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Predicting Length of Stay and Mortality in Acute Exacerbation of Chronic Obstructive Pulmonary Disease at the Intensive Care Unit

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ABSTRACT

Introduction: Chronic obstructive pulmonary disease (COPD) is a worldwide public health challenge because it affects more than 5% of the population. Early identification of the patients at risk of severe disease or death gives the clinician the chance to initiate rapid and aggressive treatment, and thereby save lives.

Methods: This was a single-center observational retrospective study. We included all patients aged ≥40 years admitted to the respiratory intensive care unit with a diagnosis of acute exacerbation of COPD (AECOPD) between January 2014 and December 2018.

Co-morbidities, hemogram and biochemistry values, and inflammatory markers were evaluated in both survivor and non-survivor groups. Results were evluated with SPSS.

Results: A total of 1,454 patients were assessed, 315 (21.6%) patients died during the hospital stay, and 1,139 (78.3%) patients were discharged. In the non-survivor group, mean white blood cell counts were higher than in survivors [14.1 (9.7-20.3), vs 11.8 (8.5-16.1), p<0.001]. However, the survivor group had significantly higher hemoglobin count [12.3 (10.6-14) vs 11.5 (9.8-13.2), p<0.001], lymphocyte % [6.9 (3.9-11.7) vs 5.2 (2.8-10.6), p=0.001], and eosinophil % [0.20 (0.00-0.90), vs 0.10 (0.00-0.60), p=0.001]. Additionally, C-reactive protein, and neutrophil to lymphocyte ratio were significantly lower in the survivor group on admission.

Conclusion: The findings of the current study may provide crucial information on several variables associated with in-hospital mortality for AECOPD patients.

Keywords: Chronic obstructive pulmonary disease, mortality, predictors, length of stay

Introduction

Chronic obstructive pulmonary disease (COPD) is a worldwide public health challenge due to it affecting more than 5% of the population (1,2). Approximately 10% of people aged 40 years or older have COPD which is which is expected to become the third major cause of death worldwide by the year 2030 (3).

An exacerbation of COPD, defined as a worsening of the patient's symptoms and the requirement of additional clinical treatment, is associated with accelerated lung function decline, quality of life impairment, and high hospital mortality (4-6). Early identification of the patients at risk of severe disease or death gives the clinician the chance to initiate rapid and aggressive treatment, and thereby save lives. Several identified factors, including congestive heart failure, older age, requirement of mechanical ventilation, nutritional status, and arterial oxygen and carbon dioxide partial pressure at entry have been independently associated with hospital mortality due to COPD exacerbations (7-10).

The decision to admit acute exacerbation of COPD (AECOPD) patients for the respiratory intensive care unit (RICU) were included according to the following GOLD guidelines: Hemodynamic instability, derangements in mental status, severe dyspnea that responds inadequately to initial therapy, worsening or impending respiratory acidosis and/or hypoxemia, the need for invasive mechanical ventilation (IVM) (4). Although, independent prognostic factors differ between clinical trials. To our knowledge, few studies have been conducted specifically to target patients admitted to the RICU. Thus, this study determined intensive care unit (ICU) mortality rate and factors affecting the prognosis of patients with AECOPD requiring RICU admission.

Methods

Study Design and Setting

This is a single-center observational retrospective study in our 16-bed RICU, which receives about 600 to 650 inpatients/year. The study protocol was approved by University of Health Sciences Turkey, İstanbul Training

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and Research Hospital Local Ethics Committee (approval number: 1857, date: 14.06.2019) by the Declaration of Helsinki. Because of the retrospective nature of the study design, informed consent was not obtained from patients regarding the use of medical data for publication. The identity information of all patients was strictly protected.

Study Population

We included all patients aged ≥40 years admitted to the RICU with a diagnosis of AECOPD from University of Health Sciences Turkey, Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital, Clinic of Anesthesiology, between January 2014 and December 2018. AECOPD is characterized by worsening the respiratory symptoms that is beyond normal variability, and changes therapy (4). COPD patients were excluded from the study if AECOPD was not the primary diagnosis, the patient had other acute events such as tuberculosis, lung cancer, interstitial pulmonary disease. Also, we excluded patients who needed early readmissions to the hospital occurring within ≤30 days of discharge.

Data Collection

All data from this study were obtained from retrospective querying of the institutional electronic system. The following variables were collected: 1) demographic characteristics including age, and gender; 2) characteristics of ICU stay, including the length of MV, length of ICU stay, 28-day mortality 3) blood tests, including red cell count and white blood cell count, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, C-reactive protein (CRP), creatinine, uric acid. All blood samples were collected within 24 h of admission.

Outcome Measures

The criteria for admission of AECOPD to the RICU did not change during the study period. The most common indications of AECOPD patients for RICU admission are worsening or impending respiratory failure and haemodynamic instability. The endpoint of this research was all-cause RICU mortality.

Statistical Analysis

All data were analyzed using SPSS 15.0 for the Windows program. Descriptive statistics; numbers and percentages for categorical variables, mean, standard deviation, median, and interquartile range for numeric variables. Since the numerical variables met the normal distribution condition, the comparisons of the two independent groups were made with the Mann-Whitney U test. Rates in the independent groups were compared with chi-square analysis. Relationships between numerical variables were made using Spearman correlation analysis since the parametric test condition was not met. The statistical alpha significance level was set as $p<0.05$.

Results

A total of 1,454 patients were assessed, 315 (21.6%) patients died during a hospital stay, and 1,139 (78.3%) patients were discharged.

The patients were divided into two groups based on in-hospital mortality: Survivors and non-survivors. Table 1 shows the demographics and comorbidities data of patients in the survival and non-survival groups. The majority were male in both groups, and survivors were younger than non-survivors [66 (58-75.2), vs. 69 (61-78), $p<0.001$]. The non-survivor group had significantly higher IVM requirements (51.1% vs 15.4%, $p<0.001$). The length of stay in the ICU was significantly longer in the non-survivor group. It was 7 (2-17) days in the non-survivor group and 4 (2-8) days in the survivor group ($p<0.001$). Comorbidities were similar in both groups and the most prevalent comorbidity was hypertension (<0.001).

Table 1. Clinical features and comorbidities

Variables	Survivors (n=1,139)	Non-survivors (n=315)	p-value
Male, n (%)	788 (69.2)	203 (64,4)	0.110
Age, years	66 (58-752)	69 (61-78)	<0.001
Requirement for IMV, n (%)	175 (15.4%)	161 (51.1%)	<0.001
Comorbidities, n (%)			
Hypertension	391 (34.3)	116 (36.8)	0.410
Diabetes	152 (13.3)	43 (13.7)	0.888
CHF	148 (13.0)	51 (16.2)	0.144
CKD	18 (1.6)	6 (1.9)	0.689
ICU length of stay	4 (2-8)	7 (2-17)	<0.001

Data presented as the median and interquartile range (25^{th}-75^{th} percentile) unless otherwise indicated. ICU: Intensive care unit, CHF: Chronic heart failure, CKD: Chronic kidney disease, IMV: Invasive mechanical ventilation

Table 2. Laboratory results of patients within 24 h after admission

Variables	Survivors (n=1,139)	Non-survivors (n=315)	p-value
Hemogram values			
WBC x10^9/L	11.8 (8.5-16.1)	14.1 (9.7-20.3)	<0.001
Neutrophil, (%)	83.7 (68.3-89.6)	85.1 (70.2-90.7)	0.125
Monocyte, (%)	4.7 (2.5-7.6)	4.3 (2.5-6.5)	0.059
Lymphocyte, (%)	6.9 (3.9-11.7)	5.2 (2.8-10.6)	0.001
Eosinophil, (%)	0.20 (0.00-0.90)	0.10 (0.00-0.60)	0.001
Basophil, (%)	0.20 (0.10-0.30)	0.10 (0.10-0.30)	0.078
Hemoglobin g/dL	12.3 (10.6-14)	11.5 (9.8-13.2)	<0.001
Hematocrit, (%)	38.9 (33.45-44.6)	35.9 (30.1-40.5)	<0.001
Mean platelet volume fL	87.9 (83-92.6)	88 (83-92.5)	0.712
Platelet count 10^9 L	235 (174-317)	228 (160-304)	0.062
Mean platelet volume fL	9.4 (8.4-10.3)	9.5 (8.3-10.4)	0.504
Biochemistry			
Blood glucose mg/dL	150 (119-203)	159.5 (127-195.75)	0.575
BUN mg/dL	41 (21.7-62)	55 (25.5-90.2)	<0.001
Serum creatinine mg/dL	0.71 (0.45-1.08)	0.88 (0.5-1.32)	<0.001
AST U/L	27 (19-43)	38.5 (24-74.75)	<0.001
ALT U/L	21 (14-37.25)	29 (16-55)	<0.001
Inflammatory markers			
CRP mg/dL	41.5 (9.2-121.7)	90.3 (16.5-195.1)	<0.001
NLR	11.7 (6.3-19.5)	15 (7.5-27.5)	0.002
PLT/MPV	26.5 (19.1-37.9)	25.9 (17.5-35.8)	0.079

Data presented as the median and interquartile range (25^{th}-75^{th} percentile) unless otherwise indicated. ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, BUN: Blood urea nitrogen, CRP: C-reactive protein, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, PLT/MPV: Platelet to mean platelet volume, WBC: White blood cell count

The hemogram, biochemistry values, and inflammatory markers on admission are shown in Table 2. It was discovered in our study that white blood cell count, hemoglobin count, lymphocyte %, eosinophil %, was significantly different in both groups. In the non-survivor group, mean white blood cell counts were higher than in survivors [14.1 (9.7-20.3), vs 11.8 (8.5-16.1), p<0.001]. However, the survivor group had significantly higher hemoglobin count [12.3 (10.6-14) vs 11.5 (9.8-13.2), p<0.001], lymphocyte % [6.9 (3.9-11.7) vs 5.2 (2.8-10.6), p=0.001], and eosinophil % [0.20 (0.00-0.90), vs 0.10 (0.00-0.60), p=0.001]. Additionally, CRP, and neutrophil to lymphocyte ratio (NLR) were significantly lower in the survivor group on admission. No significant differences were in platelet-to-mean platelet volume ratio values were noted.

Discussion

Our study identified several risk factors for death in adult patients treated in the RICU for AECOPD. In particular, age, requirement of IMV, white blood cell count, lymphocyte %, eosinophil %, CRP, NLR, aspartate aminotransferase, alanine aminotransferase, serum creatinine (SCr), blood urea nitrogen was associated with mortality in the ICU.

Knowledge about the prognosis of the disease and factors that will cause poor outcome helps physicians plan treatment and advise patients about the expected natural course. Different risk factors predicting death from AECOPD have been identified in previous studies. For example, the relationship between CRP, NLR, PLR, D-dimers value, N-terminal proBrain natriuretic peptide, and in-hospital mortality in AECOPD patients has been reported (11-14).

Similar to the study by Ai-Ping et al. (15), gender was not related to mortality in our study. We noted that increasing age associated with in-hospital mortality, as a reason given for that is the patients' forced expiratory volume in the first second (FEV1) decreases at a more accelerated rate in elderly patients with COPD than in younger ones (16). In our study, the age was 69 (61-78) years among the nonsurvivors and 66 (58-75.2) years among the survivors (p<0.001).

Comorbidities were not correlated with mortality in our study, this finding is consistent with Connors et al. (17). In this study, several laboratory parameters were investigated for their potential prognostic properties, some of our observations were supported by past studies rising of SCr (18), eosinopenia (19), and anemia (20).

As far as we know, few studies based on lymphocytopenia to predict mortality have been conducted in AECOPD patients. In elderly patients with moderate-to-severe COPD, a relative lymphocyte count ≤20% was related to a higher risk of mortality (21). In another study, the lymphocyte counts of patients who died from AECOPD were lower than those who survived, but the lymphocyte count was not an independent risk factor for death (22). In this study, lymphocyte percentage was found to be a factor affecting in-hospital mortality in patients with AECOPD. Several factors should be considered for the mechanisms of lymphocytopenia predicting mortality in patients with AECOPD. In the elderly, lymphocyte count may be decreased (23), and the elderly are also a risk factor for death in hospitalized COPD patients (9).

This study suggests that CRP and NRL are useful laboratory biomarkers for prognosis in patients with AECOPD. Xiong et al. (22) and Sørensen et al. (24). Noted that elevated NLR may be related to death in patients with AECOPD. To the fact that CRP's relevance to mortality is inferior to that of NLR, it is still correlated with mortality (22).

When the need for respiratory support is established, candidates for noninvasive respitarory ventilation should be screened for possible contraindications. Generally, gastrointestinal hemorrhage, recurrent vomiting, and impairment swallowing are risk factors for vomiting, they are probably unsuitable (25). Also, patients, who are unable to protect their airway due to derangements in mental status, are poor canditates (25). Additionally, patients in AECOPD with cardiovascular instability are probably poor canditates (26). In spite of that, carbon dioxide narcosis in AECOPD should not be considered contraindication (27). We shown that the requirement for IMV was associated with in-hospital mortality. This finding is consistent with that of Brown et al. (9), and Ongel et al. (28); however, five other studies failed to find any association between IMV and in-hospital mortality (29-33). Several factors should be considered in this association; it is probably related to disease severity, and patients who require IMV rather than non-invasive ventilation are in a severe disease stage. Seneff et al. (32) demonstrated that IMV does not affect short- or long-term mortality when controlling for the severity of ilness.

We noted that the length of stay (LOS) in the ICU was related to in-hospital mortality. To our knowledge, predicting mortality based on ICU LOS in adult patients treated for AECOPD has been reported in only a few studies. Ai-Ping et al. (15) shown that LOS in the hospital was associated with mortality, while Hill et al. (34) reported that patients with COPD who died had significantly shorter LOS than those who survive. This is probably related to end-of-life practices, which differ significantly between ICUs.

Study Limitations

Our study also has some limitations. Due to retrospective design at a single center, our results may not be generalized. Additionally, data collection was limited to existing medical records, and not all study variables could be collected. However, the results of this study include many patients with COPD, who are valuable for this specific disease and deserve consideration.

Conclusion

The current study findings may provide crucial information on several variables associated with in-hospital mortality of AECOPD patients. The results may become important for medical decisions to decrease mortality and the LOS in patients with AECOPD requiring RICU admission.

Ethics Committee Approval: The study protocol was approved by University of Health Sciences Turkey, İstanbul Training and Research Hospital Local Ethics Committee (approval number: 1857, date: 14.06.2019) by the Declaration of Helsinki.

Informed Consent: Retrospective study.

Peer-review: Internally peer-reviewed.

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