

# Non-Invasive Positive Pressure Ventilation Compared To Invasive Mechanical Ventilation Among Patients With COPD Exacerbations In An Inner City MICU – Predictors Of NPPV Use

S Venkatram, S Rachmale, B Kanna, A Soni

## Citation

S Venkatram, S Rachmale, B Kanna, A Soni. *Non-Invasive Positive Pressure Ventilation Compared To Invasive Mechanical Ventilation Among Patients With COPD Exacerbations In An Inner City MICU – Predictors Of NPPV Use*. The Internet Journal of Pulmonary Medicine. 2009 Volume 12 Number 1.

## Abstract

Introduction: Non-invasive positive pressure ventilation (NPPV) has been shown to be effective in selected patients with severe exacerbations of chronic obstructive pulmonary disease (COPD) and can obviate the need for mechanical ventilation, avoid the complications, and reduce Intensive Care Length of Stay. NPPV is increasingly used among patients with Acute Respiratory Failure (ARF), but is under-utilized. We studied the utilization of NPPV in patients with COPD exacerbations and impact on patient outcome at our MICU which is staffed 24/7 by intensivists.

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease state that is characterized by partially reversible airflow obstruction. COPD exacerbations characterized by a change in the patient's usual respiratory symptoms occur frequently and require a change in management, including hospital admission.

Non-invasive positive pressure ventilation (NPPV) has been shown to be effective in selected patients with severe exacerbations of chronic obstructive pulmonary disease<sup>1-6</sup>. Patients that are managed with NPPV do not suffer the complications associated with endotracheal intubation and mechanical ventilation and spend fewer days in the critical care units. NPPV has also been shown to reduce recurrent admissions and mortality. The key to successful outcomes is by initiating therapy early<sup>7</sup>. But while NPPV is increasingly used among patients with Acute Respiratory Failure (ARF)<sup>5, 8, 9</sup>, it is also underutilized. Underutilization of NPPV may be related to physician staffing and expertise, as appropriate patient selection and titration of the ventilation are key to its success. In addition to the usual staffing by house officers, the MICU at our institution is staffed 24/7 by on site intensivists. Our goal was to determine if the presence of intensivists resulted in greater utilization of NPPV and improvement in outcomes.

## METHODS AND MATERIALS

### DESIGN

This is a retrospective study of patients with COPD in acute respiratory failure admitted to the Medical Intensive Care Unit (MICU). Patients admitted from January 2005 to December 2007 were enrolled in the study.

### SETTING

Lincoln Medical Center is a hospital that serves the inner city population, which has a high prevalence of obesity, smoking, illicit drug use and other comorbid conditions such as HIV infection and Hepatitis C. The 20 bed closed MICU is staffed 24/7 by a team of American board-certified intensivists, nursing staff-patient ratio of 1: 2 and other ancillary services staff. The MICU also hosts graduate resident training rotations from post-graduate PG1 to PG3 levels from the Internal medicine and emergency medicine training programs. In our MICU, NPPV is administered by Bi-level positive pressure ventilation (BIPAP).

### INCLUSION CRITERIA

All patients with COPD exacerbations in acute respiratory failure that required ventilatory support – either non-invasive positive pressure ventilation (NPPV) or invasive mechanical ventilation (IMV) – on admission to the MICU were included. Patients hospitalized due to pneumonia, pulmonary

edema, or causes other than a COPD exacerbation and patients with a history of asthma were excluded from this study. In all cases, triage decisions pertaining to ICU care was done by the on site pulmonologist/intensivist.

## DATA COLLECTION

Data for this study was extracted from a detailed critical care clinical database of all patients admitted to the MICU service. The database prospectively recorded demographic variables, admission diagnoses, APACHE II scores, mechanical ventilation, days on ventilator, and the complications and outcomes of all patients admitted to the MICU. The director of critical care oversaw the standardized updates of the database daily and reviewed it monthly with the MICU team to ensure complete and accurate data collection.

In addition to this database, data regarding patient weight, presence of comorbid illnesses (such as Congestive heart failure, Obstructive sleep apnea), days on NPPV, NPPV failures, and Arterial blood gas (ABG) values on admission were extracted from medical records by independent observers. NPPV failure was then defined as a need for endotracheal intubation at any time during ICU stay. The primary outcome measures were NPPV utilization in patients with COPD exacerbations admitted to the MICU and NPPV failures in the MICU. Secondary outcomes were duration of ventilatory support (NPPV or MV) and hospital mortality. Data was also analyzed to study the relationship between presence of obesity, history of congestive heart failure (CHF) or obstructive sleep apnea (OSA) with the choice of mode of ventilatory support. We defined obesity as a weight of > 100kgs (height was not available for all patients and a weight of > 100 kilograms would approximate a BMI of > 30 with a height range of 60 to 74 inches). The study was approved by the hospital institutional review board and informed consent was waived.

## STATISTICAL ANALYSIS

After descriptive analysis, univariate analysis was performed using the unpaired t-test to examine differences in continuous variables. Multivariable logistic regression was used to analyze the independent effect of each variable on the outcome (use of NPPV). For all analysis, a two-tailed p-value of < 0.05 was considered statistically significant.

## RESULTS

In the 3 year study (2005 to 2007), 3749 patients were admitted to the MICU. Out of these, 266 patients with

COPD and acute respiratory failure required supportive ventilation. 110 patients were managed with NPPV and 156 underwent endotracheal intubation and were mechanically ventilated. Demographics and admission characteristics are summarized in Table 1. Forty one percent of patients with ARF received NPPV as the initial mode of ventilation.

### Figure 1

Table- 1: Demographics and Admission Characteristics of patients treated with NPPV versus IMV

	NPPV	Mechanical Ventilation	P-Value	95% CI
Total (n)	110	156		
APACHE II score (Mean+/-SD)	13.7+/-4.7	16.48+/-5.58	0.001	- 4.06 to -1.49
Age (yr+/- SD)	62.44+/-12.33	67.44+/-11.88	0.001	-7.95 to -2.04
Male (%)	38.18%	40.38%	0.89	
Female (%)	61.82%	59.72%		
PaCO <sub>2</sub> at admission (Mean+/-SD)	70.47+/-20	67.94+/-25.24	0.94	-65.28 to 70.34
pH at admission (Mean+/-SD)	7.29+/-0.07	7.28+/-0.11	0.94	-0.27 to 0.29
Weight (Mean+/-SD)	104.2+/-40.19	91+/-38.8	0.007	3.54 to 22.85

## ADMISSION CHARACTERISTICS

The mean admission APACHE II score was lower in NPPV as compared to IMV group (13.7 vs 16.4, p= 0.001). The patients in the NPPV group were found to be younger than those in the IMV group (62.4 vs 67.4, p=0.001). Women patients were predominant in both groups. Mean patient weight was higher in NPPV than the IMV group (104.2 vs 91, p = 0.007). There was no difference in the mean PaCO<sub>2</sub> value (70.47 vs 67.94, p=0.94) or arterial Ph (7.28 vs 7.27, p=0.94) in the two groups at admission.

## COMORBID CONDITIONS

Obesity and OSA were more common in the NPPV group. Also, CHF as a comorbid condition was found to be similar in both groups and did not appear to influence the choice of ventilatory support (Table 2).

### Figure 2

Table- 2: Co-morbid conditions of patients treated with NPPV versus IMV

	NPPV	Invasive Mechanical Ventilation	P-Value
Total (n)	110	156	
CHF n (%)	46 (41.81%)	79 (50.64%)	0.17
Obesity n (%)	50 (45.45%)	45 (28.84%)	0.006
OSA n (%)	38(34.54%)	30(19.23%)	0.007

## OUTCOMES

The duration of ventilatory support with NPPV was lower compared to mechanical ventilation (NPPV=2.5 vs IMV=3.9, p = < 0.001). There was no significant difference in the in-hospital or ICU all-cause mortality in the two

groups. While there were no deaths in the NPPV group, there were five deaths in the MV group. Six patients who were originally managed with NPPV (5.45%) clinically deteriorated and underwent endotracheal intubation and mechanical ventilation. All survived to hospital discharge (Table 3).

**Figure 3**

Table- 3: Outcomes among patients treated with NPPV versus IMV

	NPPV	Mechanical Ventilation	P-Value	95% CI
Total (n)	110	156		
Days of therapy (Mean +/-SD)	2.54+/-1.56	3.9+/-3.9	<0.001	-2.13 to -0.58
Mortality n (%)	0	5 (3.2%)	0.079	
NPPV Failure n (%)	6 (5.45%)	--	---	

**DISCUSSION**

NPPV ventilation was utilized in management of 41% of patients with COPD and ARF in our study. The management was successful in 94.5% of patients with 5.45% who required a change to MV. NPPV utilization appeared to have been influenced by the presence of younger age, coexisting obesity and OSA. A history of CHF did not play a role in the choice of ventilator support.

**NPPV UTILIZATION AND FAILURE**

The benefit of NPPV over MV has been proven unequivocally in selected patients with acute on chronic respiratory failure secondary to COPD<sup>4, 8, 10, 11</sup>. NPPV has been shown to decrease need for endotracheal intubation, decreased ICU and hospital stay as well as decreased mortality<sup>8, 12, 13</sup>. Additional benefits of NPPV use include lower infectious complications and reduced length of stay, accounting for lower health care costs<sup>14, 15</sup>. However, NPPV is under- utilized in patients with respiratory failure overall in acute care settings, with 20 percent of ICU’s not using NPPV<sup>16</sup>. An observational survey by Demoule<sup>17</sup> in French ICU’s demonstrated that NPPV use increased from 16 percent to 24 percent in all ICU patients receiving ventilatory support from 1997 to 2002. The changes in relative use of NPPV were higher in patients with acute on chronic respiratory failure and denovo respiratory failure. Maheshwari et al showed the NPPV utilization varied among different acute care hospitals from none to 50 percent and overall 20% in the US<sup>18</sup>. However, data on NPPV use on the percentage of patients with acute on chronic respiratory failure is sparse. There have been no studies to date which have looked into ICU staffing patterns and NPPV use. Availability of physicians on site may be a factor in the

underutilization of NPPV, which requires the selection of appropriate patients and titration of the support. Intensivist staffing 24/7 is a valuable resource available in less than 5% of all ICUs in the US and may account for the increased utilization of NPPV in our cohort of patients.

Also, our NPPV failure rate of 5.45% is significantly lower than that reported in previous studies<sup>19</sup>. The first randomized controlled trial comparing NPPV to standardized treatment with oxygen via a mask revealed intubation rates of 25% in the NPPV group<sup>1</sup>. Subsequent studies<sup>2, 4, 18, 19</sup> have shown a NPPV failure rates between 7-62.5%. NPPV failures can be accountable to both patient factors and system factors. Predictors of NPPV failure include Glasgow Coma Score <11, acute physiology and chronic health evaluation (APACHE) II>29, respiratory rate >30 breaths/min and pH at admission < 7.25<sup>20</sup>. System issues relate to ICU staffing with intensivists 24/7, availability of respiratory therapists and nursing staff. Low NPPV failure rates in our study could be attributed to both early initiation of NPPV by the in-house intensivists and titration at bed side. Younger age and lower APACHE scores may have also contributed to the success of NPPV in our study; however, there was no significant difference in the admission pH and pCO<sub>2</sub> in the two groups. When comparing the duration of ventilator support of the NPPV group to the MV group, patients with COPD showed lower days on NPPV rather than on MV.

Our study validates earlier studies reporting similar findings<sup>20, 21</sup>.

**COPD, OBESITY AND VENTILATORY SUPPORT**

Steuten et al<sup>22</sup> reported that 18% of COPD patients were obese with the highest prevalence in GOLD stages 1 and 2. In a multiethnic cohort of patients with early COPD, a higher prevalence of 54% was reported by Eisner et al in California<sup>23</sup>. Although a potential link between obesity and COPD is also increasingly recognized<sup>24</sup>, the effect of obesity on COPD exacerbations is unknown. Literature on the use of ventilatory support in obese patients with COPD exacerbations is meager. In our study, the mean weight of COPD patients on NPPV were higher compared to MV; presence of obesity was associated more with NPPV use than with MV. The reasons for this is unclear but may be related to a higher prevalence of OSA in this cohort of patients.

**COPD, COMORBIDITIES AND VENTILATORY**

## **SUPPORT**

Patients with COPD have many complex comorbidities. COPD is considered to be a predisposing condition for developing a new distinct disorder called chronic systemic inflammatory syndrome<sup>25</sup>. The components of this syndrome include congestive heart failure and OSA. It is estimated that 20 % of patients with OSA have COPD<sup>26</sup>. The role of OSA on natural history of COPD is well known. Patients with overlap syndrome (COPD & OSA) have a higher risk of developing pulmonary hypertension, respiratory failure and chronic cor pulmonale, compared to patients with COPD alone. We found that patients with COPD exacerbations with a history of OSA had higher use of NPPV than MV. This may represent a provider familiarity with NPPV use in patients with OSA. Patient familiarity and tolerance for NPPV use were also probable contributing factors.

Similarly, COPD is associated with congestive heart failure in 20% of patients<sup>27,28</sup>. Distinction of etiological diagnosis in this group of patients with acute breathless is difficult. The use of NPPV in CHF exacerbations is controversial. Studies using CPAP revealed a rapid improvement in vital signs, oxygenation and a decreased need for endotracheal intubation<sup>29,30</sup>. However, a subsequent study comparing CPAP with Bi-level Positive Pressure Ventilation (BIPAP) revealed a higher incidence of acute MI in the BIPAP group<sup>31</sup>. It would seem intuitive that BIPAP use would be lower in patients with COPD exacerbations with a comorbid history of CHF. In our study, a history of CHF was not associated with an increased use of either form of ventilatory support.

There were no deaths in the NPPV group, and mortality in the MV group was 3.2%. This is lower than reported in literature<sup>32-34</sup>. The admission APACHE scores were lower than reported in other studies and most likely accounted for the lower mortality seen in our study. Of the mechanically ventilated patients, 141 of 151 survivors were extubated and 10 patients underwent tracheostomy and were transferred to long-term ventilatory institutions.

The limitations of our study include a single center retrospective study and a lack of randomization. Patients in the NPPV group were younger and had lower APACHE scores. Our ICU is covered 24/7 by intensivists and the results cannot be generalized to units not having this valuable resource. We did not record the height of patients and could not calculate actual BMI and used > 100 kilograms as morbidly obese.

In conclusion, NPPV utilization in patients with COPD exacerbations is higher in ICU's staffed 24/7 by intensivists. Younger age, obesity and history of OSA favored the use of NPPV over IMV. A history of CHF was not associated with preferential use of either form of ventilatory support. It would be tempting to attribute 24/7 staffing by intensivists for the lower hospital mortality, lower days of ventilatory support, high extubation rates and lower NPPV failure, but this has to be validated in prospective studies.

## **References**

1. Kramer, N., Meyer TJ, Meharg J et al., Randomized, prospective trial of noninvasive positive pressure ventilation in acute respiratory failure. *Am J Respir Crit Care Med*, 1995. 151(6): p. 1799-806.
2. Squadrone, E., frigerio P, Fogliati C 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): p. 1303-10.
3. Peter, J.V., Moran JL, Hughes JP, Noninvasive ventilation in acute respiratory failure--a meta-analysis update. *Crit Care Med*, 2002. 30(3): p. 555-62.
4. Bott, J. Carroll MP, Conway JH et al., Randomised controlled trial of nasal ventilation in acute ventilatory failure due to chronic obstructive airways disease. *Lancet*, 1993. 341(8860): p. 1555-7.
5. Antonelli, M., Conti G, Rocco M et al., A comparison of noninvasive positive-pressure ventilation and conventional mechanical ventilation in patients with acute respiratory failure. *N Engl J Med*, 1998. 339(7): p. 429-35.
6. Ambrosino, N., Noninvasive mechanical ventilation in acute on chronic respiratory failure: determinants of success and failure. *Monaldi Arch Chest Dis*, 1997. 52(1): p. 73-5.
7. Early use of non-invasive positive pressure ventilation for acute exacerbations of chronic obstructive pulmonary disease: a multicentre randomized controlled trial. *Chin Med J (Engl)*, 2005. 118(24): p. 2034-40.
8. Brochard, L., Mancebo J, Wysocki M, et al., Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *N Engl J Med* 1995. 333(13): p. 817-22.
9. Hillberg R.E., Johnson DC, Noninvasive ventilation. *N Engl J Med* 1997. 337(24): p. 1746-52.
10. Plant PK, Owen JL, Elliott MW. Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: a multicentre randomized controlled trial. *Lancet* 2000; 355: 1931-1935.
11. Conti G, Antonelli M, Navalesi P, et al. Noninvasive versus 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: 1701-1707.
12. Wysocki M, Tric L, Wolff MA, et al. Noninvasive pressure support ventilation in patients with acute respiratory failure: a randomized comparison with conventional therapy. *Chest*, 1995; 107:761-768
13. Kramer N, Meyer TJ, Meharg J, et al. Randomized, prospective trial of noninvasive positive pressure ventilation in acute respiratory failure. *Am J Respir Crit Care Med* 1995; 151: 1799-1806
14. Plant PK, Owen JL, Elliott MW. Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards:

a multicentre randomised controlled trial. *Lancet* 2000; 355: 1931–1935.

15. Plant PK, Owen JL, Parrott S, et al. Cost effectiveness of ward based non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease: economic analysis of randomised controlled trial. *BMJ* 2003; 326: 956.

16. Carlucci A, Richard J-C, Wysocki M et al: Noninvasive versus conventional mechanical ventilation: and epidemiological survey. *Am J Respir Crit Care Med* 2001, 163: 874-880.

17. Demoule A, Girou Ewe, Richard J-C El al. Increased use of noninvasive ventilation in French intensive care units. *Intensive care Med*, 2006; 32:1747-1755

18. Maheshwari V, Paioli D, Rothaar R, et al. Utilization of non invasive ventilation in acute care hospitals: a regional survey. *Chest* 2006; 129:1226–1233

19. Lightowler JV, Wedjicha JA, Elliott MW et al: 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, 326:185-187

20. Confalonieri M, Garuti G, Cattaruzza MS, et al. A chart of failure risk for noninvasive ventilation in patients with COPD exacerbation. *Eur Respir J* 2005; 25:348–355

21. L Brochard, D Isabey, J Piquet et al. Reversal of acute exacerbations of chronic obstructive lung disease by inspiratory assistance with a face mask. *NEJM* Volume 323:1523-1530, 1990

22. Steuten LM, Creutzberg EC, Vrijhoef HJ, et al. COPD as a multicomponent disease: inventory of dyspnoea, underweight, obesity and fat free mass depletion in primary Care. *Prim Care Respir J* 2006; 15:84–91.

23. Eisner MD, Blanc PD, Sidney S, et al. Body composition and functional limitation in COPD. *Respir Res* 2007; 8:7.

24. Poulain M, Doucet M, Major GC, et al. The effect of obesity on chronic respiratory Diseases: Pathophysiology

and therapeutic strategies. *CMAJ* 2006;174:1293–9.

25. Fabbri LM, Rabe KF. From COPD to chronic systemic inflammatory syndrome? *Lancet* 2007; 370: 797–799.

26. Fletcher EC. Chronic lung disease in the sleep apnea syndrome. *Lung* 1990; 168: Suppl., 751–761.

27. Rutten FH, Moons KG, Cramer MJ, et al. Recognising heart failure in elderly patients with stable chronic obstructive pulmonary disease in primary care: cross sectional diagnostic study. *BMJ* 2005; 331: 1379.

28. Rutten FH, Cramer MJ, Lammers JW et al. Heart failure and chronic obstructive pulmonary disease: an ignored combination? *Eur J Heart Fail* 2006; 8: 706–711.

29. Bernstein AD, Holt AW, Vedig AE et al. Treatment of severe Cardiogenic pulmonary edema with continuous positive pressure delivered by face mask. *NEJM* 325:1825-1830.1991

30. Rasanen J, Heikkila J, Downs J ET all. Continuous positive air way pressure by face mask. In acute cardiogenic pulmonary edema. *Am J cardiol* 1985;55:296-300.

31. Mehta S, Jay GD, Woolard RH ET all. Randomized prospective trial of Bilevel versus continuous positive air way pressure in acute pulmonary edema. *Crit care med* 1997; 25:620-628.

32. Gunen H, Hacievliyagil SS, Kosar F, et al. Factors affecting survival of hospitalised patients with COPD. *Eur Respir J* 2005; 26:234–41.

33. Connors AF Jr, Dawson NV, Thomas C, et al. Outcomes following acute exacerbation of severe chronic obstructive lung disease. The SUPPORT investigators (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments). *Is J Respir Crit Care Med* 1996; 154:959–67.

34. Breen D, Churches T, Hawker F, et al. Acute respiratory failure secondary to chronic obstructive pulmonary disease treated in the intensive care unit: a long term follow up study. *Thorax* 2002; 57:29–33.

**Author Information**

**Sindhaghatta Venkatram, MD, FCCP**

Director, Critical Care Units, Bronx Lebanon Hospital Center

**Sonal Rachmale, MD**

Fellow, Critical Care Medicine, Mayo Clinic

**Balavenkatesha Kanna, MD, MPH**

Assistant Program Director, Internal Medicine, Lincoln Medical and Health Center

**Anita Soni, MD, FACP**

Chair Person, Department of Internal Medicine, Lincoln Medical and Health Center