

How Successful is Non-Invasive Ventilation Treatment that is Initiated in the Emergency Department in Cases of COPD Exacerbations with Acute Hypercapnic Respiratory Failure? Can We Predict Treatment Failure?

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Abstract

Objective: We aimed to investigate the success rate of non-invasive ventilation (NIV) in wards and the predictors of failure in cases of chronic obstructive pulmonary disease (COPD)-related acute hypercapnic respiratory failure (AHRF).

Methods: The was a retrospective study conducted in a tertiary teaching hospital between May 2011 and 2013. Patients who were admitted to the emergency department (ED) because of COPD with AHRF were evaluated; 544 patients who initially received NIV in ED and were transferred to wards were included. Patient characteristics, baseline and follow-up pH values, and partial arterial carbon dioxide (PaCO₂) values were recorded. Baseline pH values were categorized as severe (pH<7.26), moderate (pH≥7.26–7.30), and mild (pH≥7.30) acidosis. According to the in-hospital outcome, patients were classified in 2 groups: Group 1: home discharge, Group 2: death or intensive care unit transfer.

Results: Treatment resulted in success in 477 (88%) patients. Albumin levels were significantly low and the mean Charlson index (CI) score was significantly high in Group 2. Admission pH and PaCO₂ values did not affect the treatment outcome. Patients in Group 2 had higher PaCO₂ and lower pH values as well as a lower level of decrease in PaCO₂ values within 2 hours of treatment in ED. Similarly, higher PaCO₂ and lower pH values at the end of the first day in wards were indicative of NIV failure (p<0.05).

Conclusion: The success rate of NIV in wards in cases of AHRF is high. Patients with low albumin levels and higher CI scores have worse response to treatment. pH or PaCO₂ values after a few hours of treatment and not the baseline pH or PaCO₂ values are better predictors than the baseline pH and PaCO₂ values.

Keywords: Acute hypercapnic respiratory failure, arterial blood gas, chronic obstructive pulmonary disease, non-invasive ventilation



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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a chronic progressive disease and a leading cause of mortality and morbidity (1). Acute exacerbations of COPD worsen the quality of life, increase hospital admissions, and enhance the rate of mortality (2). Respiratory failure is observed in 1 out of 5 patients with COPD exacerbations, and non-invasive ventilation (NIV) has been the primary treatment choice for these patients (3, 4).

The use of NIV for the treatment of acute hypercapnic respiratory failure (AHRF) is mostly reported in intensive care units (ICUs) or specialized respiratory care units, and the use of NIV outside the ICU remains controversial (5-10). However, the limited number of available beds in the ICU, the higher cost of treatment, and the fact that not all patients have a poor general condition requiring close monitoring necessitate NIV treatment outside the ICU (11). A number of studies have investigated the success of NIV treatment in non-ICU clinics. The reported success rates vary in a wide range between 44% and 90% according to the management units, patient groups, and disease stages (12, 13). Little is known on the predictive factors of NIV failure in wards. Male gender, advanced age, and baseline and follow-up arterial blood gas (ABG) values are the reported parameters that predict NIV failure

in wards (14-17). Still, because the data on these parameters are insufficient to provide foresight on NIV failure, clinicians struggle with regard to the decision of the care unit.

In the present study, we investigated the success rate and the factors that would allow an accurate prediction of NIV failure in cases of COPD exacerbations with AHRF in wards.

METHODS

Patient Inclusion and Study Protocol

The present study was a retrospective study conducted between May 2011 and 2013 in a training and research hospital, which is a reference center for chest diseases. Patients admitted to the emergency department (ED) because of COPD exacerbation with AHRF were investigated. Patients were selected via the hospital electronic database with an intervention code of NIV implementation. Among these, patients having an ICD-10 code of COPD (J44) were included in our study. Patients with an ICD-10 code of pneumonia (J15), interstitial lung disease (J84), and restrictive lung disease (M41) were excluded. Patients who were directly transferred to the ICU were not included. Patients who were admitted more than once in the study period were included only with regard to their first applications. The inclusion criteria of this cohort have been described previously (18). Treatment results were evaluated, and patients leaving the hospital on their own decision and those ones transferred to other health units for non-respiratory indications were excluded from the study. A total of 544 patients were included in the present study (Figure 1).

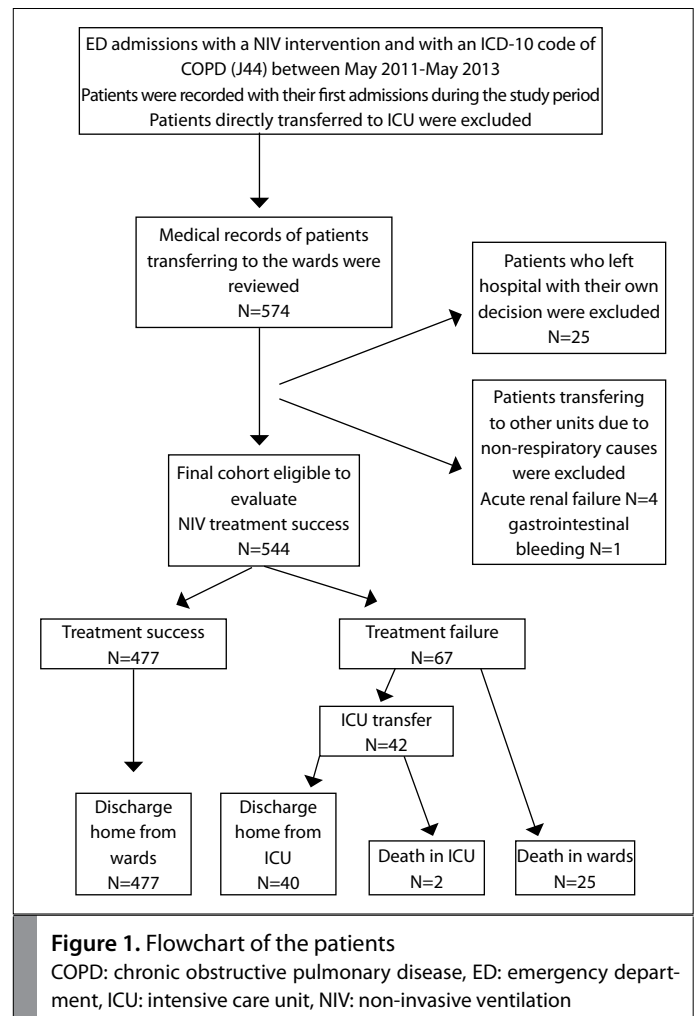
COPD was diagnosed by a pulmonologist evaluating airflow obstruction on spirometry (i.e., a forced expiratory volume in 1 second of $\leq 70\%$ predicted and a forced expiratory volume in 1 second to forced vital capacity ratio of $\leq 70\%$) in patients with a compatible history (1). AHRF had been diagnosed with moderate or severe dyspnea, tachypnea, accessory muscle use, abdominal paradoxical respiration, ABG $\text{pH} < 7.35$, partial arterial carbon dioxide (PaCO_2) > 45 mmHg (19).

Demographical and clinical data of all the patients were recorded from medical records. Charlson index (CI) was calculated for each patient (20). The current status of using long-term oxygen treatment (LTOT) or NIV at home was recorded.

Baseline ABGs were measured under nasal oxygen treatment according to the pulse oximeter oxygen saturation values. Baseline laboratory data of complete blood count, albumin levels, and ABG values on admission and within the first 2 hours of treatment in ED and at the end of the first day of treatment in wards were recorded. The subtraction values of pH and PaCO_2 values at presentation and within 2 hours of treatment were recorded. pH values at admission were classified in 3 groups as follows: $\text{pH} < 7.26$ (severe), $7.26 \leq \text{pH} < 7.30$ (moderate), and $\text{pH} > 7.30$ (mild) (14). Spirometry findings could not be recorded due to lack of data.

Treatment results of the patients were evaluated, and the success rate of NIV treatment was investigated. According to the treatment outcome, the patients were classified in 2 groups:

Group 1: Success outcome: NIV treatment was entitled as “success” in patients who were successfully discharged to their homes from wards.



Group 2: Failure outcome: NIV treatment was entitled as “failure” in patients who either died or whose clinical status deteriorated and were transferred to the ICU (19).

Demographics and baseline and follow-up parameters of the outcome groups were compared, and the predictive factors of NIV failure were analyzed. The study protocol was approved by the hospital’s local ethics committee and was in accordance with the Declaration of Helsinki. All data were collected retrospectively from the hospital database. Because of the retrospective study design, informed consent was not obtained.

Organization of ED and Wards

Our center has a highest inpatient bed capacity (628 beds) in the country with a tertiary respiratory ICU. A pulmonologist provides 24/7 care in ED, clinics, and the respiratory ICU. All personnel are regularly provided with training sessions on NIV implementation. In ED, NIV implementation is given by pulmonologists on the basis of the clinical status and ABG values (19). Both in ED and in wards, NIV is applied through an oronasal mask using a bi-level ventilator (Respironics, Inc. Murrysville, USA) set in a spontaneous/timed mode.

In ED, standard medical treatments are concomitantly initiated in patients receiving NIV (1). The acute response is evaluated within the first 2 hours. In case of improvement of the clinical condition and

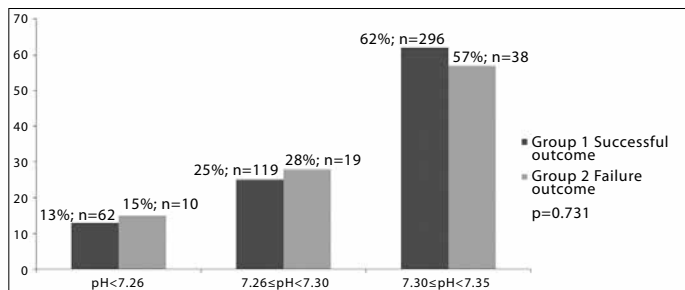


Figure 2. Categorization of baseline pH values according to treatment success

ABG values, patients are transferred to wards. Otherwise, patients are transferred to the ICU. The decision to transfer to the ICU is made by pulmonologists and on ICU consultation.

Statistical Analyses

Number Cruncher Statistical System (NCSS) 2007 and Power Analysis and Sample Size (PASS) 2008 Statistical Software (Utah, USA) programs were used for statistical analyses. Descriptive statistics (mean, standard deviation, median, frequency, ratio, minimum, and maximum) were calculated to evaluate recorded data. Student’s t test was used to compare normally distributed data, and Mann–Whitney U test was used to compare non-normally distributed quantitative data. Paired sample test and Wilcoxon signed-rank test were used to perform in-group comparisons of normally and non-normally distributed data, respectively. Pearson chi-square test, Fisher’s exact test, Fisher–Freeman–Halton test, and Yates’ continuity correction test (Yates’ corrected chi-square) were used to compare qualitative data. Statistical significances were analyzed at a p value of <0.05.

RESULTS

Of all the 544 patients, 333 (61%) were men, and the mean age was 68±11 years. In total, 22% of the patients had never smoked. At presentation, 314 (58%) patients were using LTOT, while 120 (22%) patients were using NIV at home. The mean CI was calculated as 2.2±1.8. The mean baseline ABG values were as follows: pH: 7.316±0.05 (min–max, 7.192–7.386), PaCO₂: 66.5±10.6 mmHg (50.2–98.8), PaO₂: 62.0±31 mmHg (30.1–92.5) and std. HCO₃: 27.8±5.1 (min–max, 20.1–38.4). The mean leukocyte count was 10.8±4.7×10⁹ l, hematocrit was 44.7±7.6%, and albumin level was 3.1±0.5 g/dL.

Baseline pH values were grouped as severe (pH<7.26) in 72 patients (14%), moderate (pH between 7.26 and 7.30) in 138 (25%), and mild (pH>7.30) in 334 (61%) (Figure 2).

In ED, the mean inspiratory positive airway pressure (IPAP) was 20.8 (16–30 mmHg) and the mean expiratory positive airway pressure (EPAP) of NIV implementation was 5.6 (4–8). After NIV implementation in ED, within 2 hours, the mean ABG values were 7.358±0.04 for pH and 57.5±10.1 for PaCO₂. At the end of the first day, the mean pH value was 7.371±0.05 and the mean PaCO₂ value was 60.2±15.7 for all the patients. The mean duration of hospital stay in wards was 9.2±5 days.

After transfer to the wards and providing NIV treatment along with medical treatment, 477 (88%) patients were successfully discharged to their homes (Group 1). Twenty-five (4%) patients died in the wards,

Table 1. Comparisons of demographics and baseline laboratory values between the groups

Variables	Group 1 Successful outcome (n=477)	Group 2 Failure outcome group (n=67)	p
Age (years)	68±11	70±10	0.79
Male, n (%)	291 (87)	42 (62)	0.184
Smoking status current/ex/never (n, %)	46/331/100	6/43/18	0.833
Charlson Index	2.1±1.8	2.6±2.0	0.045
LTOT (n, %)	281 (59)	33 (49)	0.134
Long-term home NIV (n, %)	107 (22)	13 (19)	0.687
Baseline laboratory values			
Leukocyte count (10 ⁹ l)	10.7±4.6	11.6±5.4	0.214
Hematocrit (%)	44.8±7.7	43.9±7.1	0.393
Albumin (g/dL)	3.2±0.5	2.8±0.5	0.001

LTOT: Long-term oxygen treatment; NIV: non-invasive ventilation

whereas 42 (8%) patients had been transferred to the ICU. These 67 (12%) patients with treatment failure were grouped as Group 2. In the follow-up in the ICU, 2 patients died, whereas 40 patients were discharged to their homes.

Comparisons of the groups did not show any significant difference in terms of the mean age, gender, smoking status, previous LTOT, and home NIV use. The CI score was significantly higher (p=0.045) in Group 2. The baseline white blood cell count and hematocrit levels did not affect the outcome, whereas the baseline albumin levels were significantly lower in Group 2 (p=0.001) (Table 1).

Baseline pH and PaCO₂ values did not correlate with NIV failure. In addition, the categorization of baseline pH values did not show any significance. Failure rates were similar in patients with baseline severe, moderate, and mild acidosis (14%, 14%, and 11%, respectively) (p=0.73). Within the first 2 hours of NIV implementation, patients in Group 2 had statistically significant lower pH and higher PaCO₂ values (p=0.008 and p=0.014, respectively). Similarly, Group 2 patients had significantly lower pH and higher PaCO₂ values at the end of the first day of treatment in the wards (p=0.001 and p=0.001, respectively) (Tables 2, 3).

Comparison of the ABG values after NIV treatment in ED revealed that in both the groups, pH values increased and PaCO₂ values decreased. The mean level of decrease in the PaCO₂ value was 10.1 mmHg in Group 1 and 6.4 mmHg in Group 2. The mean level of decrease in the PaCO₂ value was significantly lower in Group 2 (p=0.032) (Figure 2).

Table 2. Comparison of the baseline and follow-up ABG values according to treatment success

Variables	Group 1 Successful outcome (n=477)	Group 2 Failure outcome (n=67)	p
Initial ABG values (ED)			
pH	7.31±0.05	7.31±0.05	0.928
PaCO ₂ (mmHg)	66.46±10.6	66.42±10.2	0.980
PaO ₂ (mmHg)	60.92±29.5	69.68±40.7	0.236
Within 2 hours of NIV treatment (ED)			
pH	7.36±0.04	7.34±0.05	0.008**
PaCO ₂ (mmHg)	57.1±10.2	60.9±9.6	0.014**
PaO ₂ (mmHg)*	66.9±30.9	58.9±16.4	0.105
After 24 hours of NIV treatment (wards)			
pH	7.38±0.05	7.31±0.09	0.001**
PaCO ₂ (mmHg)	58.8±12.1	70.7±19.6	0.001**
PaO ₂ (mmHg) *	67.9±26.6	69.79±48.3	0.288
ED: Emergency department; NIV: non-invasive ventilation; PaCO ₂ : partial arterial carbon dioxide; PaO ₂ : partial arterial oxygen; std. HCO ₃ : standard bicarbonate * PaO ₂ (mmHg): nasal oxygen, according to the pulse oximeter oxygen saturation values; **Statistically significant			

Table 3. Comparison of differences in ABG values at baseline and within 2 hours of treatment in the emergency department

	Group 1 Successful outcome (n=477)		Group 2 Failure outcome (n=67)		Comparison between the groups
	Difference	p	Difference	p	p
pH	-0.06±0.05	0.001	-0.05±0.04	0.001	0.169
PaCO ₂	10.1±10.5	0.001	6.4±8.3	0.001	0.032
PaCO ₂ : partial arterial carbon dioxide					

DISCUSSION

The present study showed that NIV treatment in wards in cases of COPD exacerbations with AHRF has a high success rate of 88%. Treatment failure was found to be related to higher CI scores, lower baseline albumin levels and pH values and higher PaCO₂ values within 2 hours of NIV treatment and at the end of the first day of treatment. In addition, the importance of the level of decrease in the PaCO₂ value within the initial hours was demonstrated. Baseline pH and PaCO₂ values did not affect NIV treatment failure with numerical or categorical values. To our knowledge, the present study involved one of the largest study samples to evaluate the efficacy and predictive outcome factors of NIV treatment in cases of COPD exacerbations, giving important clues to the clinician with regard to the decision of the follow-up unit.

In the literature, the success rate of NIV treatment in ED and wards has been reported to vary on a large scale between 44% and 90% (12-14, 21). This rate depends on the patient-management unit, patient population, and experience of the medical caregivers. Wood et al. (12) have evaluated the efficacy of NIV in reducing the need for endotracheal intubation and reported a NIV failure rate of 44% in a small number of patients. Schneider et al. (21) have analyzed the efficacy of NIV in ED and reported a failure rate of 60%. However non-COPD diagnoses and patients directly transferred to the ICU were included in this cohort. On the other hand, when COPD exacerbation patients were assessed alone, the success rate was reported to be higher. In a recent study by Fiorino et al. (14), COPD patients with acute respiratory failure were found to have a high success rate of NIV of 82% when treated in wards. The highest rate of NIV success reported so far is 90% in a relatively small number of patients. In that study, a medical emergency team implemented NIV at various localizations outside the ICU (13). Carlucci et al. (22) compared the efficacy of NIV with experience. They compared the success rates of NIV implementation outside the ICU and noted that the success rate of NIV therapy increased by 3-fold in 4 years.

In the present study, the success rate of NIV was higher (88%) than that in most studies (12, 14, 21). The reason for this high rate may be that more homogenous COPD exacerbations were included in the present study. The other reason may be prompt NIV implementation by medical caregivers with an experience of more than 10 years during the study period, both in ED and wards. In our opinion, NIV treatment should be considered for suitable patients in wards as long as the staff is well-trained and close monitoring of the patients is feasible.

Male gender and older age were found to be related risk factors for endotracheal intubation requirement after NIV implementations outside the ICU (15). Fiorini et al. (14) reported that NIV failure increases with age. In that study, the mean age was 80 years and the majority of patients had severe acidosis. However, other reports did not find a correlation between age, gender, and NIV failure (16, 23). Similarly, in the present study, treatment outcome did not correlate with age or gender. We could not encounter direct literature on the smoking status, but in the present study, we did not identify any correlation with the smoking status. These findings indicate that age, gender and smoking status are irrelevant for NIV failure prediction in the acute phase despite their use in long-term prognosis and effect on frequent exacerbations.

Previous studies have reported that 40%–95% of COPD patients have comorbidities, which affect the success of NIV (24). Only a few studies have evaluated the CI score on NIV success. Fiorino et al. (14) have not found a significant relation between the CI score and NIV success. Conversely, in the present study, the mean CI was found to be significantly higher in patients with NIV failure. Additional diseases are considered to have an influence on the development of acute cases, but we believe that new series are needed to establish the role of this score on the success rate of NIV.

Long-term oxygen and home NIV treatment have been shown to improve the quality of life and shorten the hospital stay (25, 26). To the authors' knowledge, there are no data on the effect of home oxygen and NIV therapy on COPD exacerbations. In the present study, LTOT and NIV use at home did not affect NIV success.

Serum albumin levels have been accepted as an indicator of acute-phase protein response. Therefore, it has been suggested that low levels of this protein may reflect a deterioration of the clinical status and increased persistent inflammation during acute exacerbations of COPD (26). The relation between lower albumin levels and NIV failure has been reported in some studies on this issue (14, 16, 17). Similarly, in the present study, decreased albumin levels were found to be indicative of NIV failure. In line with the relevant literature, we believe that albumin level is a guiding factor for prognosis in the acute phase and that the success rate of NIV may be low in wards.

The predictive ABG values in COPD patients with AHRF have been evaluated, and different results have been reported. Lower baseline pH levels have been shown to predict NIV failure in the study of Ambrosino et al. (17). A study performed in England concluded that NIV is not safe in patients with baseline pH levels lower than 7.30. The authors suggested that NIV can be safely implemented at wards only in patients with mild-moderate acidosis (27). However, other reports have not established a relationship between baseline pH and PaCO₂ values and NIV failure. Crummy et al. (28) have classified baseline pH values as severe and moderate acidosis and found NIV success rates to be similar in both the groups. In a recent prospective study performed in wards, the success rate of NIV was found to be 76% among patients with pH < 7.26 and 84% among patients with pH 7.26–7.30. The researchers concluded that NIV can be safely used in wards (14). A study performed in Canada reported that 16 out of 17 patients with pH 7.15–7.24 showed improvement after NIV implementation in wards (29). In line with recent reports, the present study did not find any correlation between baseline pH and PaCO₂ values and NIV failure, either by absolute value or by categorization.

An improvement trend in pH values and a decreasing trend in PaCO₂ values within the initial hours of NIV implementation were reported to affect NIV success. Several studies have demonstrated that a rapid improvement in pH levels is crucial for NIV success (10, 30). In the prospective study of Confalonieri et al. (31), the most significant indicators of NIV failure were reported to be pH and PaCO₂ levels that did not improve within 1–4 hours. Similarly, the present study showed that pH values remained lower and PaCO₂ values remained higher within the first 2 hours in patients with NIV failure. The present study also showed that the level of decrease in the PaCO₂ value can be a guiding factor as an absolute value. These results suggest that rather than the baseline pH and PaCO₂ values, ABG parameters showing acute response to NIV treatment in ED play an important role in the decision of the follow-up unit. It was also found in the present study that pH and PaCO₂ values at the end of the first day are important for determining NIV failure. The relationship between ABG values at the end of the first day can help clinicians determine the convenience of ward follow-up continuation.

There were some limitations to this study. Firstly, it was a retrospective, single-center study; therefore, many important factors affecting NIV success cannot be evaluated, e.g., spirometric data, body mass indices, and infectious parameters such as sputum purulence, amount of sputum, and C-reactive protein levels. Logistic regression analysis was not performed because of the few significant parameters. The strength of the present study is its large sample size and the fact that only pulmonologists and pulmonology fellows had been working in ED and the wards.

CONCLUSION

The success rate of NIV in wards in COPD patients with AHRF is high. NIV failure is significantly higher in patients with lower albumin levels and higher CIs. Baseline ABG values and categorized pH values do not seem to affect the treatment outcome. However, response to treatment within the first 2 hours based on pH and PaCO₂ values and the level of decrease in the PaCO₂ value are valuable to predict NIV failure. These parameters may be taken into account for the decision of the treatment unit, and these patients may need closer monitoring during hospitalization.

Ethics Committee Approval: Due to the retrospective design of the study, ethic committee approval was not taken. Local Academic Committee approval was taken from Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital.

Informed Consent: Due to the retrospective design of the study, informed consent was not taken.

Peer-review: Externally peer-reviewed.

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