*Disaster Medicine and Public Health Preparedness*

**www.cambridge.org/dmp**

# High-PEEP Noninvasive Ventilation By Means of Mask as the Respiratory Support in COVID-19 ARDS Patients: Experience From General Hospital Slavonski Brod

Matija Jurjević MD, Ivan Mirković MD, PhD, Jasminka Kopić MD, PhD, Natalija Mrzljak Vučinić MD, Marcela Špehar Kokanović MD and Tonka Bujas Ćorluka MD

Department of Anesthesiology and Intensive Medicine, General Hospital Dr Josip Benčević, Slavonski Brod, Croatia

**Brief Report**

**Cite this article:** Jurjević M, Mirković I, Kopić J, Mrzljak Vučinić N, Špehar Kokanović M, Bujas Ćorluka T. High-PEEP noninvasive ventilation by means of mask as the respiratory support in COVID-19 ARDS patients: experience from general hospital Slavonski Brod. *Disaster Med Public Health Prep*. **17**(e151), 1–4. doi: https://doi.org/10.1017/dmp.2022.102.

**Keywords:**
COVID-19; ARDS; noninvasive ventilation; positive end expiratory pressure

**Corresponding author**: Jasminka Kopić, Email: jasminka.kopic@bolnicasb.hr.

## Abstract

**Objective:** Despite widespread use of noninvasive ventilation (NIV) in some coronavirus disease 2019 (COVID-19) hypoxemic patients, its clinical application is still subject of debate.
**Methods:** This is a retrospective, observational study with data collected from 91 consecutive patients treated in COVID intensive care unit (ICU) in our institution between October 2020 and February 2021. Outcomes were represented as ventilation hours, ICU and hospital length of stay, and ICU and hospital mortality.
**Results:** Patients' mean age was 66 ± 11 y and severe COVID-19 pneumonia with mean $paO_2/FiO_2$ 137 ± 57 was observed in 90% of the patients. High positive end-expiratory pressure (PEEP) NIV by means of total face mask was initially applied in 58 (64%) patients, high flow oxygen therapy (HFOT) in 25 (27%) patients, whilst invasive mechanical ventilation (IMV) started at the moment of admission in 8 (9%) patients. NIV and high flow oxygen therapy (HFOT) have been kept on throughout ICU stay in 50 (55%) patients, while 41 (45%) patients were put on IMV. Overall ICU mortality was 41%, while ICU mortality of patients on NIV was 14%.
**Conclusions:** High PEEP NIV was convenient and safe as initial respiratory support and in some COVID-19 ARDS patients remained an optimal respiratory support throughout their disease.

Despite many controversies and unsolved questions regarding the use of noninvasive ventilation (NIV) in coronavirus disease 2019 (COVID-19) patients with acute respiratory distress syndrome (ARDS),[1–3] many centers reported its successful use in some patients.[4–6] There are at least 2 arguments for making the NIV suitable for respiratory support in these patients, but all are dependent upon the availability of experienced staff and timely switch to invasive mechanical ventilation (IMV).

The first argument is the fact that, initially, most patients present with an isolated respiratory failure and usually preserved other vital functions, including good mental function. That allows clinicians to keep patients on spontaneous breathing, thus avoiding endotracheal intubation, sedation, and other deleterious effects of IMV.

The second argument is the fact that IMV in COVID-19 ARDS patients has been connected with a high mortality rate. Meta-analysis of 57,420 patients in 69 studies has reported the case fatality rate (CFR) among COVID-19 patients on IMV around 45%, but final hospital outcome was provided on only 13,120 patients, or 22,8% of the total IMV patients, and overall heterogeneity of included studies was very high.[7]

The most important challenge of spontaneous breathing, regardless the type of ventilation (noninvasive or invasive), is how to mitigate the patient self-inflicted lung injury (P-SILI), generated by high respiratory drive. It is crucial to recognize at the bedside intense inspiratory effort and high respiratory rate as the most important signs of high respiratory drive. Intense inspiratory effort, which can be observed by the negative swings in esophageal pressure ($P_{ES}$), causes high swings in transpulmonary pressure ($P_L$) with subsequent inflation of large tidal volumes (TV) in reduced aeration lung compartments, causing volutrauma as well as atelectrauma.[8,9] Moreover, negative deflection in pleural pressure induced by huge muscle effort may cause negative pressure pulmonary edema due to increased transmural vascular pressure and further impair respiratory function.[10]

It has been shown that high positive end-expiratory pressure (PEEP) could recruit and keep the lungs open, and in this way, decreases atelectrauma, increases functional residual capacity (FRC), decreases pulmonary edema, and altogether mitigates P-SILI.[11]

During the second wave of COVID-19 pandemic in Croatia, which has lasted from October 2020 to February 2021, a total of 91 critically ill COVID-19 patients with acute hypoxemic respiratory failure were treated in the intensive care unit (ICU) of the Department of Anesthesiology and Intensive Care, General Hospital Dr Josip Benčević, Slavonski Brod. Due to the long-lasting experience in NIV use in patients with a wide spectrum of acute respiratory failure (ARF) conditions, we have used NIV by means of total face mask as the first choice ventilation in most COVID-19 hypoxemic patients and, afterward, made switch to IMV if it had been required.

## Methods

### Patients

In this retrospective, observational study we have collected data from 91consecutive patients treated in COVID ICU in our institution between October 2020 and February 2021.

Data collecting from medical records and their retrospective analysis were approved by the local ethics committee under number 04000000/21-59.

All patients included in the study had positive polymerase chain reaction (PCR) test on severe acute respiratory syndrome coronavirus disease 2 (SARS-CoV2), and in most cases the reason for admission to the ICU was acute hypoxemic respiratory failure due to COVID-19 pneumonia. Of 91 patients, there were only 4 patients who had a positive PCR test, but other reasons for their ICU admission (polytrauma, acute stroke, and need for postoperative ICU treatment).

### Inclusion Criteria

All patients who had indication for admission to the COVID ICU were included in the study. Indications for admission were severe COVID-19 pneumonia with signs of respiratory failure which were: high respiratory rate (higher than 30/min), subjective feeling of difficulty breathing and inadequate oxygenation ($SpO_2$ lower than 90%), despite respiratory support with HFOT at flow of 60 L/min and $FiO_2$ at 0.5; and/or unstable vital functions due to other reasons in PCR positive patients.

### Outcomes

Outcomes were represented as ventilator hours, ICU and hospital length of stay, and ICU and hospital mortality.

### Protocol of Treatment

Before the admission to the ICU, all patients underwent thoracic computed tomography (CT) scan or, in case of suspected pulmonary embolism, CT scan with pulmonary angiography. Upon the admission, all patients were given central venous (CV) catheters and arterial catheters for invasive blood pressure monitoring as well as serial blood gas analysis. electrocardiogram (ECG), $SpO_2$, and end-tidal $CO_2$ were continuously monitored.

The type of respiratory support (HFOT, NIV, or IMV) and respiratory support parameters were adjusted according to patient's respiratory distress severity and blood gas analysis results. HFOT was applied as initial trial to some patients. In case of a failed HFOT, NIV by means of total face mask was started. Two settings were used in all NIV patients: the first 1 was CPAP, the second 1 was pressure support (PS) ventilation with usually minimal support of 2 to 3 cm $H_2O$.

NIV was applied by means of total face mask connected to the respirator with included NIV mode. For each patient on NIV, PEEP was individually optimized upon admittance and optimization continued throughout ICU stay, targeting it to achieve patient's subjective relief as well as to calm down work of breathing. Clinical signs of the beneficial effect of the adequate PEEP were lowering the breath rate and decreasing the deflections on pressure curves. Maximal values of PEEP were recorded as PEEP max. For the patients noncompliant to face mask, continuous sedation was titrated to achieve tolerability. Continuous infusion of dexmedetomidine or target controlled infusion (TCI) of propofol were most frequently used.

Switch to IMV was indicated in case of deteriorating patients' respiratory, hemodynamic or mental condition as well as inability to tolerate mask ventilation.

Remdesivir was prescribed to all patients admitted to the ICU within the first 5 d of the onset of symptoms and dexamethasone 6-8 mg intravenously after the 7th d of the disease onset. Other medications were enoxaparin-natrium at dose 1 mg/kg, pantoprazole 40 mg intravenously, and a balanced electrolyte infusions. All patients were fed with standard hospital diet and oral nutrition support products, depending on their respiratory function and their appetite.

### Data Analysis

Data were presented as absolute numbers as well as mean ± SD.

## Results

Ninety-one patients were included in the study. Their mean age was 66 ± 11 y; 88% of the patients had at least 1 chronic disease, while more than half (53%) of the patients had 2 or more comorbidities. Mean duration of symptoms before admission to the ICU was 8 ± 4 d. On admission to the ICU, 25 (27.5%) patients had severe hypoxemia with $paO_2/FiO_2$ score $\leq 100$ and 57 (62.6%) patients had a moderate hypoxemia with $paO_2/FiO_2$ score between 100 and 200. Of 9 patients with mild hypoxemia, 4 patients had other health problems as the cause of their critical condition (1 had polytrauma, 1 hemorrhagic stroke, and 2 were postoperative patients after urgent surgery). Mean $paO_2/FiO_2$ score of all patients was 137 ± 57. The patients' characteristics are presented in Table 1.

Respiratory support was started immediately after ICU admission in all patients. NIV was applied as initial respiratory support in 58 (64%) patients, HFOT in 25 (27%) patients, and IMV as the first respiratory support was applied in 8 (9%) patients.

In severely hypoxemic patients ($PaO_2/FiO_2 \leq 100$) HFOT was not successful at all (100% failure rate), while NIV failed in 62.5% of patients in the same group. In patients with moderate hypoxemia ($PaO_2/FiO_2$ 101-200), HFOT success rate was 25% and NIV failed in approximately one-third of the treated patients (35.4%). In the mild ARDS group ($PaO_2/FiO_2$ 201-300 and higher), HFOT, when applied initially, was 100% successful, and 1 patient with NIV trial required intubation.

The most frequent type of respiratory support throughout ICU stay was NIV by mask, which had 43 patients (47%), and 7 patients (8%) had HFOT as adequate respiratory support throughout ICU stay, while 41 (45%) patients were on IMV.

Switch to IMV had to be made in 33 (43.4%) of 76 NIV patients and in 8 (9%) patients IMV was the first respiratory support.

https://doi.org/10.1017/dmp.2022.102 Published online by Cambridge University Press

**Table 1.** Patients´ demographics and respiratory characteristics at admittance: joint data and data divided in groups according to $PaO_2/F_iO_2$ score

| | All the patients included | $PaO_2/F_iO_2 \leq 100$ | $PaO_2/F_iO_2$ 101-200 | $PaO_2/F_iO_2$ 201-300 and higher |
|---|---|---|---|---|
| Number of patients included in the study | 91 | 25 | 57 | 9 |
| Male | 57% | 52% | 56% | 66% |
| Age (mean ± standard deviation [SD]) | 66 ± 11 | 67 ± 8 | 65 ± 12 | 63 ± 15 |
| 2 or more comorbidities | 53% | 60% | 52% | 33% |
| Without comorbidities | 12% | 12% | 9% | 33% |
| $PaO_2/F_iO_2$ (mean ± SD) | 137 ± 57 | 79 ± 17 | 143 ± 26 | 257 ± 65 |
| Respiratory rate (mean ± SD) | 34 ± 12 | 37 ± 11 | 33 ± 11 | 23 ± 9 |
| Day of disease at admittance (mean ± SD) | 8 ± 4 | 8 ± 4 | 9 ± 4 | 7 ± 4 |

**Table 2.** Outcomes and ventilation modes: joint data and data divided in $p_aO_2/F_iO_2$ groups

| | All the patients included in the study | $p_aO_2/F_iO_2 \leq 100$ (25 pts) | $p_aO_2/F_iO_2$: 101-200 (57 pts) | $p_aO_2/F_iO_2$: 201-300 and higher (9 pts) |
|---|---|---|---|---|
| PEEPmax (mean ± standard deviation [SD]) cm $H_2O$ | 16 ± 2 | 17 ± 2 | 16 ± 2 | 12 ± 6 |
| Ventilator hours (mean ± SD) | 214 ± 108 | 268 ± 178 | 216 ± 108 | 139 ± 115 |
| ICU days (mean ± SD) | 10 ± 5 | 12 ± 6 | 10 ± 5 | 8 ± 4 |
| Hospital days (mean ± SD) | 15 ± 7 | 15 ± 6 | 17 ± 8 | 13 ± 5 |
| ICU deaths (ICU mortality) | 37 (41%) | 15 (60%) | 20 (35%) | 2 (22%) |
| Hospital deaths (hospital mortality) | 39 (43%) | 15 (60%) | 22 (39%) | 2 (22%) |
| IMV | 41 (45%) | 16 (64%) | 22 (39%) | 3 (33%) |
| NIV | 43 (47%) | 9 (36%) | 31 (54%) | 3 (33%) |
| HFOT | 7 (8%) | 0 | 4 (7%) | 3 (33%) |

Mean of the maximal PEEP level was 16 ± 2. In the mild ARDS group, it was 12 ± 6, and in moderate and severe hypoxemic patients' group, 16 ± 2 and 17 ± 2, respectively.

Patients with severe hypoxemia required longer period of mechanical ventilation and more ICU days.

During their ICU stay, 11 patients (12%) suffered pulmonary thromboembolism and pneumothorax was observed in 10 patients (11%).

ICU mortality of the entire group was 41% and hospital mortality was 43%. In the group of patients with mild hypoxemia, ICU mortality was 22%, whereas in the group with severe hypoxemia ICU, mortality was 60% and in the group with moderate hypoxemia 35%. One patient with $paO_2/FiO_2$ higher than 201 suffered hemorrhagic stroke with fatal outcome, the other 1 died from diffuse malignancy. Outcomes are presented in Table 2.

## Discussion

NIV by means of total face mask was applied at the moment of admission to the ICU, or very soon after HFOT trial, in most of our patients (76 or 84% of all patients) irrespective of the severity of hypoxemia. In 43 (47%) patients, NIV was adequate respiratory support throughout their disease and HFOT was used throughout their ICU stay in 7 (8%) patients.

The most frequent reasons for endotracheal intubation and switch to IMV were thromboembolic events, pneumothorax, septic complications, and noncompliance of the patients to mask ventilation.

According to last ISARIC report from February 2021 with data of 26,160 patients treated in the ICUs, 47.8% of patients received some type of NIV, while 60.7% of patients were on IMV.[12] Comparing our data with ISARIC report, our patients received NIV and HFOT more frequently.

ICU mortality rate of our patients (41%) was similar to reported mortality rate in previous studies (45% mortality in meta-analysis of patients requiring IMV by Lim et al.[7]; and 33.7% mortality in the study by Nicholson et al. of 404 patients with mechanical ventilation and 36% mortality in the similar age group to our patients[13]).

The most favorable outcome was in the group of 43 patients in which NIV was used throughout their ICU stay. ICU mortality in this group was 14%, while hospital mortality was 16%. On the contrary 26 of 33 patients (79%) in the failed NIV group died.

According to our experience, the most important initial goal of respiratory support was to decrease high respiratory drive and it was achieved by appropriate PEEP level selection as well as adequate sedation. We observed that applying appropriate PEEP level resulted in a gradual decrease of the rate of breathing and calmed down the forceful inspiration. On the contrary to the usual PEEP levels (5 to 10 cm $H_2O$) which are applied in patients with chronic obstructive pulmonary disease (COPD) or heart failure, in COVID-19 hypoxemic patients, PEEP levels were in range from 15 to 20 cm $H_2O$. Surprisingly, patients have tolerated such high PEEP levels very well and stated that they felt comfortable and breathed easier, while their oxygenation improved. In our experience, the most suitable device for NIV with such high PEEP levels was total face mask with silicone edge, which has adhered to the skin pretty well and leakage was rare.

Our approach and subsequent observations that injurious effects of spontaneous ventilation could be blunted by enough high PEEP levels have been in accordance with experimental work by Morais et al.[11] They have shown that recruitment of dependent

https://doi.org/10.1017/dmp.2022.102 Published online by Cambridge University Press

pulmonary regions by higher PEEP has decreased the inspiratory effort, lowered $V_T$, and thus made spontaneous breathing less injurious.[11,14]

According to our experience, high PEEP level should be kept long enough, which usually lasted 5 to 7 d, and thereafter, should be decreased very slowly, 2-3 cm $H_2O$ per d. Otherwise, in case of faster PEEP lowering, respiratory function was deteriorated.

The weak point of our study is that it is observational, retrospective 1, but we hope that our clinical data would be useful for future meta-analysis on the NIV use in COVID-19 ARDS patients. Our plan is to set up prospective study on NIV use in patients with COVID-19 ARDS.

**Author contributions.** Matija Jurjević, Ivan Mirković, and Jasminka Kopić participated in preparing and writing manuscript equally. Natalija Mrzljak Vučinić, Marcela Špehar Kokanović, and Tonka Bujas Ćorluka collected patients' data from medical record documentation equally.

**Conflicts of interest.** None.

## References


1. **Dobler CC, Murad H, Wilson ME.** Noninvasive positive pressure ventilation in patients with COVID-19. *Mayo Clin Proc.* 2020;95:2594-601.
2. **James A, Verdonk F, Bougle A, *et al.*** Noninvasive ventilation for acute respiratory failure (in COVID-19 patients): the non-ending story? *Anaesth Crit Care Med.* 2020;39:549-550.
3. **Rahmanzade R, Rahmanzadeh R, Tabarsi P, *et al.*** Noninvasive versus invasive ventilation in COVID-19: one size does not fit all! *Anesth Analg.* 2020;131:e114-e115.
4. **Avdeev SN, Yaroshetskiy AI, Tsareva NA, *et al.*** Noninvasive ventilation for acute hypoxemic respiratory failure in patients with COVID-19. *Am J Emerg Med.* 2021;39:154-157.
5. **Sivaloganathan AA, Nasim-Mohi M, Brown MM, *et al.*** Noninvasive ventilation for COVID-19-associated acute hypoxemic respiratory failure: experience from a single centre. *Br J Anaesth.* 2020;125:e368-e371.
6. **Ferreyro BL, Angriman F, Munshi L, *et al.*** Association of noninvasive oxygenation strategies with all-cause mortality in adults with acute hypoxemic respiratory failure: a systematic review and meta-analysis. *JAMA.* 2020;324:57-67.
7. **Lim ZJ, Subramaniam A, Reddy MP, *et al.*** Case fatality rates for patients with COVID-19 requiring invasive mechanical ventilation. A meta-analysis. *Am J Respir Crit Care Med.* 2021;203:54-66.
8. **Brochard L, Slutsky A, Pesenti A.** mechanical ventilation to minimize progression of lung injury in acute respiratory failure. *Am J Respir Crit Care Med.* 2017;195:438-442.
9. **Gattinoni L, Marini JJ, Pesenti A, *et al.*** The "baby lung" became an adult. *Intensive Care Med.* 2016;42:663-673.
10. **Bhattacharya M, Kallet RH, Ware LB, *et al.*** Negative-pressure pulmonary edema. *Chest.* 2016;150:927-933.
11. **Morais CC, Koyama Y, Yoshida T, *et al.*** High-positive end-expiratory pressure renders spontaneous effort noninjurious. *Am J Respir Crit Care Med.* 2018;197:1285-1296.
12. **Escher M, Hall M, Baillie K, *et al.*** ISARIC Clinical data report. February 10, 2021. https://isaric.org/research/covid-19-clinical-research-resources/evidence-reports/
13. **Nicholson CJ, Wooster L, Sigurslid HH, *et al.*** Estimating risk of mechanical ventilation and in-hospital mortality among adult COVID-19 patients admitted to Mass General Brigham: The VICE and DICE scores. *EclinicalMedicine.* 2021;33:100765.
14. **Borges JB, Morais CCA, Costa ELV.** High PEEP may have reduced injurious transpulmonary pressure swings in the ROSE trial. *Crit Care.* 2019;23:404.


https://doi.org/10.1017/dmp.2022.102 Published online by Cambridge University Press