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ORIGINAL RESEARCH **INTENSIVE CARE**

Prognosis and evaluation of patients with chronic obstructive pulmonary disease intubated in intensive care unit

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Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) is the third most common cause of death worldwide. It is important to prevent this problem from a human as well as an economic point of view. With ever-increasing number of people requiring hospitalization, there is a need to increase intervention and treatment facilities and to develop new treatment approaches necessary to reduce mortality. We evaluated the course of the disease of patients who were already admitted to the intensive care unit with respiratory failure due to COPD, underwent acute exacerbation requiring intubation and invasive mechanical ventilation (IMV).

Methodology: Our study included 149 patients who were admitted to the intensive care unit with respiratory failure due to COPD exacerbation only, who underwent intubation and IMV while being followed up in the intensive care unit. The demographic data of patients diagnosed with COPD before hospitalization, length of stay in the intensive care unit and service, comorbid diseases, type of respiratory support device before IMV, current pneumonia status during exacerbation, and laboratory values were recorded. The relationship between the in-hospital exacerbation in COPD and the prognosis was evaluated.

Results: The mean intensive care unit stay of these patients was 3.74 ± 4 days. Reintubation was needed in 56 patients (37.6%), 30 patients (20%) could not survive. A statistically significant difference was found between pneumonia developing in the hospital and the mortality (P = .01).

Conclusion: While studies are ongoing for the prevention of COPD exacerbations, more studies are needed to develop approaches and treatments for patients with COPD who develop acute respiratory failure due to their existing disease and need intensive care, as the associated mortality is very high.

Abbreviations: COPD - Chronic obstructive pulmonary disease; IMV - Invasive mechanical ventilation; HFNC - High Flow Nasal Cannula; NIMV - Non-invasive mechanical ventilation; CRP – C-Reactive protein; GOLD - Global Initiative for Chronic Obstructive Lung Disease

Key words: Intubation; Invasive mechanical ventilation; Chronic Obstructive Pulmonary Disease; COPD; High Flow Nasal Cannula; HFNC

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1. Introduction

According to the GOLD (Global Initiative for Chronic Obstructive Lung Disease) report, which is updated every year and is widely accepted, chronic obstructive pulmonary disease (COPD) is characterized by persistent airflow limitation and respiratory symptoms due to persistent airway and/or alveolar disruptions, usually caused by severe exposure to harmful particles or gases and host factors including abnormal lung development.[1] When exposure to risk factors such as increased air pollution, low socioeconomic conditions, and smoking is combined with genetic factors, this disease, which occurs with permanent airway damage in some people, increases the intensive care occupancy rates, especially during winters, with secondary infections.[2] Each episode and each hospitalization in the intensive care unit (ICU) causes an increased mortality and morbidity for the patient, and a heavy economic burden on the hospitals.

Endotracheal intubation and invasive mechanical ventilation (IVM) are the gold standard methods used to protect the airway and maintain respiration in cases of acute respiratory failure, where support devices such as non-invasive mechanical ventilation (NIMV) or high-flow nasal cannula (HFNC) do not help.[3] As with every invasive procedure, intubation has some complications and can increase mortality.[4]

In patients hospitalized with COPD exacerbation and acute respiratory failure, the first treatment approach is usually NIMV.[1] Regular and continuous use of NIMV shortens hospitalization and reduces mortality.[5] Despite all this, in cases where pharmacological and NIMV support is not adequate, IMV offers a chance to ensure continuous oxygenation. Predicting the length of hospital stay in a patient who is intubated and connected to IMV, and continuing the treatment and follow-up is important. Equally important are to determine the right extubation time. Much depends upon the foresight and experience of the intensive care physician, as well as the professional grooming of the ICU team to protect the patient from the complications of intubation and IMV. In addition, many factors such as the patient's current infection status, comorbid diseases, time of arrival at the hospital, and the nutritional status also determine the effect of IMV on mortality and morbidity.

We evaluated the prognosis during and after intubation in COPD patients who had to be intubated and shifted to IMV after acute exacerbations and to determine the factors that may affect the prognosis in this cohort of the patients.

2. Methodology

After approval by the local ethics committee, patients followed up with the diagnosis of 'COPD exacerbation and acute respiratory failure' in our ICU were examined from our hospital's electronic data system between January 2017 and October 2021. Data of 377 patients was retrieved from the electronic system of our hospital and examined.

Inclusion criteria in our study was; patients over the age of 18 y, who were previously diagnosed with COPD by a pulmonologist and were followed up in our ICU within the above-mentioned date range. Patients who could not be weaned off an invasive mechanical ventilator, undergoing tracheostomy were excluded. Patients diagnosed with myocardial infarction, acute cerebrovascular accident, acute decompensated heart failure, acute kidney injury, acute pulmonary embolism that may affect the clinical situation, were also excluded. In addition, patients who were intubated before being admitted to our ICU were also excluded from the study. This decision was taken due to the problems of previously intubated patients to reach the reasons for intubation. In addition, it was difficult to obtain treatment data before intubation. After scrutiny, a total of 149 patients were included in our study.

The patient's demographic data (age, gender), comorbidities, and the years since diagnosed with COPD were noted. Other data recorded, included the duration of intubation, the type of support ventilator (HFNC, NIMV) used before IMV (if any), and the number of days in the tertiary ICU, the recurrent intubation status, the number of hospital admissions in the last one year, the presence of infection and the prognosis after tertiary ICU. The relationship between the first hospitalization and last hospitalization laboratory values, e.g., white blood cell, albumin, CRP, hematocrit, hemoglobin, sodium, potassium, creatinine, aspartate transaminase (AST), alanine aminotransferase (ALT), related to the poor prognosis of the patients and mortality were evaluated. The relationship between the presence of infection and the prognosis was evaluated. The laboratory tests show the malnutrition and infection status of the patients. HFNC therapy and NIMV therapy are applied to patients admitted to our ICU with a diagnosis of COPD before IMV. We also prefer one of the NIMV or HFNC therapies for COPD patients after weaning off IMV. In mild acute hypercapnic patients who had difficulty in adapting to NIMV, the HFNC therapy was first applied. NIMV therapy was preferred primarily in patients with severe respiratory acidosis and no contraindications for NIMV application. HFNC therapy is used for patient comfort and to avoid pneumothorax complications as far as possible.

Statistical analysis

The data were analyzed with the SPSS 28.0 package. Continuous variables were expressed as mean ± standard deviation, and categorical variables as numbers and

Table 1: Frequency of co-existing diseases

Disease	N (%)
Cardiovascular diseases (hypertension, coronary artery disease, congestive heart failure)	84 (56.4)
Endocrinological diseases (diabetes, chronic kidney disease)	35 (23.5)
Diabetes mellitus	32 (21.4)
Chronic kidney isease	3 (0.2)
Malignancy	13 (8.7)
bladder cancer	1 (0.6)
Lung cancer	12 (6.9)
Breast cancer	1 (0.6)
Multiple myeloma	1 (0.6)
pulmonary embolism	8 (5.4)
neurological diseases	13 (8.7)
Alzheimer's Disease	4 (2)
Epilepsy	1 (0.6)
CVA	8 (5.4)

percentages. The differences between the categorical variables were analyzed by Chi-square analysis. The distribution of variables was measured with the Kolmogorov Smirnov test. The Mann-Whitney U test was used in the analysis of quantitative independent data. $p < 0.05$ was considered statistically significant in the analyses.

3. Results

A total of 149 patients, 40 of whom were females (26.8%), were included in our study. The mean age of the patients was 71.2 ± 11.37 years. They were followed for COPD for a mean of 8.7 ± 6.7 y. The average frequency of admission was 5 times in the last one year, and 103 (69.1%) patients had additional diseases detailed in Table 1.

The patients stayed in the 3rd level ICU for an average of 9.54 ± 6 days. The stay was for a minimum of 5 days. A total of 30 (20%) patients expired.

The mean intubation time was 3.74 ± 4 days; re-intubation after extubation was required in 56 (37.6%) patients. HFNC was given to 33 (22.1%) patients before intubation. The remaining 116 (77.9%) patients received NIMV support before intubation. When intubation time and mortality were compared, no statistically significant relationship was found between them (P = 0.77). Similarly, when the intubation time and mortality of the patients, who received HFNC support before intubation were compared, no statistically significant differences was found between them (P = 0.334 and P = 0.441 respectively).

Signs of pneumonia were found in 38 (22.5%) patients in addition to COPD exacerbation, the infection suspected to have developed in 95 (63.8%) patients

Table 2: Relationship between first hospitalization laboratory values and intubation time. length of stay in ICU. re-intubation status. mortality

Parameter	Average value (Initial hospitalization values)	Re-intubation status (P)*	Intubation time (P)	Mortality (P)*	Number of hosp days in 3rd level ICU (P)	Number of hosp days in chest ICU
WBC count (10^3/ml)	12.3 (n=149)	0.127	0.46	0.248	0.336	0.531
CRP (mg/L)	20.9 (n=148)	0.018	0.18	0.02	0.02	0.871
Hb (g/dL)	11.7 (n=147)	0.227	0.89	0.148	0.266	0.06
Sodium (mEq/L)	140.2 (n=148)	0.201	0.3	0.43	0.182	0.673
Potassium (mEq/L)	4.2 (n=148)	0.028	0.39	0.205	0.16	0.483
ALT (U/L)	42.8 (n=148)	0.899	0.36	0.07	0.109	0.492
AST (U/L)	46.1 (n=148)	0.926	0.4	0.07	0.12	0.649
Creatinine (mg/dL)	30.3 (n=148)	0.708	0.795	0.701	0.127	0.293
Albumin (U/L)	1.2 (n=147)	0.011	0.097	0.14	0.27	0.001

**Mann Whitney U test*

Table 3: Relationship between discharge laboratory values and intubation time. length of stay in intensive care units. re-intubation status. mortality

laboratory values	average value Discharge values)	Re-intubation status (P)*	Intubation time (P)	Mortality (P)*	Number of hosp days in the 3rd level ICU (P)	Number of hosp days in chest ICU
WBC count (10^3/ml)	10.6	< 0.001	0.443	0.007	0.346	0.046
CRP (mg/l)	35	< 0.001	0.825	< 0.001	0.953	0.335
Hb (g/dL)	10.6	0.209	0.001	0.753	0.198	0.559
Sodium (mEq/l)	138	0.01	0.189	< 0.001	0.853	0.681
Potassium (mEq/l)	4	0.701	0.148	0.069	0.250	0.212
ALT (U/l)	36	0.171	0.865	0.032	0.380	0.44
AST (U/l)	38	0.159	0.796	0.004	979	0.353
Creatinine (mg/dl)	1.1	0.209	0.352	0.416	0.818	0.576
Albumin (U/l)	16.7	0.222	0.492	0.002	0.833	0.005

**Mann Whitney U test*

during hospitalization. When the intubation time and pneumonia development status were examined, no statistically significant difference was found (P = 0.167).

A statistically significant difference was found between pneumonia and hospitalization and mortality of the patients (p < 0.01). There was also significance co-relationship between hospital acquired pneumonia and the mortality (P = 0.01).

The statistical correlations between laboratory findings of the patients at the hospitalization and discharge are shown in Tables 2 and 3. The lab data shows values of white blood cell count, C-Reactive protein (CRP), hemoglobin, sodium, potassium, albumin, creatinine, ALT, and AST. The mortality rate, intubation time, frequency of reintubation, and number of hospitalization days are also given.

4. Discussion

While COPD was the 6th most common cause of death in the 90s, the data for the year 2020 shows that this disease is now the 3rd leading cause of death.[6] Contrary to what was previously known, not only smoking but also air pollution, sociodemographic differences, occupational factors, and infections are risk factors for this disease. It has such a widespread risk factors, and continues to be a curse for the societies and governments due to loss of workforce, economic losses, and high morbidity and mortality.

The female preponderance (26%) and the mean age of all patients (71 y) in our study was similar to the earlier studies.[7,8]

Our patients with a diagnosis of COPD who needed tertiary level intensive care were in ICU for approximately 10 days, and they stayed in the second level chest ICU. The maximum period was about 3 weeks, and it is a serious burden for both the physician and the healthcare staff. As the length of the stay of each patient in the hospital increases, it also increases the economic burden for the hospital. We could collect adequate information regarding the length of hospitalization of patients with respiratory failure diagnosed with COPD and hospitalized in the ICU. In a study conducted by Li et al. published in 2021, 1116 patients were examined and the average hospital stay was found to be 12.28 days.[9] We think that the higher number of days spent in ICUs is due to the low number of patients participating in our study and the fact that only patients requiring intensive care and intubation were included in our study.

As is known, the frequency and the severity of COPD is increased with advanced age, and it usually co-exists with cardiovascular and metabolic diseases together.[10] In our study, 56% of our patients had cardiovascular disease and 23% had a metabolic disease. This concurrence can further complicate the course of the disease and the management.

Patients with a diagnosis of COPD admitted to the ICU with respiratory failure should receive either NIMV or HFNC if they do not require emergency intubation according to availability in the hospital. HFNC has become popular recently, especially in respiratory failure due to COVID-19. It was applied to 33 (21%) of our patients who presented with respiratory failure due to COPD and did not have type-2 respiratory failure, had

no compliance problems. No significant statistical relation was found with it by the intubation time and the mortality (P = 0.334 and P = 0.441).[11,12] In the study of Cortegiani et al., it was stated that HFNC could be used in some COPD cases with mild to moderately severe COPD, yet its advantage over NIMV could not be demonstrated.[13]

Pneumonia is one of the most important causes of mortality, especially in elderly patients with comorbidities. Considering that COPD is also associated with a disease seen after middle age and many additional comorbidities, finding a statistically significant difference between hospital-acquired pneumonia and hospitalization and mortality shows parallelism with different studies (P = 0.01).[14] Some studies have shown that the duration of intubation and intensive care stay is increased with hospital-acquired pneumonia, there are no studies has shown that COPD exacerbations secondary to pneumonia can prolong the current intubation period.[15–17]

As a result; COPD is still the third most common cause of death in the world. It is undoubtedly very important to prevent respiratory failure due to COPD exacerbations, which deteriorates the quality of life of people for many years and is a heavy economic burden on the state and health institutions. However, it is very important to develop different treatment methods for people who are already diagnosed with COPD and to develop appropriate intensive care protocols for these patients in ICUs in terms of reducing mortality and comorbidities. This study allowed us to review the literature on COPD in the last 10 years. In the last 5 years, we have not seen a sufficient number of studies on evaluations and intensive care approaches, especially with the causes of COPD exacerbations. We believe that more research is needed in COPD and intensive care follow-up to develop different respiratory support device models, investigating the factors of community-acquired pneumonia, and taking appropriate prevent measures. Also, according to our study, there was no statistically significant difference in mortality between HFNC and NIMV applications in COPD patients before intubation.

5. Conclusion

In conclusion, according to our study, there was no statistically significant difference in mortality between HFNC and NIMV applications in COPD patients before intubation. Therefore, we believe that the severity of respiratory acidosis and patient comfort should be taken into account in the choice of HFNC and NIMV. We believe that it would be more appropriate not to delay endotracheal intubation in patients with severe respiratory failure.

6. Data availability

Numerical data involved in this study is available with the authors.

7. Conflict of interest

The authors declare no conflict of interest

8. Authors contribution

MK: Planning, design and writing of the study

MY: Data collection, literature review

OM: Data collection, getting study ready for publication, making revisions

GD: Data collection, interpretation of statistical data

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