Does admission from different sources have any influence on intensive care unit outcome in COPD patients?

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ÖZET

KOAH'lı hastaların farklı servislerden kabul edilmeleri yoğun bakım ünitesi sonuçlarını etkiler mi?

Bu çalışmanın amacı; yoğun bakım ünitesi (YBÜ)'nde takip edilen kronik obstrüktif akciğer hastalığı (KOAH) olan hastaların bu üniteye gelmeden önce takip edildikleri bölümlerin ve bu bölümlerle ilgili faktörlerin hastaların prognozunu nasıl etkilediğini araştırmaktır. Retrospektif, gözlemsel kohort çalışması. Hastaların demografik özellikleri, hastalıklarının ve hava yolu obstrüksiyonlarının ağırlığı, komorbiditeleri, hangi bölümlerden YBÜ'ye kabul edildikleri [göğüs hastalıkları servisi (GHS), acil servis (AS)], entübasyon öncesi ve sonrası dönemde noninvaziv mekanik ventilasyon (NIMV) kullanımları ve kan gazları kaydedildi. İstatistiksel analiz olarak t-test, ki-kare testi ve lojistik regresyon analizi kullanıldı. Çalışmaya YBÜ'de takip edilen, 52'si GHS'den, 52'si AS'dan kabul edilen toplam 104 KOAH'lı hasta alındı. İki grup karşılaştırıldığında yaş, cinsiyet, komorbidite, hava yolu obstrüksiyonunun ağırlığı ve yatış "Acute Physiology Assessment and Chronic Health Evaluation (APACHE)-II" skoru açısından anlamlı farklılık bulunmadı. AS'dan kabul edilen hastalar daha hipoksemikti ve daha sık toplum kökenli pnömoni ile başvurmuşlardı; GHS'den kabul edilen hastalarda ise daha sık entübasyon öncesi ve sonrası dönemde NIMV kullanımı ($p< 0.001$) ve daha yüksek HCO_3^- değerleri mevcuttu. Potansiyel risk faktörlerinden yüksek APACHE-II skoru ve mekanik ventilasyon süresi mortalite için bağımsız risk faktörleri olarak saptandı. KOAH'lı hastaların bazı yatış yeri özellikleri anlamlı farklılık göstermesine rağmen GHS'den veya AS'dan kabul edilmeleri prognozlarını ve YBÜ sonuçlarını olumsuz etkilememektedir.

Anahtar Kelimeler: *KOAH, yoğun bakım ünitesi, yatış yeri, prognoz.*

SUMMARY

Does admission from different sources have any influence on intensive care unit outcome in COPD patients?

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Influence of admission source and admission source related factors on intensive care unit (ICU) outcome have not known much in patients with chronic obstructive pulmonary disease (COPD). The aim of the study was to investigate if admission source and related factors have any impact on ICU outcome in patients with COPD. A retrospective observational cohort study. Demographics of the patients, severity of admission disease and airflow limitation, comorbidity, source of admission [pulmonary ward (PW), emergency department (ED)], noninvasive mechanical ventilation (NIMV) therapies in the pre-and post-intubation period, and blood gases were recorded. T-test, chi-square test and logistic regression analysis were used for statistical analysis. One hundred and four patients were included in the study. Fifty two of them were admitted from PW and 52 from ED. There were no significant difference between age, gender, comorbidity, severity of airflow limitation and admission Acute Physiology Assessment and Chronic Health Evaluation (APACHE)-II scores among the patients admitted from PW and ED. While the patients admitted from ED were more hypoxemic, admitted with community acquired pneumonia more frequently, the patients admitted from PW, received NIMV trial in pre-intubation and post-extubation period more frequently ($p< 0.001$) and had higher HCO_3^- levels. There was no significant difference in the ICU survival across the groups. Among these potential risk factors higher APACHE-II scores and duration of mechanical ventilation were independent risk factors for the mortality. These results suggest that while some of the admission characteristics were significantly different, admission from ED or PW did not have negative influence on ICU course and outcome in patients with COPD.

Key Words: *COPD, intensive care unit, admission source, outcome.*

Mortality associated with hospitalization for chronic obstructive pulmonary disease (COPD) can be considerable. In-hospital mortality is more than 20% among patients who require admission to intensive care unit (ICU) (1,2). Hospital acquired infections, weaning failure and prolonged mechanical ventilation increase mortality in these patients. Prospective randomized controlled studies have shown that addition of noninvasive mechanical ventilation (NIMV) to standard treatment reduces the need for endotracheal intubation, lowers hospital mortality and shortens the length of stay in selected patients with COPD (3-5). There have been many studies that investigate the factors associated with ICU mortality in patients with COPD and, older age, higher Acute Physiology Assessment and Chronic Health Evaluation (APACHE)-II scores, comorbidities, ventilator associated pneumonia (VAP), severity of airflow limitation, and prolonged mechanical ventilation (MV) have been reported as risk factors (6,7). On the other hand the effects of admission source and admission source related factors on ICU outcome have been studied less in these studies. The proportion of COPD patients admitted to ICU from pulmonary wards (PWs), emergency departments (EDs) other ICUs and wards and impact of these transfers on ICU outcome have not been known much yet. The aim of the study is to investigate if admission source related characteristics have any impact on ICU outcome in patients with COPD.

MATERIALS and METHODS

The study was conducted at a pulmonary ICU of a 1500 bed university hospital. All patients with respiratory failure were admitted to this pulmonary ICU and followed by an intensivist and one or two residents of pulmonary diseases. For this study, the medical records of 104 mechanically ventilated COPD patients were evaluated retrospectively. When patients were admitted to ICU, APACHE-II, sequential organ failure assessment (SOFA) score, pneumonia patient outcomes research team (PORT) severity index were calculated and noted to database (8). Besides comorbidities (heart failure, hypertension, coronary artery and neurological disease, chronic renal failure and diabetes mellitus), pulmonary function test (PFT) results, presence of community-acquired pneumonia (CAP), duration of MV, ICU, hospital stay, data related to the trial of pre-intubation NIMV, blood gases recorded before and after NIMV therapy, the use of long term oxygen therapy (LTOT), prior stay in the ED or PW were also recorded.

For the diagnosis of COPD, post-bronchodilator or best-recorded forced expiratory volume in 1 second (FEV_1) less than 70% predicted, with FEV_1/FVC less than 70% measured were accepted (9). Radiographic evidence of hyperinflation or typical clinical history of chronic cough and dyspnea in a smoker combined with compatible physical signs such as wheezing and persistent airflow limitation pattern on ventilator flow-volume curves were accepted as supportive of the diagnosis of COPD, in the absence of lung function measurements. Sixty-five (63%) of the 104 patients had PFTs.

Medical Therapy and NIMV Protocols

In our institution for the management of respiratory failure due to COPD, NIMV is administered in the PW and invasive mechanical ventilation in the ICU. NIMV is not routinely prescribed in the ED. In both PW and ED, patients received oxygen therapy, inhaled beta-agonists, ipratropium bromide, antibiotics and intravenous steroids (40-60 mg/day prednisone, for one week) at first. In the ED patients were intubated depending on the arterial blood gas analysis results, clinical status and the state of consciousness usually with the decision of the emergency medicine physician. In the PW NIMV was first tried to patients with pH < 7.35 or arterial CO_2 tension > 45 mmHg in the absence of metabolic acidosis; arterial O_2 tension < 60 mmHg or O_2 saturation < 90% with less than 50% supplemental FiO_2; respiratory rate > 35/minute and to patients using accessory respiratory muscles. NIMV was performed with BiPAP S/T (Respironics), Cesar, Horus (Teima), Vela (Viasys) ventilators. The ventilatory support system was initiated at a level of 5 cmH_2O of expiratory positive airway pressure (EPAP or PEEP) and a pressure support (PS) level of 10 cmH_2O in a spontaneous mode, than pressure support level was titrated in increments of 2 cmH_2O. Trained pulmonary residents performed NIMV therapies with close pulse oxymetry and blood gas monitoring. Patients who were unresponsive to NIMV therapy (pH < 7.35, less than 15-20% decrease in $PaCO_2$ while O_2 saturation ≥ 90%, < 20% decrease in respiratory rate compared with the spontaneous respiratory rate) and who had altered mental status were accepted to ICU and intubated with the decision of the intensivist or the pulmonary residents.

After extubation if patients' blood gases were stable they were transferred to the PW; if they were hypercapnic or hypoxemic they were treated with NIMV in ICU and then transferred to the ward after stabilization with this therapy.

Statistical Analysis

Data are reported as means ± standard deviations (SD). Categorical variables were compared by Fisher's exact or Chi-Square tests. A value of $p< 0.05$ was considered to be statistically significant. Student's t-test was used for continuous variables. Nonparametric analysis using the Mann-Whitney U test was used for data with abnormal distributions.

Logistic regression analysis (LR) was used to evaluate the impact of potential risk factors on the mortality, controlling for the remaining variables. Stepwise backward deletion method was used to eliminate nonsignificant candidates from the LR model. The potential independent risk factors were those variables found to have ≤ 0.05 in univariate analysis. Odds ratios (OR) and 95% confidence interval (CI) were calculated in accordance with the standard methods. During the LR 3 categorical (pre-intubation NIMV, CAP, LTOT) and 3 numerical variables (APACHE-II, age, duration of MV) were entered for analysis. These were variables that were found to have a significant impact ($p< 0.05$) on development of acute respiratory failure (ARF) in univariate analyses. All potential explanatory variables included in the LR were subjected to a correlation matrix for analysis of co linearity. Variables in association with each other were not included in the LR ($p< 0.05$, $r> 6$).

The final multivariate model was evaluated for calibration using the Hosmer-Lemeshow goodness-of-fit statistic (in which $p> 0.05$ indicates a good fit). All data were analyzed using SPSS release 11.5.

RESULTS

Fifty-two (50%) patients admitted from PW and 52 patients from ED (50%), a total of 104 COPD

patients were included in the study. Three patients admitted from other ICUs, 2 from home and 2 from other wards were excluded from the study. The causes of ICU admissions were COPD acute exacerbations in 60 (59%), CAP in 37 (35%) and cardiac ischemia in 7 (7%) of them. Patients from ED were admitted to ICU for MV and none of them had received NIMV before intubation. Among the patients from PW, 36 (69%) of them had received NIMV before their admission to ICU. Mean arterial blood gas values of the patients before NIMV trial were as follows as mean ± SD; pH: 7.32 ± 0.3, PaO_2: 53 ± 13 mmHg, $PaCO_2$: 68 ± 17 mmHg, O_2 saturation %: 82 ± 12, PaO_2/FiO_2: 180 ± 61 mmHg. Patients with unsuccessful NIMV trial received NIMV for a mean of four days (median 1), 4 hours in a day (median 3) and three times a day (median 2.5). The mean maximum inspiratory and expiratory pressures used were 13 and 6 cmH_2O respectively.

Mean PORT severity index of the patients with CAP was 150 ± 51. Mean WBC counts in patients with and without CAP were 13995 ± 5837 and 10563 ± 4567 mm^3/mL respectively (p= 0.003).

There were no significant difference between age, gender, comorbidity, severity of airflow limitation, and admission APACHE-II scores between the patients admitted from PW and ED (Table 1). While the patients admitted from ED had lower pre-intubation PaO_2/FiO_2 values, admitted with the CAP diagnosis more frequently, patients admitted from PW had higher HCO_3^- levels, received NIMV trial in pre-intubation and post-extubation period more frequently (p< 0.001) (Table 2). There was no significant difference in the duration of prior stay in the PW or ED, MV, ICU, hospital stay or ICU survival across the groups. Table 3 shows the potential risk factors for the mortality. Among these potential risk factors admission from PW or ED did not enter into the LR since it was not significantly different across the groups in univariate analysis. Serum HCO_3^- levels were not entered into LR since it is highly correlated with unsuccessful NIMV. While the duration of MV and APACHE-II were significant predictors for mortality, unsuccessful NIMV trial was not. Even patients with unsuccessful NIMV trial had better survival than the others.

DISCUSSION

The ICU outcomes of patients with COPD show no difference depending on being admitted from ED or PW and receiving NIMV first for a while in PW. To the best of our knowledge no study has assessed the influence of admission source on the outcome of patients with COPD before. However patients with COPD may be admitted from very different sources such as ED, PW, other ICU or wards, chronic care facilities and operation rooms to ICU. Recent studies have reported that admission source may have important impact on ICU outcome. For example Combes and coworkers have found in a recent study that referral from another ICU was a strong and independent predictor of ICU death in their mixed ICU population (10).

Table 1. Baseline characteristics of the patients admitted from PW or ED.

	Admissions from the PW (n= 52, mean ± SD or %)	Admissions from the ED (n= 52, mean ± SD or %)	p
Age	67 ± 8	68 ± 10	0.603
Gender, female (%)	8 (15)	14 (27)	0.123
APACHE-II	19 ± 4	19 ± 5	0.882
SOFA	4 ± 1	6 ± 3	0.185
Comorbidity (%)	21 (40)	26 (50)	0.307
FEV_1 (% predicted)	35 ± 13	39 ± 12	0.182

PW: Pulmonary ward, ED: Emergency department, APACHE-II: Acute Physiology Assessment and Chronic Health Evaluation-II, SOFA: Sequential Organ Failure Assessment, FEV_1: Forced expiratory volume in 1 second.

Table 2. ICU admission characteristics of the patients.

	Admission from the PW (n= 52, mean ± SD or %)	Admission from the ED (n= 52, mean ± SD or %)	p
Pre-intubation blood gases			
pH	7.28 ± 0.11	7.28 ± 0.14	0.979
PaO_2	48 ± 13	52 ± 18	0.331
$PaCO_2$	71 ± 21	61 ± 24	0.051
SaO_2%	75 ± 13	78 ± 20	0.413
PaO_2/FiO_2 (mmHg)	190 ± 51	157 ± 60	0.031
HCO_3^- (mEq)	34 ± 7	27 ± 7	0.0001
Pre-intubation stay in ED or PW (days)	4 ± 6	2 ± 2	0.090
CAP (%)	11 (23)	26 (50)	0.008
Previous NIMV trial (%)	36 (69)	0	0.001
Post-extubation NIMV (%)	25 (48)	7 (13)	0.001
Duration of MV	13 ± 8	14 ± 10	0.608
Length of ICU	19 ± 23	21 ± 23	0.737
Length of hospital stay	36 ± 36	29 ± 26	0.297
Mortality (%)	11 (20)	17 (32)	0.131

ICU: Intensive care unit, PW: Pulmonary ward, ED: Emergency department, CAP: Community-acquired pneumonia, NIMV: Noninvasive mechanical ventilation, MV: Mechanical ventilation.

Table 3. Assessment of potential risk factors for the mortality with univariate and logistic regression analyses results.

Variable	Survivors n= 70 (mean ± SD or %)	Nonsurvivors n= 34 (mean ± SD or %)	p	OR (95% CI)	p
APACHE-II	18 ± 4	21 ± 5	0.0001	1.3 (1.02-1.56)	0.004
Age (years)	72 ± 9	66 ± 9	0.001	0.9 (0.91-1.08)	0.935
FEV_1 (%)	36 ± 14	40 ± 11	0.245		
Comorbidity (%)	28 (39)	23 (68)	0.007	3.5 (0.7-16)	0.111
CAP (%)	20 (33)	17 (57)	0.029	1.3 (0.3-5.8)	0.721
NIMV trial (%)	31 (44)	6 (18)	0.009	0.026 (0.08-0.74)	0.026
Duration of MV (days)	12 ± 8	17 ± 10	0.012	1.5 (1.04-1.3)	0.004
PaO_2/FiO_2 (mmHg)	179 ± 66	165 ± 54	0.401		
HCO_3-(mEq)	32 ± 8	27 ± 8	0.002		
$PaCO_2$ (mmHg)	71 ± 22	58 ± 21	0.004		
Admission from PW (%)	30 (47)	8 (42)	0.714		

APACHE-II: Acute Physiology Assessment and Chronic Health Evaluation-II,
CAP: Community-acquired pneumonia, NIMV: Noninvasive mechanical ventilation, MV: Mechanical ventilation.

ICUs admit patients from different sources in different proportions depending on the institutional policies and characteristics. Nevins and coworkers reported that they admitted 81% of patients from home, 13% from chronic care facilities, and 1% from acute care hospitals (11). Results of our study showed that, similar proportions of patients were admitted from ED and PW to our

ICU and admission source does not have any influence on ICU outcome in patients with COPD. While patients admitted from the ED had significantly more frequent community acquired pneumonia and they were more hypoxemic; patients admitted from PW were more hypercapnic, received NIMV in pre-intubation and post-extubation period more frequently, but they had similar mortality rate. Even patients with unsuccessful NIMV trial had better survival than the other patients.

Studies have shown that, the use of NIMV on respiratory wards is both feasible and clinically effective at reducing the demand for invasive ventilatory support and in-hospital mortality in patients with COPD. A survey of hospitals in 1997 showed that, where it was being used, NIMV was being undertaken on a general ward in 16%, on a respiratory ward 24%, on high dependency unit 12%, on ICU in 13% and in a combination in 34% (12). Nevertheless, NIMV is not successful in all cases, with a reported failure rate of 7-50% (13). Patients with moderately severe exacerbations of COPD who receive NIMV on a general or respiratory ward with experienced nursing staff and physicians do appear to benefit compared to controls. However, patients with more severe exacerbations (pH< 7.30) treated in such a setting with NIMV did not derive a mortality benefit compared with controls (5). Moreover, these patients had a mortality rate greater than twice that of similar patients in other studies treated with NIMV in the ICU (4). Hence, patients with more severe exacerbations benefit from closer monitoring in a high dependency unit or ICU to evaluate the response to treatment and to facilitate the endotracheal intubation with NIMV failure. ICU outcome of patients with COPD who treated with NIMV previously has been less extensively studied in literature. In a recent observational study Esteban et al. found that patients with ARF who were intubated after having first received NIMV had a higher mortality rate than those who were intubated without having received NIMV (48% vs. 31%, p= 0.01) (14). On the other hand, among patients with COPD ventilated because of ARF, ICU mortality was similar in those intubated after a failed attempt at NIMV and in those treated with MV (27% vs. 24%, p= 0.91) (14).

Sixty-one percent of the patients required NIMV after extubation in our study. Despite this, mortality was low in this group. The use of NIMV to avert the need for reintubation in patients with respiratory failure after extubation has been studied in several studies. Two randomized controlled trials have suggested that the use of NIMV did not significantly alter the need for reintubation (15,16). But patients with COPD were not evaluated in these studies. In an uncontrolled case series Hilbert et al. described a decreased rate of intubation compared with historical controls among COPD patients who developed respiratory distress after extubation who were treated with NIMV (17). Our results are similar to these results but our aim was not to test this hypothesis and data was not randomized and controlled.

The major limitation of our study is that it is retrospective and not randomized controlled or case-control. Because of these reasons distribution of some factors such as CAP, unsuccessful NIMV, hypercapnia and hypoxemia among the groups are not balanced. To compensate this problem we used multivariate logistic regression analyses. Another limitation is that, our results are derived from the data collected in only one center. Therefore, our results may not be applicable to other hospitals or ICUs with different case mixes and admission policies.

In conclusion, results of this study showed that, patients admitted from ED were more hypoxemic compared to those admitted from PW who were more hypercapnic with compensated respiratory acidosis. This was linked to increased diagnosis of CAP in patients admitted from ED. But these characteristics of the admission source did not influence ICU outcome in patients with COPD. Even unsuccessful NIMV trial did not influence ICU outcome negatively. Influence of different ICU admission policies on ICU outcome in patients with COPD is not clear yet. Multicentric studies and meta-analyses that will compare the policies of different centers are needed.

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