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Original Article

Predictors of in-hospital mortality in patients with acute exacerbation of COPD requiring ventilation: a retrospective study

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Abstract: Background: Previous studies sought to identify survival or outcome predictors in patients with chronic obstructive pulmonary disease (COPD) requiring mechanical ventilation (MV), but their findings are inconsistent. This study aims to identify clinical predictors of in-hospital mortality among these patients. Material and methods: We conducted a retrospective cohort study of 146 patients admitted to intensive care unit who required IMV for acute exacerbation of COPD between July 2010 and June 2014. Results: The mean age of the study population was 68 ± 11 years. Ninety-six of the patients accepted IMV immediately. Non-invasive positive pressure ventilation (NIPPV) was used in the 50 patients who refused to accept intubation. Of these, 21 patients accepted IMV when deterioration of their vital signs was observed, and 29 patients were given NIPPV continuously. The in-hospital mortality rate was 37.0% for the entire cohort, 29.2% for patients who accepted IMV immediately, 52.4% for patients who accepted IMV on deterioration of their vital signs, and 52.7% for patients given NIPPV continuously. Using binary logistic regression analysis, the in-hospital mortality rate of all 146 patients was positively correlated with multi-organ dysfunction syndrome (MODS), higher APACHEII (acute physiology and chronic health evaluation) score at the beginning of MV, delayed intubation, multidrug resistant organisms (MDRO), higher levels of brain natriuretic peptide (BNP) and the presence of Aspergillus. Conclusions: MODS, higher APACHE II score at the beginning of MV, delayed intubation, MDRO, higher levels of BNP and Aspergillus may be risk factors for mortality in patients who require IMV for acute respiratory failure attributable to COPD.

Keywords: Acute respiratory failure, COPD, exacerbation, ventilation, mechanical, mortality

Introduction

Chronic obstructive pulmonary disease (COPD) is a major public health problem. It is the fourth leading cause of chronic morbidity and mortality in the United States and is projected to rank fifth in the order of diseases in terms of its contribution to global burden in 2020 [1]. The natural history of COPD is characterized by a progressive decline in pulmonary function and recurrent exacerbations [1]. Many COPD patients require admission to an intensive care unit (ICU), in which 26-74% patients receive mechanical ventilation (MV), and average hospital and ICU stays are long and costly. In a recent study, independent predictors of need for MV in patients with COPD with acute respiratory failure were underlying disease severity as assessed by an Acute Physiology and Chronic Health Evaluation II (APACHE-II) score ≥11.5, pH ≤7.28, and $PaCO_2$ ≥68.6 mmHg on admission and premorbid functional status [2].

The prognosis of patients with COPD exacerbations requiring MV in hospital emergency departments or the ICU is poor. The in-hospital mortality rate for patients with acute exacerbation of COPD is estimated to be 20-50% [3-6]. Previous studies on predictors of in-hospital mortality for these patients have focused on physiologic variables associated with severity of disease including increased age [3, 4], baseline dyspnea or use of inspiratory accessory muscles or paradoxical breathing [3, 4, 6], altered mental status or Glasgow Coma Scale (<15 points) [3-5], previous need for long-term

home oxygen therapy or non-invasive mechanical ventilation (NIV) [3, 4], need for intubation, duration of MV, development of acute renal failure [5, 6], cardiac comorbidities, cachexia [7], clinical subtypes C and D of patients experiencing exacerbations of COPD [8], readmission within 30 days of discharge [9], comorbid ischemic heart disease (IHD) [10], and NIV failure and transition from NIV to invasive mechanical ventilation (IMV) [11, 12]. Other studies have tried to use a clinical scoring system to evaluate the prognosis of these patients, including APACHE II scores, the DECAF score, a validated classification and regression tree (CART), and the pneumonia severity index (PSI) [13-17] as well as the presence of invasive pulmonary aspergillosis (IPA) [18, 19], hyperuricemia, and ventilator associated pneumonia (VAP) [20, 21].

The objective of this retrospective study was to investigate in-hospital mortality rates and predictors of in-hospital mortality for patients treated with IMV for acute exacerbation of COPD, and identify possible prognostic factors associated with in-hospital mortality.

Materials and methods

Study population

This retrospective study included all patients admitted to the ICU of the Second Hospital of Hebei Medical University for IMV due to acute exacerbation of COPD between July 2010 and June 2014. COPD was diagnosed clinically from the patient's history and from pre-morbid pulmonary function testing results, or, if unavailable, from results of a physical examination, in accordance with the American Thoracic Society guidelines and GOLD [1]. Exacerbation was defined as dyspnea, cough, and sputum purulence severe enough to warrant hospital admission. COPD patients with respiratory failure due to a specific cause, such as pneumonia, bronchial asthma, restrictive pulmonary disease, and pulmonary embolism, were excluded.

IMV was indicated when one or more of the following conditions were met: severe dyspnea with the use of accessory muscles, paradoxical respiration, respiratory arrest, and respiratory frequency >35 breaths/minute, impaired mental status, respiratory acidosis (pH <7.26), hypoxemia (PaO_2 <60 mmHg), resistance to oxygen supplied through a mask, and hemodynamic instability [1]. Non-invasive positive pressure ventilation (NIPPV) was used for patients who refused to accept IMV for personal reasons. All patients received standard treatment with broad-spectrum antibiotics, inhaled or aerosol bronchodilators, theophylline, and systemic corticosteroids. Weaning from IMV commenced as soon as possible after patients were capable of initiating a spontaneous breath with pressure support ventilation.

This study was approved by the Ethics Committee of the Second Hospital of Hebei Medical University.

Data collection

Demographic and clinical characteristics: Patient demographic characteristics including age, gender and smoking status were documented. The presence and number of co-morbid conditions such as diabetes mellitus, cardiovascular disease (CVD), hypertension, chronic renal disease and chronic liver disease were recorded. The long-term use of oral corticosteroids was defined as ≥5 mg/day of prednisolone or an equivalent during the month before hospitalization.

Hospital admission: Serum albumin, APACHE II score and mental status were noted at the time of ICU admission. Arterial blood gas measurements including pH, $PaCO_2$ and PaO_2 were documented directly before intubation. Serum albumin levels after treatment and the presence/absence of fungal infection were also recorded. Multi-organ dysfunction syndrome (MODS) was diagnosed when two or more organs failed according to the following criteria: (a) respiratory: mechanical ventilation (MV) required; (b) cardiovascular (CV): sepsis shock requiring inotropic support; (c) renal: hemodialysis required or serum creatinine >3.5 mg/dL; (d) gastrointestinal: intestinal perforation, hemorrhagic necrotizing pancreatitis, or gastrointestinal bleeding requiring ≥2 transfusions of packed red blood cells; (e) neurological: score without sedation on Glasgow Coma Scale <8; (f) hepatic: total bilirubin >3 mg/dL and transaminases more than twice the upper limit of normal; (g) hematological: <3,000 leukocytes/μL or platelet count <50,000 platelets/μL. Ventilator-associated pneumonia (VAP) was defined as the presence of two of the following

Table 1. Demographic and clinical characteristics of patients (*n* = 146)

Characteristics	Values*
Baseline age, year	68.4 ± 10.6
Male, %	109 (74.7%)
History of smoking, year	20.8 ± 9.7
Co-morbidity	
Diabetes mellitus, %	47 (32.2%)
Cardiovascular disease, %	50 (34.2%)
Hypertension, %	54 (37.0%)
Chronic renal disease, %	35 (24.0%)
Chronic liver disease, %	11 (7.5%)
Long-term corticosteroids	37 (25.3%)
Serum albumin at admission, g/L	36.7 ± 5.0
Serum albumin after treatment, g/L	36.4 ± 4.9
BNP, pg/ml	325 ± 647.02
APACHE IIscore	23.2 ± 6.1
Pulmonary encephalopathy, %	84 (57.5%)
Arterial blood gas measurement	
PH	7.25 ± 0.10
PCO_2, mmHg	89.1 ± 30.7
PO_2, mmHg	70.4 ± 35.9
MDRO infection	43 (29.5%)
Fungi infection	
Candida albicans, %	21 (14.4%)
Aspergillus, %	8 (5.5%)
Organ failures	
Renal failure, %	36 (24.7%)
Hepatic failure, %	15 (10.3%)
Shock, %	23 (15.8%)
DIC, %	12 (8.2%)
MODS, %	24 (16.4%)
VAP, %	75 (51.4%)
Duration between NIPPV and IMV, day	1.3 ± 0.8
Duration of MV (NIPPV or IMV), day	7.5 ± 13.9
Duration of ICU stay, day	15.0 ± 20.3
Survival out of ICU (or hospital), %	92 (63.0%)

*Values are presented as mean ± SD or N (%), unless otherwise indicated. BNP = brain natriuretic peptide; APACHE = acute physiology and chronic health evaluation; MDRO = multi drug resistant organisms; DIC = disseminated intravascular coagulation; MODS = multi-organ dysfunction syndrome; VAP = ventilator associated pneumonia.

criteria: temperature >38.5°C or <36.5°C, leukocyte count >10,000/μL or <1,500/μL, purulent tracheal aspirate associated with new or progressive radiographic infiltrate, and a positive ($\geq 10^6$ cfu/mL) tracheal aspirate culture result.

Outcomes

Duration of ICU stay and MV, as well as in-hospital mortality, was determined for each patient. The duration between NIPPV and MV was recorded in patients who received NIPPV.

Statistical analysis

Statistical analyses were performed using a statistical software package (SPSS for Windows, version 13.0; SPSS Inc, Chicago, IL, USA). Descriptive data are presented as mean (± SD) or median (range). Comparisons between groups were performed using Student *t*-test and X^2 -test. Significant variables from the univariate analysis were entered into a binary logistic regression model to identify independent predictors of in-hospital mortality. A *P*-value <0.05 was considered statistically significant.

Results

A total of 146 patients were admitted to the ICU of the Second Hospital of Hebei Medical University for IMV due to acute exacerbation of COPD from July 2010 to June 2014. Of these, 96 patients accepted IMV immediately. NIPPV was used as a substitution for 50 patients who refused to accept intubation on admission. Of these, 21 patients accepted IMV after deterioration of their vital signs was observed. 29 patients refused to accept IMV for personal reasons and were given NIPPV continuously.

Demographic and clinical characteristics of the patients included in this study are shown in **Table 1**. The mean age was 68.4 ± 10.6 years, the majority were men (74.7%), and had a history of smoking (mean duration, 20.8 ± 9.7 years). 139 (89%) patients had co-morbid conditions. 37 (25.3%) patients were using long-term steroids. Mean serum albumin level at the time of ICU admission and after treatment was 36.7 ± 5.0 g/L and 36.4 ± 4.9 g/L, respectively. Mean APACHE II score at admission was 23.2 ± 6.1. 84 (57.5%) patients had hypercapnic encephalopathy before intubation; their consciousness was defined as drowsy, comatose, or respiratory arrest. Mean pH, $PaCO_2$, and PaO_2 were 7.25 ± 0.10, 89.1 ± 30.7 mmHg, and 70.4 ± 35.9 mmHg, respectively. 75 (51.4%) patients developed VAP during the

Table 2. Differences of demographic and clinical characteristics of patients between groups survivors and non survivors*

Variables	Survivors (*n* = 92)	Nonsurvivors (*n* = 54)	*t*-value or X^2-value	*P*-value
Age, year	66.6 ± 11.3	71.5 ± 8.4	2.939	0.004▲
Male	69	40	0.015	0.091
History of smoking, year	20.38 ± 9.83	21.56 ± 9.47	0.707	0.481
Co-morbidity				
Diabetes mellitus	29	18	0.051	0.821
CVD	30	27	4.324	0.038▲
Hypertension	36	28	2.237	0.135
Chronic renal disease	23	12	0.144	0.704
Chronic liver disease	4	7	3.625	0.057
Long-term corticosteroids	22	15	0.993	0.609
Serum albumin at admission, g/L	37.4 ± 5.0	35.5 ± 4.9	-2.337	0.021▲
Serum albumin after treatment, g/L	37.3 ± 4.6	35.0 ± 5.2	-2.824	0.005▲
BNP, pg/ml	208.6 ± 385.9	523.4 ± 908.8	2.421	0.018▲
APACHE II score	21.7 ± 5.4	25.6 ± 6.6	3.851	0.000▲
Pulmonary encephalopathy	84	62	1.133	0.287
Arterial blood gas measurement				
PH	7.24 ± 0.09	7.27 ± 0.12	1.724	0.088
PCO_2, mmHg	93.19 ± 26.66	82.21 ± 35.74	-1.959	0.053
PO_2, mmHg	69.13 ± 25.88	72.43 ± 48.71	0.064	0.594
MDRO infection	21	22	5.256	0.022▲
Fungi infection				
Candida albicans	14	11	0.637	0.425
Aspergillus	2	6	5.248	0.022▲
Organ failures				
Renal failure	19	17	2.148	0.143
Hepatic failure	7	9	2.861	0.091
Shock	11	14	4.679	0.031▲
DIC	7	5	0.123	0.726
MODS	7	16	12.433	0.000▲
VAP	47	31	0.546	0.460
IMV acceptance			7.354	0.007▲
Accepted without delay	68	28		
Delayed IMV	24	26		

*Values are presented as mean ± SD or N (%), unless otherwise indicated. ▲$P<0.05$. CVD = cardiovascular disease. BNP = brain natriuretic peptide; APACHE = acute physiology and chronic health evaluation; MDRO = multi drug resistant organisms; VAP = ventilator associated pneumonia; IMV = invasive mechanical ventilation.

therapy. 34 (23.3%) patients developed MODS during therapy.

Mean duration of MV (NIPPV or IMV) was 7.5 ± 13.9 days. The median duration of ICU stay was 15.0 ± 20.2 days. 54 patients died in the ICU. The in-hospital mortality rate for the entire cohort was 37.0%. Age, CVD, serum albumin level at the time of ICU admission and after treatment, use of IMV, MODS, APACHE II score, multidrug resistant organisms (MDRO), BNP level, Aspergillus, and shock were significantly different between survivors and non survivors (**Table 2**).

The mortality rate among patients who received IMV at the time of ICU admission was 29.2% (28/96). The mortality rate among patients who refused intubation on admission but accepted IMV after deterioration of their vital signs was 52.4% (11/21). The mortality rate among the patients who received NIPPV con-

Table 3. Differences in in-hospital mortality stratified by acceptance of IMV between groups

IMV acceptance	Mortality, %	Group 1	Group 2	Group 3
Group 1	29.2 (28/96)	—	$P = 0.041$▲	$P = 0.025$▲
Group 2	52.4 (11/21)	$X^2 = 4.179$	—	$P = 0.963$
Group 3	51.7 (15/29)	$X^2 = 5.022$	$X^2 = 0.002$	—

Group 1 = patients who immediately accepted IMV at the time of ICU admission. Group 2 = patients who accepted IMV after a period of NIPPV. Group 3 = patients who refused IMV until the end of the therapy. X^2-test, ▲$P<0.05$. IMV = invasive mechanical ventilation.

Table 4. Predictors of in-hospital mortality

Variables	β coefficient	Wald	Odds Ratio (95% CI※)	*P*-Value
Age	-0.038	1.828	0.963 (0.912-1.017)	0.176
CVD	-0.671	1.768	0.511 (0.190-1.375)	0.184
Shock	0.235	0.097	1.265 (0.289-5.529)	0.755
MODS	-1.587	4.18	0.205 (0.045-0.936)	0.041▲
APACHE II score	-0.138	11.658	0.871 (0.805-0.943)	0.001▲
Delayed IMV	-1.867	12.336	0.155 (0.055-0.438)	0.000▲
MDRO	-1.297	5.963	0.273 (0.097-0.774)	0.015▲
BNP	-0.002	10.188	0.998 (0.997-0.999)	0.001▲
Aspergillus	-3.130	7.556	0.044 (0.005-0.407)	0.006▲
Constant	4.680	2.478	107.804	0.115

※CI = confidence interval. ▲$P<0.05$. CVD = cardiovascular disease. MODS = multi-organ dysfunction syndrome; APACHE = acute physiology and chronic health evaluation; IMV = invasive mechanical ventilation; MDRO = multi drug resistant organisms; BNP = brain natriuretic peptide.

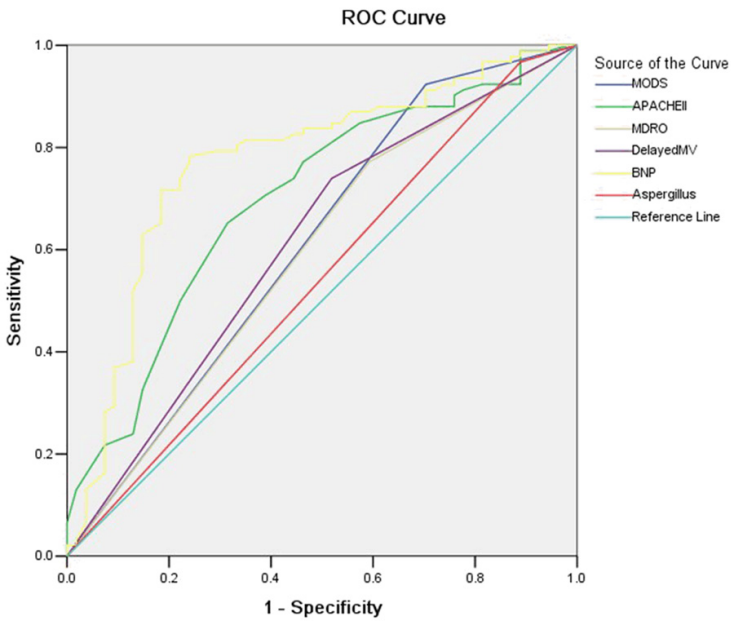

Figure 1. ROC curve.

tinuously was 51.7% (15/29). There was a significant difference in the mortality rate between patients who accepted IMV immediately and those who refused intubation (**Table 3**).

Using binary logistic regression analysis, the in-hospital mortality rate of the entire cohort was positively correlated with delayed intubation, higher APACHE II score at the beginning of MV, MODS, MDRO, higher levels of BNP, and presence of Aspergillus (**Table 4**).

Receiver operating characteristic (ROC) curves showed the area under the curve (AUC) for delayed IMV, higher APACHE II score at the beginning of MV, MODS, MDRO, higher levels of BNP value and presence of Aspergillus to predict in-hospital mortality were 0.590, 0.699, 0.610, 0.610, 0.773 and 0.539, respectively (**Figure 1**; **Table 5**).

Discussion

This is a retrospective study of patients admitted to the ICU for IMV due to acute exacerbation of COPD. The in-hospital mortality rate for patients who received intubation and IMV immediately was 29.2%, and similar to that reported in other studies [1, 3-6]. An indication of the severity of the exacerbations in the patients included in this study is given by the fact that conventional medical treatment failed in the hospital ward and emergency room. The low mortality rate (< 30%) in the patients that received IMV immediately upon admission to the ICU shows that survival can be achieved even in the presence of the severe acute physiologic derangement that occurs in patients requiring IMV for COPD. However, the likelihood of survival in these patients declines after hospital discharge. Guerrero et al [9] found that 18% of chronic COPD patients were readmitted with chronic exacerbations of COPD

Table 5. ROC curve

Test result variables	Area	Std. error	Asymptotic sig	Asymptotic 95% confidence interval
MODS	0.610	0.050	0.027▲	0.512-0.709
APACHE II	0.699	0.045	0.000▲	0.610-0.787
Delayed IMV	0.610	0.049	0.026▲	0.514-0.707
MDRO	0.590	0.050	0.071	0.492-0.687
BNP	0.773	0.042	0.000▲	0.690-0.855
Aspergillus	0.539	0.050	0.429	0.441-0.638

▲$P < 0.05$. MODS = multi-organ dysfunction syndrome; APACHE = acute physiology and chronic health evaluation; IMV = invasive mechanical ventilation; MDRO = multi drug resistant organisms; BNP = brain natriuretic peptide.

within 30 days of discharge, and 30-day readmission was an independent risk factor for mortality at 1 year. This suggests further studies on long-term mortality rates of patients treated in the ICU for acute exacerbation of COPD are warranted.

Previous studies show that increased age, baseline dyspnea, altered mental status, previous need for long-term home oxygen therapy or NIV, need for intubation, development of acute renal failure, cardiac comorbidities, IHD and cachexia, readmission within 30 days of hospital discharge, NIV failure and transition from NIV to IMV, higher APACHE II scores, and the presence of IPA or VAP are related to in-hospital mortality of COPD patients requiring IMV [3-21]. Our study added to these findings and revealed that delayed IMV, higher APACHE II score at the beginning of MV, MODS, MDRO, higher levels of BNP, and the presence of Aspergillus are also associated with higher in-hospital mortality. Because only about one third of our patients had pulmonary function testing within a year before hospital admission, the effect of this parameter was not analyzed.

Our study showed that delayed IMV was less beneficial than using NIPPV alone for acute exacerbation of COPD. The same result was seen in community-acquired pneumonia (CAP), where the delay in time to intubation from the onset of CAP symptoms was associated with outcomes in patients who ultimately required IMV [22].

The prognosis of do-not-intubate patients who receive NIPPV is controversial. Diagnosis is an important determinant of survival. Tabernero et al reported that do-not-intubate patients with obesity hypoventilation syndrome or Barthel index >50 had the best prognosis among elderly patients with multiple morbidities in a chronic disease hospital [23]. Previous studies showed that some do-not-intubate patients, particularly those diagnosed with congestive heart failure or COPD, who have a rough cough and are conscious, have a good prognosis with NIPPV. Another report suggested that NIPPV performed by an experienced team with high nurse-patient ratios that afford close monitoring in COPD exacerbation with moderate to severe hypercapnic encephalopathy, leads to similar short and long-term survivals with a reduced nosocomial infection rate and duration of ventilation compared to IMV. Do-not-intubate patients are commonly treated with NIV; however, NIV failure is associated with increased risk of in-hospital death in this patient population. One study showed that do-not-intubate patients that failed NIV were comparatively younger and had a higher APACHE II score than do-not-intubate patients in which NIV was successful, suggesting the need for a careful selection of patients that might benefit from NIV [12]. These data indicate that do-not-intubate patients with a higher disease burden are more likely to be ventilated and to receive initial IMV treatment than patients with a lower comorbidity burden; however, they also have the highest rate of NIV failure. The respiratory deterioration found in these patients may be less easily reversible, and these patients may more often deteriorate to the point where they have to be intubated [12]. One study showed that high-flow nasal cannula (HFNC) therapy, which supplies a flow of heated and humidified oxygen, may provide an effective alternative to NIV in these patients [24].

In our study, APACHE II score and hypoalbuminemia after treatment were associated with in-hospital mortality in COPD patients requiring IMV. These data are in accordance with some previous reports [13-16] but not all. Our observations add support to the recommendation that APACHE III and/or IV scores, which include albumin as a variable, are more contemporary and accurate than the APACHE II score for use in this type of research. Echevarria et al found that the Dyspnoea, Eosinopenia, Consolidation, Acidaemia, and atrial Fibrillation (DECAF) score

is a robust predictor of in-hospital or 30-day mortality [13]. The pneumonia severity indexes including PSI or CURB65 and BAP65 may also be used to evaluate the prognosis of patients with acute exacerbation of COPD. Hu et al found the PSI was a predictor of in-hospital mortality in acute exacerbation of COPD patients [16]. Some research has used a classification and regression tree (CART) to assess mortality associated with exacerbation of COPD, and has identified several easy-to-determine variables that allow clinicians to predict risk of death and provide appropriate clinical care [15].

Development of MODS was also correlated with high in-hospital mortality in our study. Our patients suffered from COPD with respiratory failure, so MODS was diagnosed when one or more other organs failed, with renal failure serving as the majority case. One study showed that renal failure was highly relevant to the prognosis of COPD patients discharged from hospital after an acute exacerbation [5, 6]. The acute changes in carbon dioxide levels play a more dominant role than oxygen levels in determining renovascular resistance. Because patients with an acute exacerbation of COPD usually have a combination of hypoxemia and hypercapnia, the importance of controlled oxygen therapy and the prevention of progressive hypercapnia should be emphasized.

Acute exacerbations of COPD are the main reason for hospitalization of patients with COPD. While most exacerbations are due to viral or bacterial infections, up to one-third have an unknown etiology. Abnormalities of the cardiovascular system have been implicated as an important factor in the prognosis of patients with COPD [25]. Epidemiological evidence suggests that left ventricular failure is a common comorbidity in these patients. In our study, there was a link between an elevated level of BNP and increased mortality in acute exacerbations of COPD. Some studies suggest that BNP or NT-proBNP could be a useful biomarker for the diagnosis of left ventricular failure, and a predictor of mortality, particularly in the short term in patients with an acute exacerbation of COPD [26, 27]. More research is needed in order to determine the clinical utility of BNP or NT-proBNP as a biomarker in these patients.

We concluded that presence of Aspergillus was independently associated with hospital mortality in our patient population. Bulpa et al [18] showed that the mortality of COPD patients with invasive pulmonary Aspergillosis (IPA) was high: 95% patients died despite 77% of patients receiving invasive ventilation and antifungal treatment. Tutar et al suggested that IPA should be taken into account in differential diagnosis, particularly in patients with severe and very severe COPD presenting with dyspnea, exacerbation, poor clinical status, and a new pulmonary infiltrate under treatment with broad-spectrum antibiotics and steroids [19]. These observations indicate that antifungal treatment should be considered in critically ill patients with COPD requiring IMV, if features of pulmonary infection are present and Aspergillus spp. are isolated from respiratory secretions.

In our study, MDRO was associated with high in-hospital mortality, and was an independent prognostic factor affecting the mortality of the patients who required IMV for acute exacerbation of COPD. A previous study reported that although multiple-drug-resistant (MDR) bacteria are not independently associated with ICU mortality, inappropriate initial antibiotic treatment is an independent risk factor for ICU mortality in patients with severe acute exacerbation of COPD. Although NIV use in severe acute exacerbation of COPD has substantially reduced the need for intubation, an important number of COPD patients are still mechanically ventilated through a tracheal tube in the ICU. Intubation is a major risk factor for lower respiratory tract colonization (LRTC) in ICU patients. At the same time, LRTC is a major risk factor for VAP, which is associated with increased mortality and morbidity in ICU patients. These observations indicate that MDR bacterial infection, especially bacteremia secondary to VAP, should be considered a risk factor for increased mortality [21, 28, 29].

Our study adds to existing literature identifying predictors of in-house mortality in patients who require IMV for acute exacerbation of COPD; however, it has several limitations. First, the study was retrospective, a single-centre design, with a small sample size. Second, we had no information on the general health status of the patients before admission. Third, there were significant differences in the average age of survivors and nonsurvivors in our study, although age was not a significant predictor of

mortality. In other studies of patients with COPD, advanced age was a prognostic factor for in-hospital mortality, although not always an independent prognostic factor.

Conclusions

We conclude that patients with COPD requiring ICU admission have a good chance of surviving to hospital discharge despite requiring the use of IMV. However, delay of IMV is associated with a higher mortality rate. Delayed IMV, higher APACHE II score at the beginning of MV, MODS, MDRO, elevated BNP levels, and presence of Aspergillus predict poorer in-hospital outcomes.

Disclosure of conflict of interest

None.

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References

[1] Vestbo J, Hurd SS, Agusti AG, Jones PW, Vogelmeier C, Anzueto A, Barnes PJ, Fabbri LM, Martinez FJ, Nishimura M, Stockley RA, Sin DD and Rodriguez-Roisin R. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2013; 187: 347-365.

[2] Kumar S, Khilnani GC, Banga A and Sharma SK. Predictors of requirement of mechanical ventilation in patients with chronic obstructive pulmonary disease with acute respiratory failure. Lung India 2013; 30: 178-182.

[3] Quintana JM, Esteban C, Unzurrunzaga A, Garcia-Gutierrez S, Gonzalez N, Barrio I, Arostegui I, Lafuente I, Bare M, Fernandez-de-Larrea N and Vidal S. Predictive score for mortality in patients with COPD exacerbations attending hospital emergency departments. BMC Med 2014; 12: 66.

[4] Quintana JM, Esteban C, Unzurrunzaga A, Garcia-Gutierrez S, Gonzalez N, Lafuente I, Bare M, de Larrea NF and Vidal S. Prognostic severity scores for patients with COPD exacerbations attending emergency departments. Int J Tuberc Lung Dis 2014; 18: 1415-1420.

[5] Alaithan AM, Memon JI, Rehmani RS, Qureshi AA and Salam A. Chronic obstructive pulmonary disease: hospital and intensive care unit outcomes in the Kingdom of Saudi Arabia. Int J Chron Obstruct Pulmon Dis 2012; 7: 819-823.

[6] Gaude GS, Rajesh BP, Chaudhury A and Hattiholi J. Outcomes associated with acute exacerbations of chronic obstructive pulmonary disorder requiring hospitalization. Lung India 2015; 32: 465-472.

[7] Ongel EA, Karakurt Z, Salturk C, Takir HB, Burunsuzoglu B, Kargin F, Ekinci GH, Mocin O, Gungor G, Adiguzel N and Yilmaz A. How do COPD comorbidities affect ICU outcomes? Int J Chron Obstruct Pulmon Dis 2014; 9: 1187-1196.

[8] Arostegui I, Esteban C, Garcia-Gutierrez S, Bare M, Fernandez-de-Larrea N, Briones E and Quintana JM. Subtypes of patients experiencing exacerbations of COPD and associations with outcomes. PLoS One 2014; 9: e98580.

[9] Guerrero M, Crisafulli E, Liapikou A, Huerta A, Gabarrus A, Chetta A, Soler N and Torres A. Readmission for Acute Exacerbation within 30 Days of Discharge Is Associated with a Subsequent Progressive Increase in Mortality Risk in COPD Patients: A Long-Term Observational Study. PLoS One 2016; 11: e0150737.

[10] Aliyali M, Mehravaran H, Abedi S, Sharifpour A and Yazdani Cherati J. Impact of Comorbid Ischemic Heart Disease on Short-Term Outcomes of Patients Hospitalized for Acute Exacerbations of COPD. Tanaffos 2015; 14: 165-171.

[11] Gacouin A, Jouneau S, Letheulle J, Kerjouan M, Bouju P, Fillatre P, Le Tulzo Y and Tadie JM. Trends in Prevalence and Prognosis in Subjects With Acute Chronic Respiratory Failure Treated With Noninvasive and/or Invasive Ventilation. Respir Care 2015; 60: 210-218.

[12] Correa TD, Sanches PR, de Morais LC, Scarin FC, Silva E and Barbas CS. Performance of noninvasive ventilation in acute respiratory failure in critically ill patients: a prospective, observational, cohort study. BMC Pulm Med 2015; 15: 144.

[13] Echevarria C, Steer J, Heslop-Marshall K, Stenton SC, Hickey PM, Hughes R, Wijesinghe M, Harrison RN, Steen N, Simpson AJ, Gibson GJ and Bourke SC. Validation of the DECAF score to predict hospital mortality in acute exacerbations of COPD. Thorax 2016; 71: 133-140.

[14] Zilz C, Blaas SH, Pfeifer M, Jorres RA and Budweiser S. Mental health, serum biomarkers and survival in severe COPD: a pilot study. Multidiscip Respir Med 2015; 11: 3.

[15] Esteban C, Arostegui I, Garcia-Gutierrez S, Gonzalez N, Lafuente I, Bare M, Fernandez de Larrea N, Rivas F and Quintana JM. A decision tree to assess short-term mortality after an emergency department visit for an exacerbation of COPD: a cohort study. Respir Res 2015; 16: 151.

[16] Hu G, Zhou Y, Wu Y, Yu Y, Liang W and Ran P. The Pneumonia Severity Index as a Predictor of In-Hospital Mortality in Acute Exacerbation of Chronic Obstructive Pulmonary Disease. PLoS One 2015; 10: e0133160.

[17] Yang H, Xiang P, Zhang E, Guo W, Shi Y, Zhang S and Tong Z. Is hypercapnia associated with poor prognosis in chronic obstructive pulmonary disease? A long-term follow-up cohort study. BMJ Open 2015; 5: e008909.

[18] Delsuc C, Cottereau A, Frealle E, Bienvenu AL, Dessein R, Jarraud S, Dumitrescu O, Le Marechal M, Wallet F, Friggeri A, Argaud L, Rimmele T, Nseir S and Ader F. Putative invasive pulmonary aspergillosis in critically ill patients with chronic obstructive pulmonary disease: a matched cohort study. Crit Care 2015; 19: 421.

[19] Tutar N, Metan G, Koc AN, Yilmaz I, Bozkurt I, Simsek ZO, Buyukoglan H, Kanbay A, Oymak FS, Gulmez I and Demir R. Invasive pulmonary aspergillosis in patients with chronic obstructive pulmonary disease. Multidiscip Respir Med 2013; 8: 59.

[20] Zhang X, Liu L, Liang R and Jin S. Hyperuricemia is a biomarker of early mortality in patients with chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis 2015; 10: 2519-2523.

[21] Hadda V, Khilnani GC, Dubey G, Nallan R, Kumar G and Guleria R. Impact of ventilator associated pneumonia on outcome in patients with chronic obstructive pulmonary disease exacerbation. Lung India 2014; 31: 4-8.

[22] Hraiech S, Alingrin J, Dizier S, Brunet J, Forel JM, La Scola B, Roch A, Papazian L and Pauly V. Time to intubation is associated with outcome in patients with community-acquired pneumonia. PLoS One 2013; 8: e74937.

[23] Tabernero Huguet E, Gil Alana P, Arana-Arri E, Citores Martin L, Alkiza Basanez R, Hernandez Gil A and Gil Molet A. [Non-invasive ventilation in 'do-not-intubate' patients in a chronic disease hospital. One year follow-up study]. Rev Esp Geriatr Gerontol 2016; 51: 221-4.

[24] Peters SG, Holets SR and Gay PC. High-flow nasal cannula therapy in do-not-intubate patients with hypoxemic respiratory distress. Respir Care 2013; 58: 597-600.

[25] Marcun R, Sustic A, Brguljan PM, Kadivec S, Farkas J, Kosnik M, Coats AJ, Anker SD and Lainscak M. Cardiac biomarkers predict outcome after hospitalisation for an acute exacerbation of chronic obstructive pulmonary disease. Int J Cardiol 2012; 161: 156-159.

[26] Chang CL, Robinson SC, Mills GD, Sullivan GD, Karalus NC, McLachlan JD and Hancox RJ. Biochemical markers of cardiac dysfunction predict mortality in acute exacerbations of COPD. Thorax 2011; 66: 764-768.

[27] Gariani K, Delabays A, Perneger TV and Agoritsas T. Use of brain natriuretic peptide to detect previously unknown left ventricular dysfunction in patients with acute exacerbation of chronic obstructive pulmonary disease. Swiss Med Wkly 2011; 141: w13298.

[28] Nseir S, Ader F, Lubret R and Marquette CH. Pathophysiology of airway colonization in critically ill COPD patient. Curr Drug Targets 2011; 12: 514-520.

[29] Brotfain E, Borer A, Koyfman L, Saidel-Odes L, Frenkel A, Gruenbaum SE, Rosenzweig V, Zlotnik A and Klein M. Multidrug Resistance Acinetobacter Bacteremia Secondary to Ventilator-Associated Pneumonia: Risk Factors and Outcome. J Intensive Care Med 2016; [Epub ahead of print].