

The Success of Noninvasive Mechanical Ventilation in Relation with Concomitant Disorders in Copd Patients with Acute Hypercapnic Respiratory Failure

Akut Hiperkapnik Solunum Yetmezliği Olan KOAH Hastalarında Eşlik Eden Bozukluklarla İlişkili Olarak Noninvaziv Mekanik Ventilasyonun Başarısı

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Abstract

Introduction: Although the benefit of non-invasive mechanical ventilation (NIMV) has been proven in the management of acute exacerbations of chronic obstructive pulmonary disease (COPD), the data are limited for other lung conditions, including pneumonia and bronchiectasis. In this study, we aimed to investigate the success of NIMV in COPD patients with acute hypercapnic respiratory failure (AHRF) and concomitant pneumonia or bronchiectasis.

Methods: Among the patients hospitalized in the intensive care unit (ICU) due to AHRF, 62 patients suitable for NIMV application were included in the study. The patients were divided into three groups: Group 1: COPD (n=34), Group 2: COPD + bronchiectasis (n=11), and Group 3: COPD + pneumonia (n=17). We evaluated the success of NIMV among those 3 groups.

Results: Three study groups were similar for NIMV success, length of stay in ICU, and mortality.

Discussion and Conclusion: There is increasing evidence for the benefit of NIMV in the management of AHRF. Although the use of NIMV in COPD exacerbations has been strongly recommended by many randomized controlled trials, more studies are needed to prove its benefit in patients with pneumonia and bronchiectasis.

Keywords: COPD; NIMV; Hypercapnic respiratory failure

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Approximately, 1 million patients with acute respiratory failure (ARF) are treated with invasive mechanical ventilation (IMV) annually in the United States.^[1]

Most of the published evidence regarding the effectiveness of NIMV for avoiding intubation applies to patients with acute chronic obstructive pulmonary disease (COPD) exacerbations.^[2] NIMV has become a usual treatment method for ARF patients, regardless of the etiology of ARF.^[3,4]

Pneumonia is the leading infectious cause of hospitalizations in the United States, resulting in more than 1 million hospitalizations annually. ARF develops in 58–87% of the patients with severe pneumonia.

The mortality rate is between 15% and 51% in patients with pneumonia requiring hospitalization in the intensive care unit (ICU). The efficacy of non-invasive mechanical ventilation (NIMV) in pneumonia is controversial, as it is associated with higher treatment failure rates compared to other causes of ARF,^[5,6] and the high mortality rate due to NIMV failure.^[7] This risk is particularly relevant for patients without pre-existing respiratory or cardiac conditions (“de novo” ARF).^[6–10] In addition, several studies have reported pneumonia as an independent risk factor for NIMV failure in patients hospitalized for acute COPD exacerbation or asthma.^[2,10,11]

NIMV may be effectively used to treat hypoxemia and hypercapnia in bronchiectasis patients with ARF. Before considering the NIMV as an option, conditions that may contraindicate NIMV should be ruled out, patients should be encouraged to expectorate their secretions, and NIMV should be interrupted every 3–4 h tolerated by the patients. In a study conducted in 2010, NIMV and IMV were compared in ICU patients with ARF due to bronchiectasis, and it was reported that NIMV patients had shorter hospital stays and more ventilator-independent days.^[12]

Although the benefit of NIMV has been proven in the management of acute attacks of COPD, there are limited data on its effectiveness in other lung disorders such as pneumonia and bronchiectasis.

In this study, we aimed to investigate the success of NIMV in patients with COPD and acute hypercapnic respiratory failure (AHRF) and concomitant pneumonia or bronchiectasis.

Materials and Methods

The patients hospitalized in the respiratory ICU of Sciences University Faculty of Medicine Atatürk Sanatoryum Training and Research Hospital, between January 2009 and January 2011 were included in the study. Ethics Committee Date/Number: April 16, 2012/381.

The patients who were hospitalized in the ICU due to AHRF were reviewed, and those who were suitable for NIMV were included in the study.

The patients were divided into the following three groups:

- Group 1: COPD (n=34)
- Group 2: COPD + Bronchiectasis (n=11)
- Group 3: COPD + Pneumonia (n=17).

In addition to NIMV, all patients were administered inhaled corticosteroids, bronchodilators, oral corticosteroids, antibiotics (if needed), and oxygen support to keep SO_2 around 90%. A respiratory physiotherapist provided respiratory physiotherapy support to all patients.

Considering that it is not possible to perform pulmonary function test in intensive care conditions in practice, it was stated that COPD was diagnosed as a result of the evaluation of clinical, radiological, and anamnesis findings.

Pneumonia was diagnosed based on the patient’s symptoms, including cough, purulent sputum, fever, and flank pain and was confirmed with a chest X-ray.

The diagnosis of bronchiectasis was made based on clinical (chronic productive cough for more than 1 year) and radiological (signet ring appearance, tram-track sign, and cystic enlargements) findings.

The patient’s age, body mass index (BMI), initial inspiratory positive airway pressure (IPAP), and expiratory positive airway pressure (EPAP) values, baseline, 1st h, 4th h, 1st ICU discharge day blood gas values, tidal volume, FiO_2 values, length of stay in the ICU and hospital, mortality and intubation rates, and causes of NIMV failure were recorded.

Exclusion Criteria

pH<7.25, GCS<8, pneumothorax, those who cannot clear their secretions spontaneously, those who cannot cooperate with NIMV, those with airway or facial deformity, and those with severe dysfunction were excluded from the study.

Diagnostic Criteria of Acute Hypercapnic Respiratory Failure

- Severe dyspnea
- Hypercapnia
- ($PaCO_2 > 45\text{mmHg}$)
- pH: <7.35 mmHg (10)

NIMV Indications

- Moderate or severe dyspnea, which requires the use of accessory respiratory muscles and causes paradoxical abdominal movements
- Tachypnea (>25/min),
- pH 45 mmHg or PaO_2/FiO_2 in arterial blood gas (ABG).^[13]

Table 1. Demographic characteristics of the patients

Characteristics	Group 1 (n=34)	Group 2 (n=11)	Group 3 (n=17)
Age (years), median	71 (19–87)	55 (27–83)	62 (20–78)
Gender			
Female	17	5	6
Male	17	6	11
Presence of concomitant disease, n (%)	13 (58.3%)	8 (8.3%)	5 (33.3%)
BMI (kg/m ²), median	28 (18–45)	27 (17–31)	25 (19–33)
APACHE II, median	19 (15–22)	18 (14–22)	18 (12–22)

BMI: Body mass index; APACHE II: Acute Physiologic and Chronic Health Evaluation.

Table 2. Length of stay in intensive care unit and hospital

Group	ICUS (days)	HS (days)
Group 1, Median (Min–Max)	13 (2–69)	22 (8–99)
Group 2, Median (Min–Max)	15 (3–75)	21 (1–60)
Group 3, Median (Min–Max)	13 (2–30)	22 (6–47)

ICUS: Intensive care unit stay; HS: Hospital stay; Min: Minimum; Max: Maximum.

NIMV Application

Masks were selected in accordance with the faces of the patients, and it was checked whether they tolerated it. Baseline IPAP and EPAP values were adjusted according to the blood gas values of the patients, and the settings were reduced as clinical findings and blood gases improved over time. NIMV was suspended in cases of eating, drinking, and expectoration.

NIMV failure was defined as the patient’s death or the need for IMV during NIMV.^[14]

Intubation Criteria

pH<7.20, pH between 7.20 and 7.25 despite 1 h NIMV, hypercapnic coma (GCS<8 and PaCO₂>8kPa), PaO₂<6 kPa despite maximally tolerated FiO₂, and cardiopulmonary arrest agitation causing mask intolerance.^[15]

Our study was conducted in accordance with the Declaration of Helsinki.

Statistical Analysis

The data were analyzed with SPSS for Windows v.15 package program. Descriptive statistics were presented in tables as the means and standard deviations.

Kruskal–Wallis test was used to compare ventilator parameters and ABG values. A Chi-square test was employed to

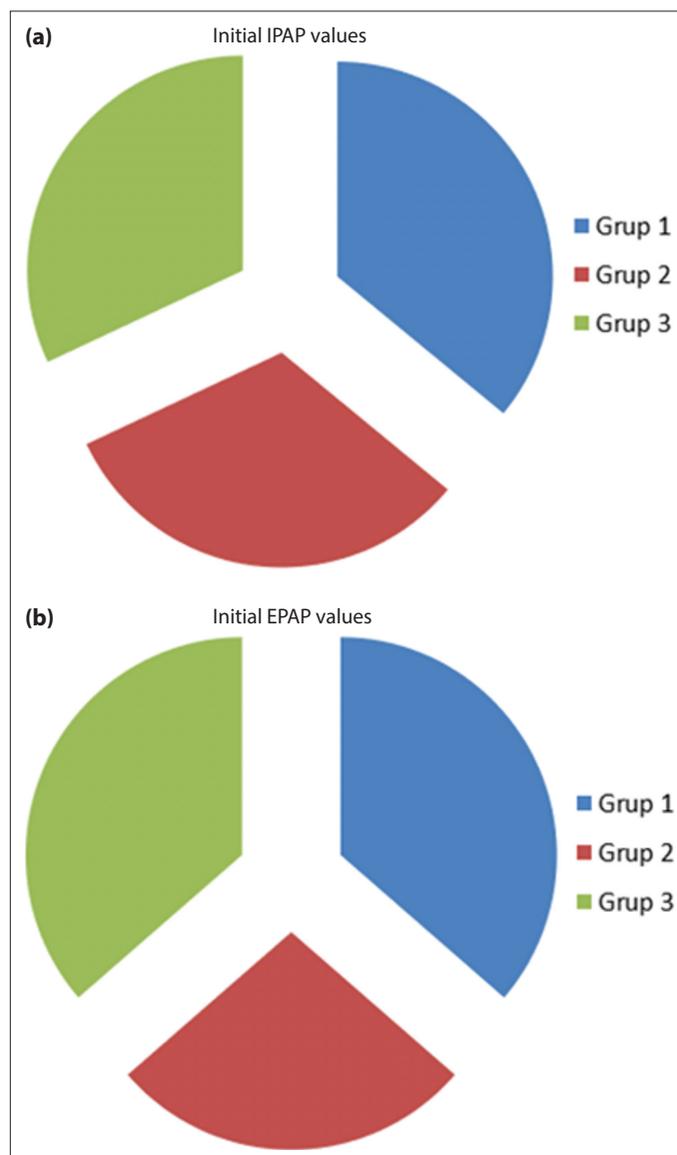


Figure 1. (a) Initial IPAP values in the study groups. (b) Initial EPAP values in the study groups.

compare mortality, intubation, and length of stay in the ICU among the study groups. The Chi-square test was used to compare the differences in pneumonia and bronchiectasis diagnoses, acute physiologic and chronic health evaluation (APACHE) II scores, and CRP levels in patients who had NIMV successful therapies. A t-test was used to compare the diagnosis rates among the groups. The result was considered statistically significant at $p < 0.05$.

Results

Thirty-four COPD (Group 1), 11 COPD+bronchiectasis (Group 2), and 17 COPD+pneumonia (Group 3) patients with acute hypercapnic respiratory failure who underwent NIMV in the ICU were included in the study.

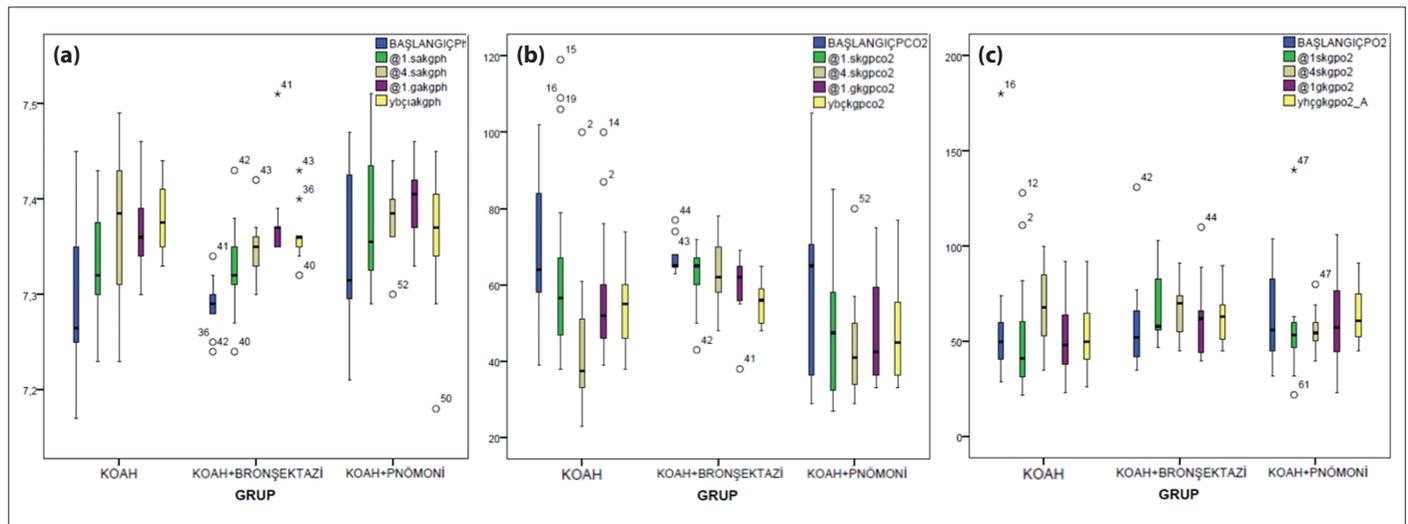


Figure 2. (a) Initial PH values by time and groups. (b) Initial PCO₂ values by time and groups. (c) Initial PO₂ values by time and groups.

There were 17 male and 17 female patients in Group 1, 5 female and 6 male patients in Group 2, and 6 female and 11 male patients in Group 3. The median mean age was 71 (19–87) years in Group 1, 55 (27–83) years in Group 2, and 62 (20–78) years in Group 3 (Table 1, demographic characteristics of the patients). There was a statistically significant difference between Group 1 and 2 in terms of mean age ($p < 0.05$); the patients in Group 1 were older than the ones in Group 2.

The median BMI was 28 (18–45) in Group 1, 27 (17–31) in Group 2, and 25 (19–33) in Group 3. There was no statistically significant difference among 3 groups in terms of BMI ($p > 0.05$).

There were comorbid disorders in 13 patients (58.3%) in Group 1, 8 patients (8.3%) in Group 2, and 5 patients (33.3%) in Group 3. There was no significant difference among the 3 study groups in terms of comorbid disorders ($p > 0.05$). Heart failure was the most frequent comorbid disorder.

The median initial IPAP value was 18 (12–25) in Group 1, 16 (13–20) in Group 2, and 16 (10–22) in Group 3. There was no statistically significant difference among the 3 groups in terms of initial median IPAP value ($p > 0.05$) (Fig. 1a).

The median initial EPAP value was 8 (5–12) in Group 1, 6 (5–10) in Group 2, and 8 (6–12) in Group 3. There was no difference among the 3 groups in terms of initial median EPAP values ($p > 0.05$) (Fig. 1b).

When the groups were compared in relation to time, there was no statistically significant difference in terms of initial pH values ($p > 0.05$). It was determined that the pH value increased over time compared to the initial value, and this was a statistically significant result ($p < 0.05$) (Fig. 2a).

When the groups were compared in relation to PaCO₂ values in time, there was no significant difference ($p > 0.05$). By time, PaCO₂ values decreased significantly ($p < 0.05$) (Fig. 2b).

PaO₂ did not show any statistically significant differences by time ($p > 0.05$). The trend was parallel, and there was no interaction in time-group analysis ($p > 0.05$) (Fig. 2c).

FiO₂ value significantly decreased over time ($p < 0.05$). When the groups were analyzed according to the time, an interaction was seen ($p < 0.05$). The FiO₂ value was significantly lower in group 1 compared to groups 2 and 3 ($p < 0.05$).

There was no statistically significant difference among 3 groups in terms of length of ICU or hospital stay ($p > 0.05$) (Table 2).

The mortality rate was 42.9% in Group 1, 42.8% in Group 2, and 14.3% in Group 3. There was no significant difference among the groups for mortality rates ($p > 0.05$).

There were no statistically significant differences among the 3 groups in terms of APACHE II ($p > 0.05$) or CRP values ($p > 0.05$).

Intubation rate was 18.4% in Group 1 (COPD). Of these patients, 2 could not adapt to NIMV, pneumothorax developed in 1, and acidosis deepened in 3 patients. The intubation rate was 35.2% in Group 2 (COPD + bronchiectasis). Acidosis deepened in 3 patients and septic shock developed in 1 patient. The intubation rate was 22.6% in Group 3 (COPD + pneumonia). Of these, 1 patient could not adapt to NIMV, and acidosis worsened in 2 patients.

Discussion

In our study, it is important to show that concomitant bronchiectasis or pneumonia does not adversely affect the success of NIMV in COPD patients with acute hypercapnic respiratory failure followed in the ICU.

AHRF has been considered the main characteristic of advanced COPD, and the benefit of NIMV has been proven in its management.^[16] Many other conditions may lead to AHRF and therefore, although most studies have been performed on patients with COPD, NIMV has also been used in a wide variety of other conditions associated with acidosis and hypercapnia.^[17]

NIMV has been used in ICU and emergency departments since the late 1980s. Brochard et al.^[18] performed the first randomized controlled trial and demonstrated that NIMV significantly reduced the need for endotracheal intubation (ETI) compared to standard medical therapy in patients admitted to the ICU with a COPD attack. It was reported that the complication rate was significantly lower in the NIMV group, the mean hospital stay was significantly shorter, and the in-hospital mortality rate was significantly reduced. A later study confirmed that NIMV was associated with lower ETI and mortality rates.^[19]

Conti et al.^[20] compared NIMV with IMV on 49 patients with COPD exacerbations in whom standard medical treatment failed. In addition, patients who can be successfully treated with NIMV have been shown to have an advantage in both reduced length of ICU stay, re-hospitalization the following year, and the need for long-term oxygen therapy.

In the study of Çiledağ et al.,^[21] NIMV was found to be successful in 41 out of 51 patients with AHRF and COPD. The authors found significant improvement in pH and PaCO₂ values starting at the 1st h of NIMV. Scala et al.^[22] used NIMV in 207 patients with AHRF. At the end of 2 h, it was determined that there was a significant improvement in blood gas values and 169 of 207 patients (81.6%) were protected from intubation. A Cochrane systematic review and meta-analysis investigated the contribution of NIMV to patients treated for acute exacerbations, and rapid improvement in PaCO₂ and pH was detected with NIMV.^[23] In the study of Söyler et al.,^[24] a significant increase in pH and a significant decrease in PaCO₂ levels were detected at the 1st and 24th h of NIMV treatment. In our study, a statistically significant improvement was found in the pH and PaCO₂ values in Group 1 (patients with COPD) compared to the baseline in accordance with the literature ($p < 0.05$), and 81.6% of the patients were protected from intubation.

In a retrospective study involving approximately 4,000 patients hospitalized for pneumonia, predominantly concomitant with COPD and requiring ventilation, NIMV treatment was associated with a 29% relative reduction in in-hospital mortality compared with IMV. The survival advantage of NIMV has been shown to remain significant in various modeling methods and sensitivity analyses. In addition, the patients treated with NIMV had a shorter hospital stay.^[25]

Several other studies have shown that patients with “de novo” ARF benefit less from NIMV than those with cardiopulmonary comorbidities such as COPD or heart failure.^[8,9] A possible explanation is that ARF may occur earlier in patients with pneumonia and concomitant COPD or CHF and respond to NIMV. In our study, significant improvements were found in pH and PaCO₂ values in Group 3 (COPD + Pneumonia) cases over time ($p < 0.05$), and the success rate of NIMV was determined as 77.4%.

Only one study investigated the efficacy of NIMV in patients with bronchiectasis. Phua et al.^[12] included 57 patients in their study. NIMV was applied to 31 patients and IMV to 26 patients. In the NIMV group, statistically significant improvements were achieved in blood gas values. The success rate was reported as 67.8%. In our study, statistically significant improvements were found in pH and PaCO₂ values in Group 2 (patients with COPD+ bronchiectasis) over time ($p < 0.05$), and 64.8% of patients were protected from intubation.

Good prognostic factors for acute NIMV applications include the young age of the patient, low APACHE score that gives information about the severity of the clinical picture, good cooperation with the patient, small amounts of secretions, breathing in harmony with the ventilator, low-air leakage, dentulous patient (important in terms of mask-face compatibility), the presence of non-severe hypercapnia ($45 \text{ mmHg} < \text{PaCO}_2 < 92 \text{ mmHg}$), non-serious acidosis ($7.10 < \text{pH} < 7.35$), improvement in heart rate, respiratory rate and effort within the first 1–2 h, and improvement in ABG values (20% decrease in respiratory rate, 20% decrease in PaCO₂, 20% increase in SO₂ or PaO₂, decrease in O₂ requirement, and improvement of acidosis).

Depending on the underlying cause, NIMV failure has been reported as 5–60%.^[1] Bhatti et al.^[26] found the failure rate as 10% in a retrospective study including 1095 patients who underwent NIMV, and it was evident that COPD and pneumonia cases constituted the majority of the failed cases. In our study, the failure rate was 22.6% in the COPD+Pneumonia group.

One of the important factors for the success of NIMV is the disease severity level at admission. APACHE II score is one of the scoring methods used as an indicator of disease severity, and a high APACHE II score was found to be associated with NIMV failure.^[2,6] In their multicenter study involving 1033 COPD attack cases, Jolliet et al.^[6] reported that an APACHE II score greater than 29 was an important predictor for NIMV failure. In our center, APACHE II score was used as an indicator of disease severity; however, APACHE II score was not found as a statistically significant predictor for NIMV failure in any of the 3 study groups ($p>0.05$).

Squadrone et al.^[27] reported a high failure rate with the use of NIMV in severely acidotic patients ($\text{pH}<7.25$). Many authors regarded a $\text{pH}<7.20$ as an indication for IMV. In a multicenter study on 1033 patients with AHRF and COPD, NIMV failure was found to be significantly higher if the pH was <7.25 .^[28] In our study, the initial pH was <7.25 in 3 patients in Group 1, and NIMV failed in those patients. In our study, the intubation rate was 18.4% in Group 1. Of these, 2 patients could not adapt to NIMV, pneumothorax developed in 1 patient, and acidosis deepened in 3 patients (initial $\text{pH}<7.25$). The intubation rate was 35.2% in Group 2. Acidosis deepened in 3 patients and septic shock developed in 1 patient. The intubation rate was 22.6% in Group 3. Of these, 1 patient could not adapt to NIMV, and acidosis worsened in 2 patients.

There was no statistically significant difference among the study groups in terms of length of ICU or hospital stay. Similarly, the 3 groups were similar for mortality rates.

In our study, it was shown that the concomitant bronchiectasis or pneumonia did not affect the success of NIMV in COPD patients with acute hypercapnic respiratory failure. However, our study has some limitations. Since the number of patients was small and it was planned as a single-center retrospective study, it may not be appropriate to generalize our results. However, we suppose that the results of the study may be valuable for similar patients since the existing patients were followed by the same chest diseases and intensive care physicians with the same protocol.

Conclusion

Evidence has been increasing on the effectiveness of NIMV in the treatment of acute hypercapnic respiratory failure. Although the use of NIMV in COPD exacerbations is now strongly recommended according to the results of many randomized controlled trials, more studies are needed on the success of NIMV in patients with pneumonia and bronchiectasis.

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Ethics Committee Approval: The Atatürk Chest Diseases and Thoracic Surgery Training and Research Hospital Ethics Committee granted approval for this study (date: 16.04.2012, number: 381).

Authorship Contributions: Concept: SK; Design: SK, SA; Data Collection or Processing: İOA, NU; Analysis or Interpretation: İOA; Literature Search: SK; Writing: SK; Critical Review: YTŞ.

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References

1. Stefan MS, Shieh MS, Pekow PS, Rothberg MB, Steingrub JS, Lagu T, et al. Epidemiology and outcomes of acute respiratory failure in the United States, 2001 to 2009: a national survey. *J Hosp Med* 2013;8(2):76–82. [\[CrossRef\]](#)
2. Lindenauer PK, Stefan MS, Shieh MS, Pekow PS, Rothberg MB, Hill NS. Outcomes associated with invasive and noninvasive ventilation among patients hospitalized with exacerbations of chronic obstructive pulmonary disease. *JAMA Intern Med* 2014;174(12):1982–93. [\[CrossRef\]](#)
3. Maheshwari V, Paioli D, Rothaar R, Hill NS. Utilization of non-invasive ventilation in acute care hospitals: a regional survey. *Chest* 2006;129(5):1226–33. [\[CrossRef\]](#)
4. Walkey AJ, Wiener RS. Use of noninvasive ventilation in patients with acute respiratory failure, 2000-2009: a population-based study. *Ann Am Thorac Soc* 2013;10(1):10–7. [\[CrossRef\]](#)
5. Hill NS. Noninvasive ventilation routine therapy for community-acquired pneumonia? Not so fast! *Intensive Care Med* 2001;27(5):797–9. [\[CrossRef\]](#)
6. Jolliet P, Abajo B, Pasquina P, Chevrolet JC. Non-invasive pressure support ventilation in severe community-acquired pneumonia. *Intensive Care Med* 2001;27(5):812–21. [\[CrossRef\]](#)
7. Keenan SP, Sinuff T, Cook DJ, Hill NS. Does noninvasive positive pressure ventilation improve outcome in acute hypoxemic respiratory failure? A systematic review. *Crit Care Med* 2004;32(12):2516–23. [\[CrossRef\]](#)
8. Carreaux G, Millán-Guilarte T, De Prost N, Razazi K, Abid S, Thille AW, et al. Failure of noninvasive ventilation for de novo acute hypoxemic respiratory failure: role of tidal volume. *Crit Care Med* 2016;44(2):282–90. [\[CrossRef\]](#)
9. Carrillo A, Gonzalez-Diaz G, Ferrer M, Martinez-Quintana ME, Lopez-Martinez A, Llamas N, et al. Non-invasive ventilation in community-acquired pneumonia and severe acute respiratory failure. *Intensive Care Med* 2012;38(3):458–66. [\[CrossRef\]](#)
10. Stefan MS, Shieh MS, Pekow PS, Hill N, Rothberg MB, Lindenauer PK. Trends in mechanical ventilation among patients hospitalized with acute exacerbations of COPD in the United States, 2001 to 2011. *Chest* 2015;147(4):959–68. [\[CrossRef\]](#)
11. Stefan MS, Nathanson BH, Lagu T, Priya A, Pekow PS, Steingrub JS, et al. Outcomes of noninvasive and invasive ventilation in patients hospitalized with asthma exacerbation. *Ann Am Thorac Soc* 2016;13(7):1096–104. [\[CrossRef\]](#)

12. Phua J, Ang YL, See KC, Mukhopadhyay A, Santiago EA, Dela Pena EG, et al. Noninvasive and invasive ventilation in acute respiratory failure associated with bronchiectasis. *Intensive Care Med* 2010;36(4):638–47. [CrossRef]
13. Bach JR, Brougner P, Hess DR, Hill NS, McIntyre N, Pearson D, et al. Consensus statement: noninvasive positive pressure ventilation. *Respir Care* 1997;42:365–9.
14. Moretti M, Cilione C, Tampieri A, Fracchia C, Marchioni A, Nava S. Incidence and causes of non-invasive mechanical ventilation failure after initial success. *Thorax* 2000;55(10):819–25. [CrossRef]
15. American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1995;152(5 Pt 2):S77–121.
16. Osadnik CR, Tee VS, Carson-Chahhoud KV, Picot J, Wedzicha JA, Smith BJ. Non-invasive ventilation for the management of acute hypercapnic respiratory failure due to exacerbation of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2017;7(7):CD004104. [CrossRef]
17. Keenan SP, Sinuff T, Cook DJ, Hill NS. Which patients with acute exacerbation of chronic obstructive pulmonary disease benefit from noninvasive positive-pressure ventilation? A systematic review of the literature. *Ann Intern Med* 2003;138(11):861–70. [CrossRef]
18. Brochard L, Isabey D, Piquet J, Amaro P, Mancebo J, Messadi AA, et al. Reversal of acute exacerbations of chronic obstructive lung disease by inspiratory assistance with a face mask. *N Engl J Med* 1990;323(22):1523–30. [CrossRef]
19. Brochard L, Mancebo J, Wysocki M, Lofaso F, Conti G, Raus A, et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *N Engl J Med* 1995;333(13):817–22. [CrossRef]
20. Conti G, Antonelli M, Navalesi P, Rocco M, Bui M, Spadetta G, et al. Noninvasive vs. conventional mechanical ventilation in patients with chronic obstructive pulmonary disease after failure of medical treatment in the ward: a randomized trial. *Intensive Care Med* 2002;28(12):1701–7. [CrossRef]
21. Ciledag A, Kaya A, Akdogan BB, Kabalak PA, Onen ZP, Sen E, et al. Early use of noninvasive mechanical ventilation in patients with acute hypercapnic respiratory failure in a respiratory ward: a prospective study. *Arch Bronconeumol*. 2010 Oct;46(10):538–42. Spanish. [CrossRef]
22. Scala R, Naldi M, Archinucci I, Coniglio G. Non-invasive positive pressure ventilation in acute hypercapnic respiratory failure: clinical experience of a respiratory ward. *Monaldi Arch Chest Dis* 2004;61(2):94–101. [CrossRef]
23. Lightowler JV, Wedzicha JA, Elliott MW, Ram FS. Non-invasive positive pressure ventilation to treat respiratory failure resulting from exacerbations of chronic obstructive pulmonary disease: Cochrane systematic review and meta-analysis. *BMJ* 2003;326(7382):185. [CrossRef]
24. Söyler Y, Akin Kabalak P, Saral Öztürk Z, Uğurman F. Comparing effectiveness of intelligent volume-assured pressure support (iVAPS) vs bi-level positive airway pressure spontaneous/timed (BPAP S/T) for hypercapnic respiratory failure in chronic obstructive pulmonary disease. *Int J Clin Pract* 2021;75(10):e14595. [CrossRef]
25. Stefan MS, Priya A, Pekow PS, Lagu T, Steingrub JS, Hill NS, et al. The comparative effectiveness of noninvasive and invasive ventilation in patients with pneumonia. *J Crit Care* 2018;43:190–6. [CrossRef]
26. Bhatti H, Ramdass A, Cury JD, Jones LM, Shujaat A, Louis M, et al. Operator dependent factors implicated in failure of non-invasive positive pressure ventilation (NIPPV) for respiratory failure. *Clin Respir J* 2017;11(6):901–5. [CrossRef]
27. Squadrone E, Frigerio P, Fogliati C, Gregoretto C, Conti G, Antonelli M, et al. Noninvasive vs invasive ventilation in COPD patients with severe acute respiratory failure deemed to require ventilatory assistance. *Intensive Care Med* 2004;30(7):1303–10. [CrossRef]
28. Bodí M, Rodríguez A, Solé-Violán J, Gilavert MC, Garnacho J, Blanquer J, et al.; Community-Acquired Pneumonia Intensive Care Units (CAPUCI) Study Investigators. Antibiotic prescription for community-acquired pneumonia in the intensive care unit: impact of adherence to Infectious Diseases Society of America guidelines on survival. *Clin Infect Dis* 2005;41(12):1709–16. [CrossRef]