ORIGINAL ARTICLE

Two-year survival of severe chronic obstructive pulmonary disease subjects requiring invasive mechanical ventilation and the factors affecting survival

Selvi Asker,[1] Bülent Özbay,[2] Selami Ekin,[3] Hanifi Yildiz,[4] Bunyamin Sertogullarindan[5]

Abstract

Objective: To investigate two-year survival rates and the factors affecting survival in patients of severe chronic obstructive pulmonary disease requiring invasive mechanical ventilation.

Methods: The retrospective study was conducted at Yuzuncuy?l University, Van, Turkey, and comprised record of in-patients with moderate to severe chronic obstructive pulmonary disease who required invasive mechanical ventilation in the intensive care unit of the Pulmonary Diseases Department between January 2007 and December 2010. Correlation between survival and parameters such as age, gender, duration of illness, history of smoking, arterial blood gas values, pulmonary artery pressure, left ventricular ejection fraction, body mass index and laboratory findings were investigated. SPSS 19 was used for statistical analysis.

Results: Of the 69 severe COPD subjects available, 20 (29%) were excluded as they did not meet the inclusion criteria. Overall in-hospital mortality rate was 42% (n:29). Of the remaining 20 (29%) who comprised the study group, 14(70%) were men and 6(30%) were women. The mortality rates at the end of 3rd, 6th, 12th and 24th months were 61%, 76%, 84% and 85.5% respectively. There was no correlation between gender and survival in time point ($p>0.05$). The only factor that affected the rate of mortality at the end of the 3rd month was age ($p<0.05$). Mortality was high in subjects with advanced ages ($p<0.05$). Duration of illness affected the survival at the end of the six month ($p<0.05$). Survival rates were high in subjects with longer illness durations ($p<0.05$). Haematocrit level was the only factor that affected mortality rates at the end of 12th and 24th months ($p<0.05$). Subjects with higher haematocrit levels had higher survival rates ($p<0.05$).

Conclusion: Age, duration of illness and haematocrit levels were the most important factors that affected survival in chronic obstructive pulmonary disease patients requiring mechanical ventilation.

Keywords: Chronic obstructive pulmonary disease, Mortality rate, Mechanical ventilation, Prognosis. (JPMA 66: 498; 2016)

Introduction

The course of chronic obstructive pulmonary disease (COPD) is marked by progressive deterioration in lung function and functional status punctuated by episodes of acute decompensation. Exacerbation of Chronic Obstructive Pulmonary Disease (eCOPD) is one of the commonest causes for hospital admission across Europe and is associated with high morbidity and mortality.[1]

Hospitalisation for subjects with acute exacerbations carries an associated in-hospital mortality of 6% to 26%, which increases to as high as 82% if ventilator support is required.[2,3] Acute exacerbation in COPD subjects is defined as progressive dyspnoea and increase in sputum volume and purulence.[4] Variables that may have prognostic value in COPD subjects include the severity of underlying lung disease, the severity of acute illness, age, nutritional status, and the level of function. While many studies appear to be contradictory in their findings, others have simply failed to identify any variables available at the time of hospital admission that predict outcomes in this population.[5]

In spite of the medical therapies, 25% cases with acute exacerbation need mechanical ventilation. Mechanical ventilation can be performed in two ways: intubated (invasive) or non-intubated (non-invasive). Concern about high mortality rates, the potential for weaning failure and prolonged mechanical ventilation (MV) has led authors to seek possible predictors of outcome that may aid physicians and subjects with decisions regarding the institution of invasive MV.[4]

There is limited data concerning the prognosis of severe COPD subjects hospitalised due to acute exacerbations, and studies show that subjects who undergo invasive MV have poor prognosis.[5] These studies reveal that mortality in mechanically ventilated subjects is related with age, advanced lung disease, exercise tolerance and pulmonary

[1,3,5]Department of Chest Diseases, Van Yuzuncu Yil University Dursun Odabas Medical Center, Van, [2]Department of Chest Diseases, Mugla University Faculty of Medicine, Mugla, [4]Department of Chest Diseases, Van Ipekyolu Government Hospital, Van, Turkey.

Correspondence: Selvi Asker. Email: selviasker@mynet.com

function tests.[6]

The current study was planned to investigate two-year survival rates and the factors affecting survival in severe COPD subjects requiring invasive MV.

Patients and Methods

The retrospective study was conducted at Yuzuncuy?l University, Van, Turkey, and comprised record of in-patients with moderate to severe COPD who required invasive MV in the intensive care unit (ICU) of the Pulmonary Diseases Department between January 2007 and December 2010. After approval from the institutional review board, diagnostic information was obtained from hospital records, including symptoms and exposures (smoking habits and/or biomass smoke exposure), physical examination findings, and pulmonary function test (PFT) results. The severity of COPD was classified according to the Global Initiative of Chronic Obstructive Lung Disease (GOLD) criteria, based on the last PFT within one year prior to admission.[7] Information on age, gender, smoking status, biomass exposure, PFT, comorbidities were collected from patient charts. Baseline findings of complete blood cell (CBC) count, blood chemistry and arterial blood gas (ABG) were recorded. The number of hospital re-admissions and survival status were determined by hospital records and by telephone contact after discharge. The name and address of patients and family members were not disclosed, and verbal informed consent was obtained from the family members by telephone contact.

Patients who had been lost to follow-up in hospital were excluded, and so were those using oxygen (O_2) concentrator, and those diagnosed with malignancy, chronic metabolic disease, systemic vascular disease, left heart failure, congenital heart diseases, cardiac valvular disease, pneumonia, kyphoscoliosis, acute respiratory distress syndrome (ARDS), lung cancer and acute pulmonary embolism. In addition, subjects who could not be contacted on phone were also excluded.

Severe dyspnoea, use of accessory respiratory muscles, a respiration rate higher than 35 per minute, confused state of mind, respiratory acidosis (pH<7.20), hypoxaemia ((partial pressure of oxygen [pO_2]<60) or desaturation (below 90%), not responding to oxygen hood therapy and haemodynamic instability were all regarded as indications for MV. All standard therapies were tried before subjects were mechanically ventilated.

Parameters such as age, gender, duration of illness, history of cigarette smoking, ABG values (during hospital stay and discharge), left ventricular (LV) functions, pulmonary arterial (PA) pressure, laboratory results (creatinine, aspartate aminotransferase [AST], alanine aminotransferase [ALT], lactate dehydrogenase [LDH] and haematocrit levels) of all subjects were recorded. Transthoracic echocardiography (Philips HD 11 XE echocardiography device, Philips Medical Systems, Bothell, WA) was performed on all subjects. LV systolic and diastolic functions, valvular structure and functions, left ventricular ejection fraction (LVEF) and PA pressure were recorded. All subjects were contacted on phone in the 24th month status was noted.

Data were analysed using SPSS 19. Parametric tests were applied to data of normal distribution and non-parametric tests were applied to data of questionably normal distribution. One-way analysis of variance (ANOVA) test was used to compare groups of independent continuous variables. The distribution of categorical variables in both groups was compared using chi-square test. Data was expressed as mean±SD or median (interquartile range [IQR]), as appropriate. Survival analyses (Kaplan Meir and log rank) were also done. All differences associated with a chance probability of 0.05 or less were considered statistically significant.

Results

Of the 69 severe COPD subjects available, 20 (29%) were excluded as they did not meet the inclusion criteria. Overall in-hospital mortality rate was 42% (n:29). Of the remaining 20 (29%) who comprised the study group, 14(70%) were men and 6(30%) were women. The mean age of the male subjects was 63±11 years, and that of the female subjects was 70±9 years. The overall mean illness duration was 10±4.9 years.

The reasons behind acute exacerbations were infections (viral and bacterial) in 13(65%) subjects, exposure to pollution and tandoori smoke in 3(15%), cardiac arrhythmia (atrial fibrillation with rapid ventricular response) in 2(10%), morbid obesity in 1(5%), and an unascertained cause in the remaining 1(5%) patient.

Table: Arterial blood gas parameters before and after intubation.

	Before intubation	After intubation
pH	7.2±0.09	7.4±0.07
PO_2	40.9±13	56±18
PCO_2	77.6±14.7	44.7±8.6
HCO_3	27±7	28±6
O_2 saturation	63±19	86.5±14.5

PO_2: Partial pressure of oxygen
PCO_2: Partial pressure of carbon dioxide
HCO_3: Bicarbonate
O_2: Oxygen

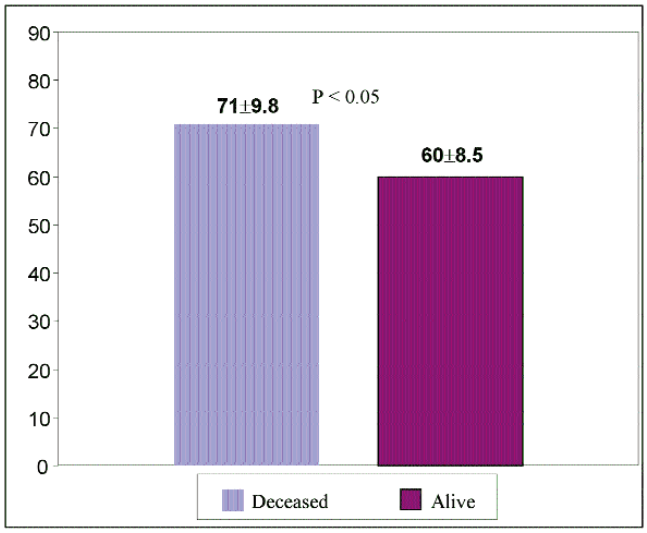

Figure-1: Average ages of deceased and alive patients (3rd month).

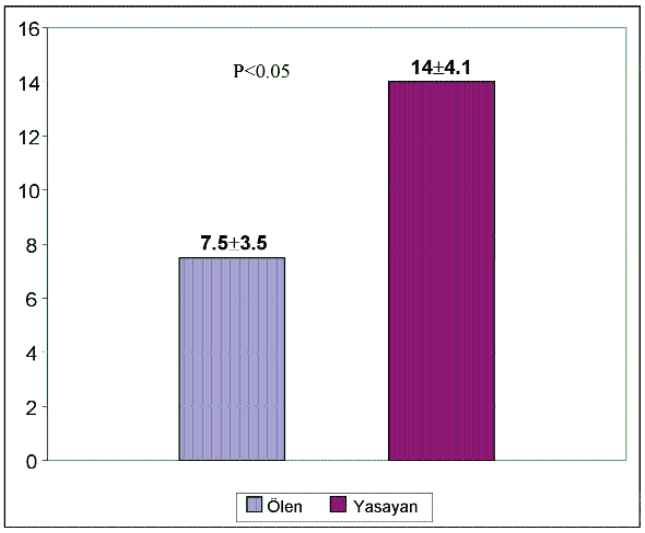

Figure-3: Average duration of illness (year) in deceased and alive patients (6th month).

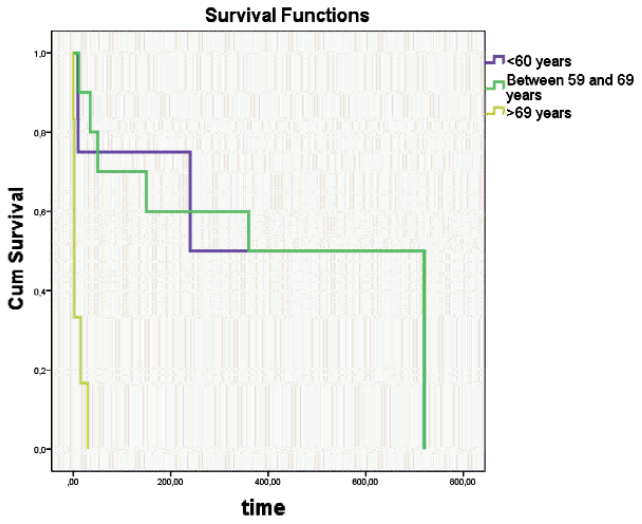

Figure-2: Two-year survival in severe chronic obstructive pulmonary disease (COPD) subjects requiring invasive mechanical ventilation by age.

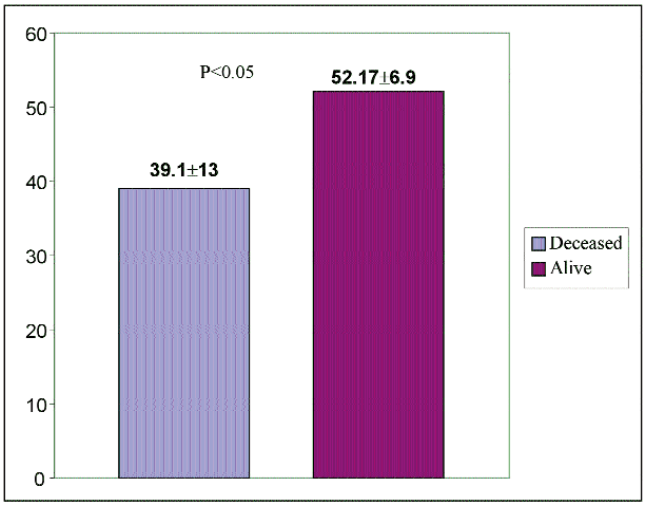

Figure-4: Average haematocrit levels in deceased and alive patients (12th month).

Mean intubation period was 5.3±6,4 days. All subjects in the study were smokers and their mean cigarette smoking duration was 58±14 pack/years. Mean pH, PO_2, partial pressure of carbon dioxide (PCO_2), Bicarbonate (HCO_3) and O_2 saturation levels of the subjects before and after intubation were noted (Table-1).

The in-hospital mortality rate was 42% (n:29), and the mortality rates at the end of the 3rd, 6th, 12th and 24th months were 61%, 76%, 84% and 85.5% respectively. There was no correlation between survival and gender in any of these periods (p>0.05). Mortality rate at the end of the third month was only affected by age (p<0.05). The mean age of the deceased was 70.67±9,8 years while the mean age of the alive was 60.20±8,5 years (Figure-1).

Survival curves showed that better prognosis was related to age below 70 (p<0.001) at the 3rd, 6th, 12th and 24th months. The mean survival time was 8.5 (95% confidence interval [CI] 0-18) days for those aged 70 or older, whereas it was 420 (95% CI 216-625) days for those aged between 59 and 69, and 422 (95% CI 73-771) days for those aged 59 or younger (Figure-2).

Duration of the illness was found to be effective on the

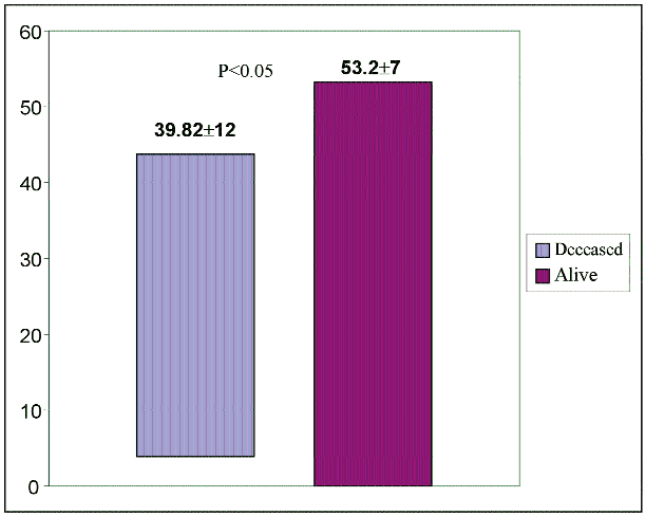

Figure-5: Average haematocrit levels in deceased and alive patients (24th month).

mortality rate at the end of the 6th month ($p<0.05$). The average illness duration of the deceased was recorded as 7.5±3,5 years, whereas this was 14±4,1 years for the subjects who were still alive (Figure-3).

Haematocrit level was the only factor that affected mortality rates at the end of the 12th and 24th months ($p<0.05$). The mean haematocrit levels of the deceased and alive subjects at the 12th months were 39.1±13% and 52.17±6,9% respectively (Figure-4). The mean haematocrit levels of the deceased and alive subjects at the 24th months were 39.82±12% and 53.2±7% respectively (Figure-5). The subjects with higher haematocrit levels had a longer survival. No statistically significant correlation was detected between the biochemical parameters of the subjects and their survival durations ($p>0.05$).

Age, duration of illness and haematocrit levels were the significant factors for survival in mechanically ventilated severe COPD subjects ($p<0.05$). The other parameters did not seem to have a substantial effect on survival ($p>0.05$).

Discussion

Data concerning the prognosis and clinical outcomes of severe COPD subjects hospitalised due to acute exacerbations is variable and insufficient and there are limited studies that show the worse prognosis of subjects who required invasive MV.

The variability in published mortality rates for subjects with COPD admitted for acute respiratory failure suggests that significant heterogeneity exists within this population. It is likely that differences in patient characteristics, more than in quality of care, account for much of the variability.

Many studies have investigated the mortality rates and factors effective on mortality in patients hospitalised with acute attacks of COPD.[8,9] Patients with comorbidities who currently used non-invasive mechanical ventilation (NIMV) or previously used NIMV or oxygen therapy for a long time were included in these studies. However, in our study, only patients included in the invasive ventilation programme were enrolled, while patients with other conditions were excluded. Most of the patients hospitalised in the ICU because of episodes of COPD are initially treated with NIMV.[10] Patients who do not respond to treatment with NIMV or those who are not suitable candidates for NIMV are connected to MVs.[8] In our ICU of 6 beds, 69 COPD patients were connected to MVs because of episodes of COPD within 2 years. Among all patients with COPD this is an expected figure. In a study, the authors stated that they applied NIMV on 75.3% of the patients, while the remaining patients underwent IMV.[10] When compared with the literature findings, our application rates are comparable. Forty-two per cent of our monitored patients died during hospitalisation. Our study also reported in-patient mortality rates and factors effective on it. In some studies performed on this subject, lower in-hospital mortality rates have been reported.[8-10] However, all patients with COPD were included in these studies. Whereas patients who underwent only IMV, those without additional diseases and patients who didn't use NIMV and/or oxygen concentrator previously or afterwards were included in our study. Mortality rates of those survived could be affected by many factors. These factors could be additional diseases or use of O_2 concentrator or NIMV. When we exclude these additional factors, the number of remaining patients is a reasonable figure. Many similar studies include these confounding factors.[11] This condition raises issues of debate. In our study the parameters of the survived and deceased patients were compared. The patients were not evaluated within themselves. Although our small sampling size is the limitation of our study, but it still conveys statistical significance. It can be a guiding tool for future studies.

In one study, the hospital mortality rate of severe COPD subjects who required MV was 52.9%.[12] Raurich et al. investigated the hospital mortalities of mechanically ventilated subjects at two years after discharge from hospital and stated that hospital mortality rate was 25.7%.[13] In the present report, hospital mortality rate was 42%, and the mortality rates at the end of the 3rd, 6th, 12th and 24th months were 61%, 76%, 84% and 85.5% respectively.

Although many studies have demonstrated age to be correlated with mortality among subjects receiving MV, but our findings revealed that advanced age increased the mortality only in the first three-month period.[10,11,14,15] Anaemia in critically ill subjects has been investigated in a number of studies, which demonstrate that anaemia is a frequent phenomenon, and that a low haemoglobin level is well tolerated by most subjects, with the possible exception of subjects with ischaemic heart disease.[16,17] Furthermore, the use of blood transfusions in critically ill subjects has been questioned because transfusions have been linked with increased mortality.[18] Chambellan et al. found a negative correlation between haematocrit and mortality/morbidity in their study.[19] In the study of Similowski et al., it was observed that low haemoglobin (Hb) levels were effective on mortality, but it was not clear why some COPD subjects had low Hb levels.[20] Lee et al. reported the fact that low Hb levels increased mortality in their series.[21] Ucgun et al. reported that low Hb level was not correlated with mortality.[12] In the present study, we revealed significantly longer survival in subjects with higher Hb levels.

Low Glasgow Coma Scores and high CO_2 levels were found to be correlated with high levels of mortality.[12] Moreover, it was concluded that sufficient metabolic compensation affected survival in a positive manner.[12] Raurich et al. have reported that high pulmonary artery pressure levels and multiorgan dysfunction increased mortality.[13] In Girgin et al.'s study, 129 COPD subjects were reviewed retrospectively and it was determined that blood gas values did not have any effect on mortality.[21] Still in a study performed by Öngel et al., an association between blood gas PO_2 and PCO_2 values and mortality, higher mortality rates were observed in patients with lower HCO3 levels.[11]

In the present study, metabolic parameters did not have any effect on survival. We did not observe any correlation among blood gas values, pulmonary artery pressures, creatinine, AST, ALT and LDH values and survival.

Despite other similar studies, we have assessed both the hospital mortality factors and the factors that affected mortality during the two-year period following discharge from hospital. We found a positive correlation between advanced age and mortality as in other studies. A study by Geneo et al. found an association between age of the patients and mortality rates.[9]

Interestingly, we also detected a positive correlation between duration of illness and survival. This correlation let us conclude that the compensatory mechanisms which evolve as the disease duration extends may have a protective effect on the subjects. The fact that subjects with higher haematocrit levels had higher survival rates supported our notion.

The main limitation of our study was its relatively small sample size. The strict intubation policy for end-stage COPD subjects in our department limited the number of these subjects in our study. Secondly, some details of history and factors that may influence the outcome may not be completely documented. Thirdly, our study findings may potentially have been influenced by confounding factors. Finally, this was a single-institution study, and although the patient population and management practice at our ICU were probably comparable with that of many other departments in the same time period, but some caution should be taken before generalising the findings to other settings. Due to these restrictions, associations should be interpreted with caution. The goal of this study and others had been to identify the important coexisting factors that help determine outcomes in subjects with COPD. A more focussed understanding of the disease will allow better utilisation of medical resources and counselling of subjects and their families regarding end-of-life decisions.

Conclusion

Age, duration of illness and haematocrit levels were the most important factors that affected survival in severe COPD subjects requiring mechanical ventilation. Other parameters were shown to have no effect on survival. It can be a guiding tool for future studies.

References

1. Saleh A, López-Campos JL, Hartl S, Pozo-Rodríguez F, Roberts CM; European COPD Audit team. The Effect of Incidental Consolidation on Management and Outcomes in COPD Exacerbations: Data from the European COPD Audit. PLoS One 2015; 10: e0134004.
2. Fuso L, Incalzi RA, Pistelli R, Muzzolon R, Valente S, Pagliari G, et al. Predicting mortality of patients hospitalized for acutely exacerbated chronic obstructive pulmonary disease. Am J Med 1995; 98: 272-7.
3. Rieves RD, Bass D, Carter RR, Griffith JE, Norman JR. Severe COPD and acute respiratory failure. Correlates for survival at the time of tracheal intubation. Chest 1993; 104: 854-60
4. Global Initiative for Chronic Obstructive Lung Disease (GOLD). [online] 2013 [cited 2014 April 17]. Avialble from: URL: http://www.goldcopd.com.
5. Moran JL, Green JV, Homan SD, Leeson RJ, Leppard PI. Acute exacerbations of chronic obstructive pulmonary disease and mechanical ventilation: a reevaluation. Crit Care Med 1998; 26: 71-8.
6. Spicher JE, White DP. Outcome and function after prolonged mechanical ventilation. Arch Intern Med 1987; 147: 421-5.
7. Global Initiative for Chronic Obstructive Lung Disease® (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. [online] 2015 [cited 2016 Jan 1]. Available from: URL: http://goldcopd.org
8. Antonelli Incalzi R, Fuso L, De Rosa M, Forastiere F, Rapiti E, Nardecchia B, et al. Co-morbidity contributes to predict mortality

of patients with chronic obstructive pulmonary disease. Eur Respir J 1997; 10: 2794-800
8. Hoo GW. The Role of Noninvasive Ventilation in the Hospital and Outpatient Management of Chronic Obstructive Pulmonary Disease. Semin Respir Crit Care Med 2015; 36: 616-29.
9 . Genao L, Durheim MT, Mi X, Todd JL, Whitson HE, Curtis LH. Early and Long-Term Outcomes of Older Adults Following Acute Care Encounters for Chronic Obstructive Pulmonary Disease Exacerbation. Ann Am Thorac Soc 2015; 12: 1805-12.
10. Aburto M, Esteban C, Moraza FJ, Aguirre U, Egurrola M, Capelastegui A. COPD exacerbation: mortality prognosis factors in a respiratory care unit. Arch Bronconeumol 2011; 47: 79-84
11. Ongel EA, Karakurt Z, Salturk C, Takir HB, Burunsuzoglu B, Kargin F, et al. How do COPD comorbidities affect ICU outcomes? Int J Chron Obstruct Pulmon Dis 2014; 9: 1187-96
12. Ucgun I, Metintas M, Moral H, Alatas F, Yildirim H, Erginel S. Predictors of hospital outcome and intubation in COPD patients admitted to the respiratory ICU fo acute hypercapnic respiratory failure. Respir Med 2006; 100: 66-7.
13. Raurich JM, Pérez J, Ibáñez J, Roig S, Batle S. In-hospital and 2-year survival of patients treated with mechanical ventilation for acute exacerbation of COPD. Arch Bronconeumol 2004; 40: 295-300.
14. Soler-Cataluña JJ, Martínez-García MA, Román Sánchez P, Salcedo E, Navarro M, Ochando R. Severe acute exacerbations and mortality in patients with chronic obstructive pulmonary disease. Thorax 2005; 60: 925-31.
15. Hébert PC, Wells G, Blajchman MA, Marshall J, Martin C, Pagliarello G, et al. A multicenter randomized controlled clinical trial of transfusion requirements in critical care. N Engl J Med 1999; 340: 409-17.
16. Corwin HL, Gettinger A, Pearl RG, Fink MP, Levy MM, Abraham E, et al. The CRIT study: Anemia and blood transfusion in the critically ill - current clinical practice in the United States. Crit Care Med 2004; 32: 39-52.
17. Vincent JL, Baron JF, Reinhart K, Gattinoni L, Thijs L, Webb A, et al. Anemia and blood transfusion in critically ill patients. JAMA 2002; 288: 1499-507.
18. Cambellan A, Chailleux E, Similowski T. ANTADIR Observatory Group. Prognostic value of the hematocrit in patients with severe COPD receiving long-term oxygen therapy. Chest 2005; 128: 1201-8.
19. Similowski T, Agustí A, MacNee W, Schönhofer B. The potential impact of anemia of chronic disease in COPD. Eur Respir J 2006; 27: 390-6.
20. Lee CM, Shieh BF, Lin FJ, Kao HT, Huang WC. Prognosis of chronic obstructive pulmonary disease after acute respiratory failure. Zhonghua Yi Xue Za Zhi (Taipei) 1989; 43: 191-6
21. Girgin NK, I?çimen R, Ar?c? S, Kahveci F, Özcan B, Kutlay O. Prognostic Factors For Patients With Chronic Obstructive Pulmonary Disease Requiring Invazive Mechanical Ventilation. Turkiye Klinikleri Arch Lung 2007; 8: 101-5.