# Does Emphysema Affect COPD Patient Compliance with Use of a Noninvasive Mechanical Ventilation Device?

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## INTRODUCTION

The use of domiciliary noninvasive mechanical ventilation (NIMV) devices by patients with chronic respiratory failure (CRF) is growing. The prevalence has been reported at 6.6/100,000.<sup>[1]</sup> The use of NIMV reduces the number of hospitalizations and the cost of treatment.<sup>[2]</sup> In addition to assisting those with chronic obstructive pulmonary disease (COPD), it is also used in cases of obesity hypoventilation syndrome (OHS), restrictive chest wall diseases, and neuromuscular diseases.<sup>[3]</sup>

The symptoms, exacerbations, response to treatment, rate of disease progression, and/or mortality vary among patients with COPD. Among the COPD phenotypes that have been defined are emphysema-hyperinflation, with frequent exacerbations; overlap asthma-COPD, with rapid loss of forced expiratory volume in I second (FEV<sub>1</sub>); a

# ABSTRACT

**Objective:** Patients with chronic obstructive pulmonary disease (COPD)-related chronic respiratory failure (CRF) are increasingly using domiciliary noninvasive mechanical ventilation (NIMV) devices. This study was an assessment of the response of COPD patients with and without emphysema to the use of such a device.

**Methods:** A cross-sectional, observational study was conducted from the outpatient clinic with COPD patients with and without emphysema who had presented at the respiratory intensive care unit between 2014 and 2018 with chronic respiratory failure and who had a thorax computed tomography image recorded within the past year and were using a domiciliary NIMV device. Data regarding demographic information, comorbidities, NIMV mode and duration of use, pulmonary function test, arterial blood gas, whole blood count, C-reactive protein level, and complications were documented from outpatient clinic records and the 2 groups were compared.

**Results:** Forty patients (male, 75%) with a median age of 66 years were included in the study. There was no difference between the groups in terms of NIMV use or NIMV pressure. The number of active smokers was statistically greater in the emphysema group (p=0.026) and the forced expiratory volume in 1 second, forced expiratory volume in 1 second/forced vital capacity, and peak expiratory flow 25–75 were lower in the emphysema group. The comorbidities of both groups were similar. The complication of skin redness due to mask pressure was observed in 1 patient in the emphysema group. There was no significant difference between groups in terms of arterial blood gas and inflammatory markers.

**Conclusion:** NIMV offers patients substantial clinical benefits and is ideal for home use. There was no significant difference in compliance with use of the device between the COPD subtypes examined.

> type seen with systemic comorbidities; and bronchiectasis-COPD. COPD with emphysema is characterized by dyspnea, exercise intolerance, hyperinflation, low body mass index (BMI), presence of emphysema on computed tomography (CT) and high-resolution CT (HRCT) images, low diffusing capacity of the lungs (DLCO)/alveolar volume, a distinct genetic component, infrequent exacerbations, and low DLCO test results.<sup>[4]</sup>

> Each patient's use of the NIMV device and the number and duration of daily applications differs. Studies on the use of NIMV at home have evaluated device use compliance in COPD patients and other disease groups.<sup>[2,5–7]</sup> However, data on patient compliance with this treatment are limited to patients with and without emphysema.<sup>[8]</sup> The present study is an examination of whether COPD patients with emphysema were less compliant with domiciliary NIMV therapy than COPD patients without emphysema.

COPD patients who presented at the respiratory intensive care unit (ICU) and were followed up at the outpatient clinic of a single center between 2014 and 2018 with a diagnosis of CRF and who used a home NIMV device were included in this retrospective cohort study. The local ethics committee approval was obtained for the study (12.07.2018/049). Ethical approval was granted according to the principles of the Declaration of Helsinki. As the study was performed retrospectively, no written consent was obtained from the patients.

#### Patients

Patients over 40 years of age who were using a NIMV device at home with a diagnosis of stable COPD and CRF with at least 10 pack-years of smoking and/or biomass history and a thorax CT image obtained within the past year were included in the study. The diagnosis of COPD was based on clinical and spirometry evaluations performed by a chest disease specialist. Patients with other causes of CRF (OHS, neuromuscular diseases, conditions leading to chest wall restriction), patients undergoing mechanical ventilation via a tracheostomy, and patients with insufficient monthly control visit data were excluded from the study. The patients were divided into 2 groups: COPD patients with emphysema as detected on thorax CT and those without emphysema.

## Definitions

COPD: Post-bronchodilator FEV<sub>1</sub>/forced vital capacity (FVC) <70% with dyspnea, cough, sputum and/or wheezing.<sup>[9]</sup>

Stable COPD: No exacerbation for 4 weeks prior to the enrollment of the patient in the study.<sup>[10]</sup>

CRF: Partial arterial oxygen pressure  $(PaO_2) < 60 \text{ mmHg}$ and partial arterial carbon dioxide pressure  $(PaCO_2) > 50 \text{ mmHg}$ .

Definition of emphysema on thorax CT: Area of emphysema that occupies more than 15% of a lung area and exhibits an attenuation of less than -950 Hounsfield units.<sup>[11]</sup>

Domiciliary mechanical ventilation: Use of NIMV at home or a care center for more than 3 months.<sup>[1]</sup>

NIMV compliance: Use of NIMV device for more than 4 hours a day.<sup>[5]</sup>

#### Follow-up

Patients who had a diagnosis of COPD exacerbation and respiratory failure in the ICU were included in the followup protocol. After the first month of follow-up, the patients were then called for a 3-month or 6-month followup visit and these data were included in the study. Bilevel positive airway pressure (BiPAP) S or BiPAP spontaneous timed (ST) models and oronasal silicone masks were used by all of the patients included in the study. The patients were asked to bring the NIMV device to the control visits.

#### Recordings

The demographic characteristics of patients such as age, gender, BMI, smoking history (pack-years, active smoker, ex-smoker status), concomitant diseases (diabetes mellitus, hypertension, coronary artery disease, arrhythmia, heart failure, neurological disease, extrapulmonary cancer, psychiatric disease, chronic renal failure) and results of pulmonary function tests were obtained from polyclinic records and recorded. Arterial blood gas values were documented based on the laboratory records at the time of discharge from the ICU (first) and the control visits. The Modified Medical Research Council (MMRC) scale and the St. George's Respiratory Questionnaire (SGRQ) were administered to assess dyspnea and quality of life, respectively. The device, mask type, and pressure values (inspiratory peak airway pressure, positive end expiratory pressure) used by the patients were recorded. In both groups, at follow-up visits, patients' statements and device usage hours were assessed. The study group was also asked about factors related to noncompliance (mask problem, exacerbation) and complications (eye dryness, sinusitis, skin redness, nasal bleeding). Visits to emergency services, and ICU or hospital admission were also noted. Spirometric assessments of the patients were made in accordance with the criteria stated in American Thoracic Society guidelines.<sup>[12]</sup>

#### Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY,

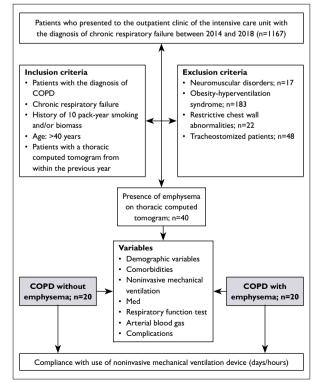


Figure 1. Algorithm of the patients (COPD: Chronic obstructive pulmonary disease).

USA). Non-normally distributed continuous variables were presented as percentiles (25–75%) and medians. The Mann-Whitney U-test was used to compare the study group data. Categorical variables were described in numbers and percentages. Pearson's chi-square test was used to analyze bimodal variables and categorical variables.

## RESULTS

Forty COPD patients at the respiratory ICU outpatient clinic with a diagnosis of COPD-CRF who were followedup with NIMV therapy were enrolled in the study. Patients using a NIMV device at home with the indications of neuromuscular disease, OHS, or restrictive chest wall disease, tracheostomized patients, and patients with incomplete third or sixth-month follow-up data were excluded. Patients included in the study were divided into 2 groups: chronic bronchitis-COPD and emphysema-COPD according to the presence of emphysema on a thorax CT (Fig. I).

The median age of the patients was 66 years and the female/male ratio was 1/4. In Table I, patients in both groups were compared in terms of age, gender, smoking history, BMI, long-term oxygen therapy (LTOT), NIMV device and compliance information, MMRC/SGRQ results, comorbidities, and mortality rates. There was no significant difference between the 2 groups in terms of age and gender. When smoking status was evaluated, there were significantly more active smokers in the emphysema group (p=0.026). No difference was found between the groups in terms of LTOT, NIMV delivery time and NIMV pressure.

While NIMV compliance was 100% in both groups, the mean duration of NIMV use was 6 hours in the chronic bronchitis-COPD group and 5 hours in the emphysema-COPD group. One patient in the emphysema group experienced the complication of reddened skin due to the pressure of the facial mask. Neurological and psychiatric diseases were not detected in either group, and the comorbidities were similar. During the study period, I patient from the chronic bronchitis group died.

Table 2 illustrates a comparison of the pulmonary function test results and arterial blood gas (ABG) characteristics of patients with chronic bronchitis and emphysema. There was no significant difference between the groups in terms of the first ABG and control ABG values; however, the FEV<sub>1</sub>, FEV<sub>1</sub>/FVC and peak expiratory flow 25–75 (PEF 25–75) values were found to be statistically significantly lower in the emphysema group.

### DISCUSSION

In this study, the results indicated that compliance with use of the domiciliary NIMV device was 100% among these study patients with COPD-CRF, and there was no significant difference between COPD patients with and 
 Table I.
 Demographic characteristics, device specifications, and comorbidities in patients with chronic bronchitis and emphysema

	Chronic bronchitis- COPD (n=20)	Emphysema- COPD (n=20)	р	
Age, years, median (IQR)	68 (61–78)	64 (57–69)	0.18	
Gender, (male), n (%)	15 (75)	17 (85)	0.42	
Smoking status, n (%)				
Former smoker	17 (85)	19 (95)	0.29	
Smoking pack-years	60 (40-80)	45 (35–80)	0.25	
Active smoker	l (5.9)	7 (36.8)	0.026	
Years since quit				
smoking	8 (4–19)	3 (1-10)	0.21	
Biomass	3 (15)	l (5)	0.29	
BMI (median)				
(IQR) (kg/m²)	28 (23–32)	23 (21–29)	0.08	
COPD (years)	5 (4–10)	6 (3–10)	0.83	
Device specifications				
LTOT (months)	7 (6–8)	7 (5–9)	0.75	
NIMV (months)	7 (6–8)	7 (5–8)	0.66	
IPAP (baseline)	27 (24–30)	28 (25–30)	0.86	
IPAP (control)	27 (24–30)	28 (25–29)	0.75	
PEEP (baseline)	5 (5–7)	5 (5–6)	0.39	
PEEP (control)	5 (5–7)	5 (5–6)	0.42	
NIMV (h/d, baseline)	6 (6–7)	6 (6–6)	0.16	
NIMV (h/d, control)	6 (5–6)	5 (4–6)	0.80	
Use of the device				
Use of the mask	20 (100)	20 (100)	0.46	
Patient satisfaction	20 (100)	20 (100)	0.52	
Complications	0 (0)	l (5)	0.31	
, MMRC/SGRQ, n (%)	( )			
	l (5.3)	l (5.6)	0.16	
2	6 (31.6)	12 (66.7)		
3	4 (21.1)	I (5.6)		
4	8 (42.1)	4 (22.2)		
Comorbidities, n (%)				
Diabetes mellitus	5 (25)	3 (15)	0.42	
Hypertension	10 (50)	8 (40)	0.52	
Coronary artery	()			
disease	3 (15)	2 (10)	0.63	
Heart failure	3 (15)	4 (20)	0.67	
Arrhythmia	0 (0)	2 (10)	0.14	
Cancer	0 (0)	L (5)	0.31	
Chronic renal failure	2 (10)	I (5)	0.54	
Mortality, n (%)	1 (5)	0 (0)	0.31	

Median (IQR 25-75%). BMI: Body mass index; COPD: Chronic obstructive pulmonary disease; IPAP: Inspiratory peak airway pressure; LTOT: Longterm oxygen therapy; MMRC/SGRQ: Modified Medical Research Council/ The St George's Respiratory Questionnaire; NIMV: Noninvasive mechanical ventilation; PEEP: Positive end expiratory pressure.

	Chronic bronchitis-COPD (n=20)		Emphysema-COPD (n=20)		р
	N		N		
Respiratory function test, median (IQR)					
FVC (mL)	20	601 (338–725)	20	725 (404–1003)	0.083
FVC (%)	20	43( 35–48)	20	38 (33–51)	0.55
FEV, (mL)	20	495 (318–840)	20	500 (348–720)	0.95
FEV (%)	20	34 (31–40)	20	27 (21–31)	0.013
FEV,/FVC	20	64 (59–70)	20	54 (47–65)	0.021
PEF <sub>25-75</sub>	19	480 (410–630)	20	345 (260–520)	0.054
PEF <sub>25-75</sub> (%)	20	18 (14–25)	20	13 (9–16)	0.013
Arterial blood gas, first, median (IQR)					
PH	20	7.45 (7.41–7.49)	20	7.44 (7.41–7.46)	0.22
PCO, (mmHg)	19	55 ( <del>4</del> 4–59)	17	54 (48–58)	0.97
PO, (mmHg)	20	71 (61–88)	20	74 (63–89)	0.75
HCO, (mmol)	20	34.0 (31.3–37.8)	20	33.3 (31.9–36.1)	0.50
FiO	20	35 (28–40)	20	36 (32–40)	0.60
PaO <sub>2</sub> //FiO <sub>2</sub>	20	220 (198–292)	20	217 (165–272)	0.58
Arterial blood gas, control, median (IQR)					
PH	20	7.39 (7.37–7.42)	20	7.40 (7.38–7.43)	0.52
PCO, (mmHg)	20	49 (44–57)	20	47 (44–57)	0.89
PO, (mmHg)	20	68 (61–89)	20	65 (52–86)	0.60
HCO <sub>3</sub> (mmol)	20	30.5 (27.0–31.5)	20	29.9 (27.2–31.8)	0.87
FiO	20	21 (21–29)	20	21 (21–32)	0.97
PaO <sub>2</sub> //FiO <sub>2</sub>	20	303 (219–370)	20	290 (224–361)	0.78

Table 2. Pulmonary function test results and arterial blood gas characteristics of patients with chronic bronchitis and emphysema

Median, (IQR); (25–75%), Mann-Whitney U test. COPD: Chronic obstructive pulmonary disease; FEV<sub>1</sub>: Forced expiratory volume in 1 second; FiO<sub>2</sub>: Fraction of inspired oxygen; FVC: Forced vital capacity; HCO<sub>3</sub>: Bicarbonate; PAO<sub>2</sub>: Partial pressure arterial oxygen; PCO<sub>2</sub>: Partial pressure of carbon dioxide; PEF: Peak expiratory flow; PO<sub>2</sub>: Partial pressure of oxygen.

without emphysema. There were more active smokers in the emphysema group, while  $FEV_1$ ,  $FEV_1/FVC$  and PEF 25–75 values were lower.

Long-term NIMV use is increasing among CRF patients. <sup>[1,13]</sup> Although the role of NIMV use during a chronic period was initially controversial in patients with COPD, NIMV is now indicated as the primary treatment option for CRF due to COPD.<sup>[14]</sup> The 2 most important criteria for long-term NIMV are persistent hypercapnia following symptomatic CRF and acute NIMV-dependent exacerbation requiring hospitalization.<sup>[14]</sup> It has been reported that NIMV treatment at home in cases of COPD has reduced the respiratory workload and eliminated alveolar hypoventilation.<sup>[15]</sup>

As a result of NIMV use, a resolution of hypercapnia and hypoxemia, improvement in respiratory function, a decrease in dyspneic symptoms, an improvement in quality of life, a decrease in hospital admissions, fewer ICU hospitalizations, reduced hospital costs, and an increase in survival time have been demonstrated in patients with COPD.<sup>[2,14,16–18]</sup> In studies, patient compliance with NIMV treatment has been reported as 77% to 96% and the results were generally good.<sup>[2,5,18–20]</sup> Örnek et al.<sup>[7]</sup> found that the daily duration of NIMV use was statistically longer in patients with a shorter life span than those for whom it was longer. In our study, NIMV compliance was found to be 100% in both groups. It has been established that patient compliance with mechanical ventilation therapy at home varies according to treated diseases. Cheng et al.<sup>[20]</sup> reported the following findings of patient compliance with NIMV treatment and daily device usage: stage 4 COPD: 40%, 8.1±3.2 h/day; overlap syndrome: 32.3%, 6.7±2.6 h/day; restrictive chest wall diseases: 10.8%, 7.8±3.0 h/day; OHS: 7.7%, 6.5±2.7 h/day; neuromuscular disorders: 3.1%, 3.1±3.9 h/day; and mixed pathologies: 6.1%, 7.3±1.7 h/day.

In our study, the duration of NIMV use was 6 hours in the chronic bronchitis-COPD group and 5 hours in the emphysema-COPD group.

It was reported in a study, due to the destruction in the lung parenchyma patients with COPD did not benefit adequetly from mechanical ventilation as expected, and compliance in COPD patients was less than that of restrictive lung patients. The 5-year compliance rate in restrictive lung disease patients was 80% and the 3-year compliance rate was 50% in COPD patients.<sup>[21]</sup>

De Becker et al.<sup>[8]</sup> investigated the question of why longterm use of NIMV in-hospital for an acute attack of CRF induced a decrease in  $PaCO_2$  and an increase in  $PaO_2$  during the day (and hence improved quality of life and survival) in some patients, while in others it did not. It was reported that in the presence of localized emphysema, both a decrease in carbon dioxide and an increase in oxygenation can be achieved, while in patients with diffuse emphysema, mechanical ventilation can improve perfusion and blood gas values. However, in order to make more accurate judgments, testing inspiratory pressures before determining whether small airways can be opened using NIMV has been suggested, and will be important for future studies.

In our study, though poor compliance was expected due to structural impairment in the group with diffuse emphysema, a difference in patient compliance with NIMV use was not be detected between patients with and without emphysema. While small airways that could be opened with inspiration pressure were not tested before NIMV treatment, patient use of the devices suggested that they benefited from use of the NIMV device.

#### Limitations

The first limitation of our study is that the data were retrospectively collected, and furthermore, the data were obtained from the files of a single center. However, the study was based on outpatient clinic data and these data were recorded by the same team. We think that this will minimize some of the deficiencies of retrospective studies. Since all of the patients had COPD, the number of centers from which data were gathered would not weaken the reliability of the study. It is thought that our results will contribute to the literature due to the number of patients investigated for a specific subject. As the study was performed in COPD patients, generalization to other patients is not appropriate.

## CONCLUSION

COPD subtypes did not make a difference in NIMV compliance in patients with advanced stage COPD with hypercarbic respiratory failure who used a NIMV device at home. Although emphysema and chronic bronchitis have some different pathophysiological features, the application of NIMV at home can provide clinical benefits to patients with chronic respiratory failure. Greater use of cigarettes and poor pulmonary function test values were more pronounced in COPD patients with emphysema compared with those with bronchitis.

#### **Ethics Committee Approval**

Approved by the local ethics committee.

- Informed Consent
- Retrospective study.

Peer-review

Internally peer-reviewed.

Authorship Contributions

Concept: E.A., B.O.; Design: E.A., B.O.; Data collection &/

or processing: E.A., B.O.; Analysis and/or interpretation: E.A., B.O.; Literature search: B.O, E.A.; Writing: E.A., B.O.; Critical review: E.A., B.O.

#### Conflict of Interest

None declared.

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# Amfizemi Olan KOAH Tanılı Hastalar Ev Tipi Noninvaziv Mekanik Ventilasyon Cihazı Kullanımı Konusunda Daha Mı Uyumsuz?

**Amaç:** Ev tipi noninvaziv mekanik ventilasyon (NIMV) cihazlarının kronik obstrüktif akciğer hastalığına (KOAH) bağlı kronik solunum yetersizliği (KSY) olan hastalarda kullanım sıklığı artmaktadır. Bu çalışmada amfizemi olan ve olmayan KOAH hastaların cihaz uyumları değerlendirilmiştir.

**Gereç ve Yöntem:** Gözlemsel kesitsel çalışmaya, 2014–2018 tarihleri arasında merkezimiz solunumsal yoğun bakım ünitesi (YBÜ) polikliniğine başvuran ve KSY tanısı ile ev tipi NIMV kullanan son bir yıl içinde çekilmiş toraks bilgisayarlı tomogafisi olan KOAH hastaları alındı. Poliklinik kayıtlarından hastaların demografik bilgileri, komorbiditeleri, NIMV modu ve kullanım süresi, solunum fonksiyon testi, arter kan gazı, tam kan sayımı, C-reaktif protein, komplikasyonlar kayıt edildi. Her iki grup bakılan parametreler açısından karşılaştırıldı.

**Bulgular:** Ortalama yaşı 66 olan 40 (erkek, %75) hasta çalışmaya alındı. Çalışmada NIMV uyumu ve NIMV basınçları açısından gruplar arasında fark saptanmadı. Amfizem grubunda aktif sigara kullanımı istatistiksel olarak daha yüksek (p=0.026) ve FEV<sub>1</sub>, FEV<sub>1</sub>/FVC ve PEF 25–75 daha düşük bulundu. Her iki grubun komorbiditeleri benzerdi ve komplikasyon olarak amfizem grubunda bir hastada yüzde maske basısına bağlı ciltte kızarıklık saptandı. Gruplar arasında arter kan gazı ve enflamatuvar markerlar açısından fark saptanmadı.

**Sonuç:** Hastalar için sağladığı klinik yarar nedeniyle evde NIMV kullanımı istenen ideal saatler arasındadır. KOAH subtipleri NIMV kompliansı üzerine bir fark yaratmamaktadır.

Anahtar Sözcükler: Amfizem; hasta uyumu; Kronik obstrüktif akciğer hastalığı; kronik solunum yetersizliği; non invaziv mekanik ventilasyon.