspiration pneumonia, 4.1% due to HIV and 13.0% due to other causes of immunocompromise. The remaining 87 immunocompetent patients were available for analysis. The 41.1% COPD patients, 45 of whom were smokers, were the subject of the

current study. The ICU mortality rate was significantly higher (30.1% versus 21.4%; p=0.05) in COPD than in non-COPD patients. A Kaplan–Meier survival curve (fig. 1) shows a significant difference (Log rank 3,69; p=0.05) in 28-day mortality for patients with and without COPD.

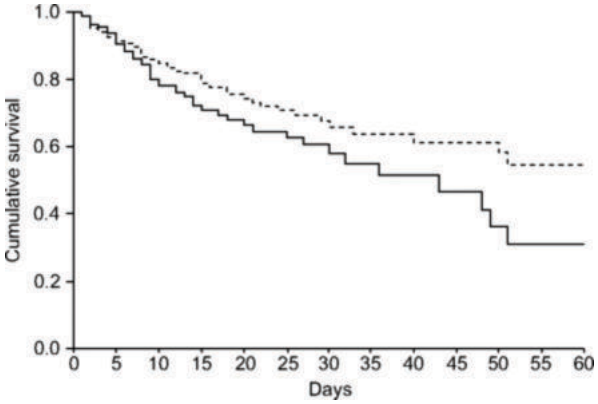

Figure 1(Kaplan–Meier survival curve)

15.7% out of the 18 COPD patients with microbiological diagnosis received inadequate empirical therapy and 57.1% died, compared with 4 deaths (25.7%; p<0.05) in COPD patients with adequate empirical regimen. The baseline characteristics of the remaining 33 COPD patients (with adequate empirical therapy and ventilated >24 h) according to the outcome. ICU mortality in COPD patients was associated with higher APS at day 1 (p=0.01), bilateral pneumonia (p<0.01), bacteraemia (p=0.04), shock (p=0.01), mechanical ventilation (p=0.001) and neurological illness (p=0.01). In this group, the Cox proportional regression analysis demonstrated that ICU mortality was independently associated with shock (OR 3.5) and bilateral pneumonia (OR 2.3). The same variables plus APS score (OR 1.06) and age (OR 1.03) were also identified for non-COPD episodes .

ICU mortality was not different for ventilated COPD and non-COPD patients (34.2% versus 28.9%; p=0.36). In COPD patients, 21 underwent endo-tracheal intubation within the first hours of ICU admission, 39% of whom died. There were 28.4% patients assigned to NIV. Of these patients, 13.6% required further intubation, and 50% of these died. The mortality rate in COPD patients with failure to NIV compared with COPD patients who underwent initial intubation had a relative risk of 1.56 (95% CI 0.6–3.8). The Kaplan–Meier survival plot at 28 days for initial intubation versus delayed intubation due to unsuccessful NIV is shown in figure 2 (log rank 1.58; p=0.23). All COPD patients with NIV who did not require intubation were discharged alive. COPD patients with successful NIV had a mean±sd ICU length of stay of 8.1±7.1 days compared with 17.8±14.0 days (p<0.05) for COPD intubated patients who survived.

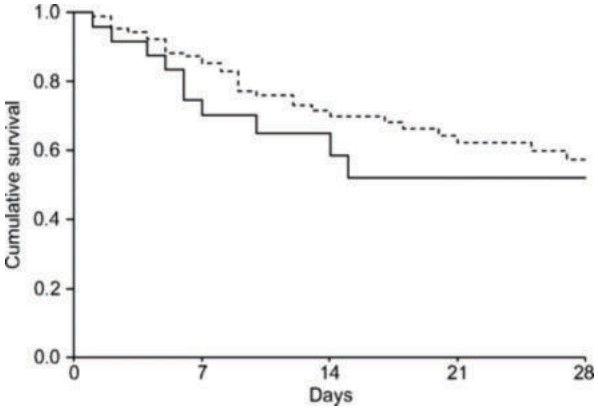

Figure 2

Microbiological documentation (definite and probable) was achieved in 50.5% COPD patients . S. pneumoniae was the most common pathogen both in patients with and without COPD. Pseudomonas aeruginosa was isolated with significantly higher frequency in COPD patients than non-COPD patients (14.6% versus 0.8%; p<0.05). No clinical variable was associated with P. aeruginosa in the subset of COPD patients. Overall, S. pneumoniae represented 54.1% of isolates in COPD patients, followed by P. aeruginosa (13.5%), Haemophilus influenzae (11.4%) and L. pneumophila (4.1%).

Invasive diagnostic methods were performed in 38.6% COPD patients, whereas 20 microorganisms (17 S. pneumoniae and three L. pneumophila) were diagnosed on the basis of urinary antigen tests. One COPD patient had pneumococcal empyema. The microorganisms isolated in COPD patients who died were as follows: S. pneumoniae (n=3); P. aeruginosa (n=2); M. tuberculosis (n=1); S. aureus (n=1); K. pneumoniae (n=1); and Proteus spp. (n=1).

The most frequent antibiotic treatments in COPD patients were: cephalosporines plus macrolide (n=57, 52.9%), cephalosporines; plus fluoroquinolone (n=20, 18.8%), other combinations (n=9, 5.2%); and monotherapy (n=41, 23.8%). Time until the first antibiotic dose was estimated to be 6.6±10.1 h. Details of antibiotic regimens are shown in table 2⇑. In total, 45.4% COPD patients received empirical anti-pseudomonal therapy and the ICU mortality rate (32.5%) was similar to episodes receiving other regimens (28.1%). No differences in ICU mortality rate were observed between COPD patients who received combination therapy or monotherapy (30.4% versus 29.3%; p=0.95). ICU mortality rate did not significantly differ with the use of a fluoroquinolone (31.4% versus 29.5%; p=0.93) or a macrolide (26.5% versus 34.6%; p=0.31) as part of the empirical regimen. Finally, antibiotic treatment was modified in 43.7% episodes: 5 due to de-escalation, 3 due to inappropriate treatment and 8 due to poor resolution . A bacterial pathogen was identifiedin 4 (3 caused by S. pneumoniae) of these episodes with changes of antibiotic therapy due to poor resolution and 50% of them ultimately died.

DISCUSSION

The findings from this large, multicentre, prospective study of SCAP suggest that COPD patients require mechanical ventilation more frequently, have a higher incidence of P. aeruginosa and higher ICU mortality rate than non-COPD patients. Patients with successful noninvasive mechanical ventilation had shorter ICU stays, but were significantly younger, with lower severity according to the APS at ICU admission, less radiographical involvement and fewer comorbidities (such as chronic heart failure). As reported elsewhere [7] a delay in adequate empirical therapy due to unexpected in vitro resistance of the responsible pathogen was associated with excess mortality, whereas with an adequate empirical regimen only bilateral pneumonia and lower APACHE II score measured on the first day of ICU admission were associated with ICU mortality.

Previous studies in COPD patients have suggested that Chlamydia pneumoniae is a frequent cause of SCAP [8] . In the present study, other atypical agents, such as Mycoplasma pneumoniae, or common organisms of the normal respiratory tract in COPD [9] e.g.Moraxella catarrhalis, were infrequently identified. This is probably due to the difference of severity in episodes requiring ICU admission. S. pneumoniae remained the most frequent pathogen and the leading cause in fatal episodes, emphasising COPD patients should be administered anti-pneumococcal vaccinations. Nontypable H. influenzae was the third most prevalent pathogen, but an uncommon cause of death.

Viruses are important agents of COPD exacerbation but none were identified, although systematic samples from nasal airways were not investigated.

P. aeruginosa was the second most common organism in patients with COPD and this is another aspect of interest. Moreover, incidence was significantly higher than in non-COPD patients and it appears to be a near exclusive problem in COPD patients. However, only 7.4% of COPD patients had P. aeruginosa and the current authors were unable to anticipate potential variables identifying COPD patients at high risk of P. aeruginosa.

The pulmonary severity index (PSI) defined from the Pneumonia Outcomes Research Team study [10] includes five comorbid conditions (cardiovascular, malignancy, cerebrovascular, renal and liver diseases), but does not include COPD as one of them. This score was designed in a cohort of patients who included a minority of patients requiring ICU admission and was primarily designed to influence the decision to hospitalise the patient. In addition, in the PSI score, COPD was analysed together with asthma and interstitial lung disease, which could be a reason why it was not identified as a risk factor for poor outcome. Another multicentre study in Spain reported low overall

mortality for COPD patients with pneumonia. However, all COPD patients with pneumonia were hospitalisedand <20% needed ventilatory support. In contrast, nearly 90% of the current cohort required mechanical ventilation. This group represents only a small proportion of hospitalised COPD patients, but it is the one with the highest mortality rates.

The present study confirms that it is crucial for physicians to initiate correct treatment if the risk of mortality is not to increase. The multivariate analysis failed to identify intervention-related factors that were able to improve survival in the subset receiving agents with adequate sensitivity. However, this study was not designed for this purpose. Moreover, factors other than the simple concept of in vitro activity alone play key roles in fighting infection. Waterer et al.23 suggested that monotherapy may be suboptimal for patients with bacteraemic S. pneumoniae pneumonia, whatever treatment is given. Further studies agree with these findings, but the controversy should be resolved by conducting a randomised clinical trial.

There were some limitations to the current study. First, it was not possible to record data regarding lung function tests or COPD disease severity. Although they can be used to classify severity and assess clinical response, these tests are usually not suitable in ICU patients . Further prospective cohort studies should determine the impact of COPD severity on survival and microbiology. Secondly, as in other studies exploring combination therapy, these results were not from a randomised controlled study. However, severity of illness measured by APS was identical. The present study cohort comprised patients with severe episodes of pneumonia requiring intensive care. Therefore, the current findings should not be extrapolated to COPD patients with pneumonia requiring hospitalisation in medical wards or with acute exacerbation. Immunocompromised patients were excluded and the current findings cannot be extrapolated to COPD patients with long-term oral steroid treatment, in whom the pathogen responsible may be an opportunistic microorganism. Patients included in the current study did not receive steroids in routine clinical practice, even those associated with septic shock. The effect of steroids in pneumonia should be further evaluated as part of randomised clinical trials. Finally, follow-up did not extend beyond the ICU stay and the continued drop in survival after ICU discharge is well documented . However, the optimal time-frame for the ascertainment of mortality should be that during which the intervention can plausibly be expected to affect survival and should encompass the potential impact of the intervention. Indeed, short- term survival can be considered a surrogate measure. In addition, long-term survival is confounded by deaths from other causes [11].

CONCLUSION

The present study demonstrates significantly higher mortality rates among patients with chronic obstructive pulmonary disease who require intensive care unit admission for acute respiratory failure due to severe community-acquired pneumonia. This selected population of patients has a higher need for mechanical ventilation and a higher incidence of Pseudomonas aeruginosa than non-chronic obstructive pulmonary disease patients.

Conflict Of Interest: - Authors declare no conflict of interest.

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