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Efficacy and Safety of High PEEP NIV in COVID-19 Patients

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Abstract

Objective: To investigate the efficacy and safety of non-invasive ventilation (NIV) with high PEEP levels application in patients with COVID–19–related acute respiratory distress syndrome (ARDS).

Methods: This is a retrospective cohort study with data collected from 95 patients who were administered NIV as part of their treatment in the COVID-19 intensive care unit (ICU) at University Hospital Centre Zagreb between October 2021 and February 2022. The definite outcome was NIV failure.

Results: High PEEP NIV was applied in all 95 patients; 54 (56.84%) patients could be kept solely on NIV, while 41 (43.16%) patients required intubation. ICU mortality of patients solely on NIV was 3.70%, while total ICU mortality was 35.79%. The most significant difference in the dynamic of respiratory parameters between 2 patient groups was visible on Day 3 of ICU stay: By that day, patients kept solely on NIV required significantly lower PEEP levels and had better improvement in PaO_2, P/F ratio, and HACOR score.

Conclusion: High PEEP applied by NIV was a safe option for the initial respiratory treatment of all patients, despite the severity of ARDS. For some patients, it was also shown to be the only necessary form of oxygen supplementation.

Original Research

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Keywords:
ARDS; continuous positive airway pressure; COVID-19; non-invasive ventilation; PEEP

Abbreviations:
ABS, acid-base status; AHRF, acute hypoxemic respiratory failure; ANOVA, analysis of variance; ARDS, acute respiratory distress syndrome; BMI, body mass index; CCI, Charlson Comorbidity Index; COVID-19, coronavirus disease; CPAP, continuous positive airway pressure; CRP, C-reactive protein; ESICM, European Society of Intensive Care Medicine; FiO_2, fraction of inspired oxygen; HACOR, heart rate, acidosis, consciousness, oxygenation, and respiratory rate; HFNO, high-flow nasal oxygen; ICU, intensive care unit; IMV, invasive mechanical ventilation; NIRS, non-invasive respiratory support; NIV, non-invasive ventilation; P/F, PaO_2/FiO_2 (ratio); PaO_2, oxygen partial pressure in arterial blood; PCR, polymerase chain reaction; PEEP, positive end-expiratory pressure; P-SILI, patient self-inflicted lung injury; RF, respiratory frequency; SOFA, Sequential Organ Failure Assessment; SpO_2, blood oxygen saturation; WOB, work of breathing

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The role of non-invasive respiratory support (NIRS) in the treatment of acute hypoxemic respiratory failure (AHRF) not due to cardiogenic pulmonary edema or acute exacerbation of chronic obstructive pulmonary disease remains inconclusive.[1] Further, the same applies to AHRF due to coronavirus disease COVID-19. NIRS is an umbrella term which encompasses the high-flow nasal oxygen (HFNO), continuous positive airway pressure (CPAP), and non-invasive ventilation (NIV).[2]

Despite the coronavirus disease pandemic lasting for over 2 years, the role of NIV in the treatment of COVID-19-related acute respiratory distress syndrome (ARDS) remains undefined by official guidelines, because of a lack of randomized trials that would provide conclusive proof of its efficacy.[1,3–6] The high mortality rate and days of intubation associated with invasive mechanical ventilation (IMV) in COVID-19 patients renewed interest in the use of NIRS.[2] The ISARIC COVID-19 clinical report from March 2022 stated that 87.6% of patients admitted to the ICU required some form of oxygen supplementation, of which 47.1% were on NIV and 61.3% required IMV.[7] Although information about NIV application in such patients is still limited, several published studies link it with significantly lower mortality compared to IMV.[8–11] The European Society of Intensive Care Medicine (ESICM) guidelines on ARDS, released in 2023, made a weak recommendation for the use of CPAP over conventional oxygen therapy, in patients with COVID-19 AHRF, to reduce the risk of intubation based on results from a randomized trial by Perkins et al. The trial reported a lower intubation rate with CPAP but no difference in mortality.[1,12] No recommendation could be made for or against the use of NIV over CPAP. A major concern regarding the use of NIRS is the potential delay in intubation, which may lead to worse outcomes including the increase in mortality.[1] Further reasons for the lower use of NIV in COVID-19 patients could be the high severity of the disease at admission, lack of resources, and concerns with aerosolization.

Another challenge when it comes to NIV is choosing the appropriate level of positive end-expiratory pressure (PEEP).[13] The ideal PEEP value should enable the preponderance of

potential benefits, such as enhanced oxygenation, over potential complications including volutrauma and hemodynamic compromise.[14] Higher PEEP levels (> 10 cmH_2O) have been suggested by guidelines for IMV use in COVID-19 patients, as it has been previously demonstrated that high PEEP improves the chance of survival in patients with ARDS of other etiologies without significantly increasing the risk of fatal barotrauma compared to lower PEEP levels.[15,16] High PEEP was found to improve oxygenation, increase functional residual capacity, and reduce atelectrauma.[17] However, varied reports of success and safety of high PEEP in COVID-19 patients exist. Some studies, with relatively small sample sizes, report a poor response to high PEEP as a result of poor lung recruitability.[18–20] Experiments on animal models showed that high PEEP reduced the risk of patient self-inflicted lung injury (P-SILI) caused by intense spontaneous breathing by lowering the necessary intensity of spontaneous breathing and reducing the amount of solid-like atelectatic lung.[21] A retrospective study by Jurjević et al. showed that patients managed with NIV and high PEEP levels exhibited good tolerance and significantly lower mortality compared to patients on IMV.[22] Based on the currently released data, ESICM could not make a recommendation for or against routine PEEP titration with a higher $PEEP/FiO_2$ strategy to reduce mortality in patients with ARDS, including ARDS due to COVID-19.[1]

This is a retrospective cohort study based on data collected from 95 patients who were treated at the COVID-19 ICU in the period of October 2021 to February 2022 at the University Hospital Centre Zagreb and who had received oxygen support with NIV and high $PEEP/FiO_2$ strategy. The aim of this study was to further investigate the efficacy and safety of NIV with high $PEEP/FiO_2$ strategy in patients with COVID-19-related AHRF, with a focus on NIV failure, mortality, and potential complications.

Methods

A retrospective cohort study was conducted in the COVID-19 ICU of the Department of Anaesthesiology and Intensive Care at the University Hospital Centre Zagreb. Patient data were collected from October 2021 to February 2022. The collected data did not include personal information and were presented respecting patient privacy and data confidentiality. This research was approved by the Ethics Committee of the University Hospital Centre Zagreb.

Inclusion Criteria

Included in the study were patients who had a positive polymerase chain reaction (PCR) test on SARS-CoV-2 and who were treated with NIV with high $PEEP/FiO_2$ strategy during their stay in the COVID-19 ICU. The most common reason for admission to the ICU was AHRF due to COVID-19 pneumonia. Indications included severe COVID-19 pneumonia with the following signs of respiratory failure: tachypnea (> 30/min), dyspnea, inadequate oxygenation ($SpO_2 < 88\%$), and PaO_2/FiO_2 or P/F ratio < 300, despite respiratory support with HFNO. Data collected from the hospital information system and medical charts were analyzed. A review of medical records excluded 15 patients for whom information on oxygen partial pressure values was missing. The final sample of the research group consisted of 95 patients.

Collected Data

Demographic data included gender, age, and body mass index (BMI).

The main data collected for each patient were the required type of ventilation, either the use of NIV throughout the entire ICU stay or the need for a switch to IMV.

For each patient, the Charlson Comorbidity Index (CCI) and SOFA score were calculated. Monitored respiratory parameters were PEEP, fraction of inspired oxygen (FiO_2), blood oxygen saturation (SpO_2), oxygen partial pressure in arterial blood (PaO_2), and respiratory frequency (RF). The laboratory parameter included was C-reactive protein (CRP) plasma concentration. For this study, values of these parameters on Days 1, 3, and 7 of the patients' ICU stay were observed. HACOR score was calculated on the same days. In patients who required a switch to IMV, HACOR was also calculated prior to intubation.[23] PaO_2 was measured upon admission to the ICU before initiation of NIV and later, on Days 1 and 3 of ventilation.

The severity of the COVID-19 disease was determined based on the P/F ratio calculated on admission to the ICU, that is, first day of NIV treatment and again on the third day. Depending on the result, patients were classified into the following categories: pneumonia/mild ARDS (200 < P/F < 300), moderate ARDS (100 < P/F < 200), and severe ARDS (P/F < 100).

Changes in the abovementioned respiratory parameters were compared based on NIV failure and disease severity.

Data on the presence of complications, which included pneumothorax, pneumomediastinum, and subcutaneous emphysema, were also collected.

Informed consent was obtained from all participants included in the study at the time of their admission to ICU for potential use of collected data during their hospitalization in future cohort studies.

Outcomes

The primary outcome was NIV failure, that is, the need for a switch to IMV. Secondary outcomes included hospital discharge and discharge from the ICU.

Treatment Protocol

Upon admission to the COVID-19 ICU, all patients received central venous and arterial catheters for invasive blood pressure monitoring and serial blood gas analysis. Electrocardiogram (ECG), saturation, and end-tidal CO_2 were continuously monitored throughout their stay in the ICU.

Conversion to NIV treatment was required when, with the use of HFNO (60-80 L/min) and FiO_2 of over 60%, SpO_2 was below 88%. Moreover, switching to NIV was required for patients in whom the work of breathing (WOB) scale had a sum greater than 5.[24] NIV was administered by Dimar "Dimax Zero" total-face mask from Dimar Medical Devices (Medolla, Modena, Italy) or F&P "Nivairo" full-face mask from Fisher & Paykel Healthcare (East Tāmaki, Auckland, New Zealand). When placing the mask, the PEEP value was set at 5 cmH_2O and FiO_2 at 70%. Patients were observed for clinical signs of improvement (reduced WOB, reduced abdominal breathing, and retraction of intercostal muscles) and a subjective feeling of more comfortable breathing. After 10 minutes, if signs of improvement appeared, patients continued ventilation with the current settings.

If there was no improvement, PEEP was increased by 5 cmH_2O and FiO_2 was reduced to 60%. From this point, every 10 minutes, a reassessment followed. If there were still no signs of improvement, PEEP was increased by 1 cmH_2O to a maximum of 25 cmH_2O and FiO_2 was reduced by 5% to a minimum of 30%. PEEP was raised

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gradually, taking into consideration physiology, esophageal and pleural pressure, and was individually optimized, with the goal of decreasing WOB as well as to achieve patient's subjective breathing comfort which was verified by using the Likert scale. Max PEEP values were recorded. In patients noncompliant to using a face mask, continuous sedation was titrated with either continuous infusion of dexmedetomidine or target controlled infusion of propofol.

If patients were able to maintain satisfactory acid-base status (ABS) results and $SpO_2 > 90\%$ on optimal PEEP value, after 24 hours, de-escalation occurred. It was performed by decreasing PEEP by 1 cmH_2O every 8 hours to a minimum of 5-7 cmH_2O. If a physiological PEEP value of 5 cmH_2O was achieved, patients were switched from NIV to HFNO with a flow of 60 L/min and FiO_2 of 45%.

In cases where optimal PEEP value with adequate therapeutic outcome could not be found, a timely switch to IMV was required. A P/F ratio and HACOR score greater than 5 were of assistance in consideration of the necessity of the IMV.

Data Analysis

The IBM SPSS Statistics v25.0 (Armonk, NY, USA) was used for statistical data analysis. Continuous variables were presented as mean (SD) (range) if normally distributed, or as median (IQR) if non-normally distributed; categorical variables were expressed as absolute numbers and relative frequencies. The normally distributed data were compared using the Student's t-test, paired samples t-test, and 1-way and 2-way repeated measures analysis of variance (ANOVA). The non-normal distributed data were compared using the Mann-Whitney U test, χ^2-test, and Friedman test. A P-value of less than 0.05 was considered statistically significant.

Results

For demographic and COVID-19-related variables, see Table 1. For observed respiratory and inflammatory parameters, see Table 2. The study included 95 patients. Clinical presentation of COVID-19 varied from mild to moderate to severe: 18 patients (18.95%) had only pneumonia or mild ARDS, 36 (37.89%) had moderate ARDS, and 41 (43.16%) had severe ARDS. For 92 out of 95 patients, information on the development of disease complications was available. Sixteen patients (17.39%) developed pneumothorax, 20 patients (21.74%) had pneumomediastinum as a complication, and in 23 patients (25.0%) subcutaneous emphysema occurred during hospitalization in the ICU. The mean day of onset for each of these 3 complications was calculated based on the collected data (see Table 1).

NIV Failure

In the study, 54 (56.84%) out of 95 patients were kept on NIV for the entirety of their stay in the ICU, while 41 (43.16%) patients required intubation. The mean total time spent on NIV was 8 days. Significantly more cases of NIV failure occurred in patients with moderate or severe ARDS ($P = 0.009$). However, when analyzing the group of 41 patients with severe ARDS, for 21 of them (51.22%), NIV was a sufficient means of ventilation.

Changes in monitored respiratory parameters between Days 1, 3, and 7 in the ICU were compared based on NIV failure and disease severity. PEEP levels administered during the first week in the ICU differed significantly between patients kept solely on NIV and patients who required intubation ($P < 0.001$) (Figure 1a). The mean value of max recorded PEEP level was 15.91. There was no significant difference detected in Day 1 PEEP levels between the 2 groups. By Day 3, however, the difference in PEEP was statistically significant ($P = 0.002$); patients who did not require intubation had significantly lower PEEP levels administered. In those patients, PEEP was decreased by 0.22 cmH_2O on average by Day 3, while patients who had to be intubated required an average increase of 1.39 cmH_2O; the difference in change of administered PEEP levels between the 2 groups between Days 1 and 3 was also significant ($P = 0.018$). The difference in PEEP dynamic during the first week in the ICU based on disease severity determined by P/F ratio calculated on Day 1 was not significant (see Figure 1b) and neither was the change in administered PEEP levels between Days 1 and 3. However, PEEP levels observed on Day 3 were found to be significantly different between patient groups of different disease severities ($P = 0.004$). Patients with mild ARDS had significantly lower PEEP values administered on Day 3 (mean value of 12.35 cmH_2O) compared to patients with moderate ($P = 0.039$) (mean value of 14.61 cmH_2O) or severe ARDS (mean value of 15.32 cmH_2O) ($P = 0.003$).

HACOR score changed significantly by Day 3 ($P = 0.001$) and by Day 7 ($P = 0.025$) when compared to the HACOR score calculated on Day 1 in the ICU; however, scores calculated on Days 3 and 7 were not significantly different. The P/F ratio increased significantly by Day 3 from 125.63 on average to 192.21 ($P < 0.001$). By Day 3 a significant difference existed in applied FiO_2 ($P < 0.001$), but also P/F ratio ($P < 0.001$), SpO_2 ($P = 0.002$), RF ($P = 0.012$), and HACOR score ($P < 0.001$) based on whether or not NIV failed. In cases where NIV was sufficient, FiO_2 was decreased by 12.07% on average between Days 1 and 3 compared to a mean decrease of 5.11% in patients who required intubation ($P = 0.050$). Patients kept solely on NIV showed a significantly higher improvement in both the HACOR score ($P = 0.017$) and SOFA score ($P = 0.003$) by Day 3. In patients in whom NIV was not a sufficient means of oxygenation, the mean HACOR score prior to the switch to IMV was 7.07.

The mean PaO_2 measured upon admission to the ICU before initiation of NIV was 7.23. That value was found to be significantly lower than PaO_2 measured on Days 1 ($P < 0.001$) and 3 ($P < 0.001$) post-initiation; the difference in PaO_2 on Days 1 and 3 was not significant. However, when comparing PaO_2 values based on NIV failure, a significant difference was found in the increase of PaO_2 from Day 1 to Day 3 between the 2 groups ($P = 0.020$). In patients kept solely on NIV, an increase of 4.55 kPa on average was visible by Day 3, while PaO_2 in intubated patients increased by only 2.20 kPa on average. PaO_2 on Day 3 was shown to be significantly higher ($P = 0.046$) in patients kept solely on NIV (mean value of 10.45 kPa) than in intubated patients (mean value of 9.71 kPa).

The Days 1 to 3 change in P/F ratio was also found to be significantly different ($P = 0.005$) in patient groups of different disease severities: In patients with severe ARDS, the increase in P/F ratio (mean value of +98.26) was significantly higher than in patients with moderate (+39.41) or mild ARDS (+39.79). Due to such a high increase, patients with severe ARDS on Day 1 had an average P/F ratio of 167.64 by Day 3. The P/F ratio on Day 3 remained significantly higher ($P < 0.001$) in patients with mild ARDS (mean value of 276.06) compared to those with moderate (mean value of 183.69) or severe ARDS (mean value of 167.64).

CRP plasma concentration decreased during the first week in the ICU ($P < 0.001$). CRP values on Days 1 and 3 ($P < 0.001$) and Days 3 and 7 ($P = 0.003$) were significantly different (Figure 2). Patients kept solely on NIV had a lower CRP plasma concentration

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Table 1. Baseline characteristics of 95 patients who participated in the study

Variables	Results
Demography	
Age, mean (SD) (range), y	67.36 (11.67) (29-87)
Sex, female/male, n (%)	44 (46.30%)/51 (53.70%)
Weight, mean (SD) (range), kg	86.63 (16.53) (42-130)
BMI, mean (SD) (range), m^2/kg	29.06 (4.78) (17.26-40.00)
Charlson comorbidity score, mean (SD) (range)	4.20 (2.21) (0-11)
SOFA score on admission to ICU, mean (SD) (range)	3.28 (1.49) (2-8)
COVID-19-related variables	
Time on NIV, mean (SD) (range), days	8.00 (4.92) (1-32)
Time spent in ICU, mean (SD) (range), days	11.80 (6.80) (0-35)
Time spent in hospital, mean (SD) (range), days	26.24 (15.90) (5-80)
Survival rate, %	51.58
Complications	
Pneumothorax, mean day of onset, days	7.00
Pneumomediastinum, mean day of onset, days	4.35
Subcutaneous emphysema, mean day of onset, days	3.83

BMI, body mass index; ICU, intensive care unit; NIV, non-invasive ventilation; and SOFA, sequential organ failure assessment.

Table 2. Respiratory and inflammation parameters observed during the first week of the ICU stay

Parameters	Day 1	Day 3	Day 7
PEEP, mean (SD) (range), cmH_2O	13.95 (2.68) (6-20)	14.48 (3.13) (7-23)	13.72 (3.62) (5-21)
PaO_2, mean (SD) (range), kPa	11.05 (4.16) (4.9-35.0)	10.15 (1.94) (7.2-17.7)	–
FiO_2, mean (SD) (range), %	53.87 (16.02) (21-100)	44.36 (15.97) (21-88)	43.02 (14.83) (25-80)
RF, mean (SD) (range), min^{-1}	27.87 (5.61) (17-40)	25.81 (6.08) (13-39)	25.43 (5.64) (14-37)
SpO_2, mean (SD) (range), %	94.49 (2.99) (84-100)	94.34 (2.44) (86-99)	93.77 (3.14) (85-98)
HACOR, mean (SD) (range)	3.56 (2.21) (0-8)	2.64 (2.30) (0-9)	3.13 (2.59) (0-12)
P/F ratio, mean (SD) (range)	123.95 (63.00) (32-299)	195.05 (79.18) (75-441)	–
CRP, mean (SD) (range), mg/L	115.58 (67.28) (9.6-346.6)	82.53 (62.76) (5.4-285.7)	69.68 (71.27) (1.6-307.9)

CRP, C-reactive protein; FiO_2, fraction of inspired oxygen; NIV, non-invasive ventilation; PaO2, oxygen partial pressure in arterial blood; PEEP, positive end-expiratory pressure; RF, respiratory frequency; and SpO_2, blood oxygen saturation.

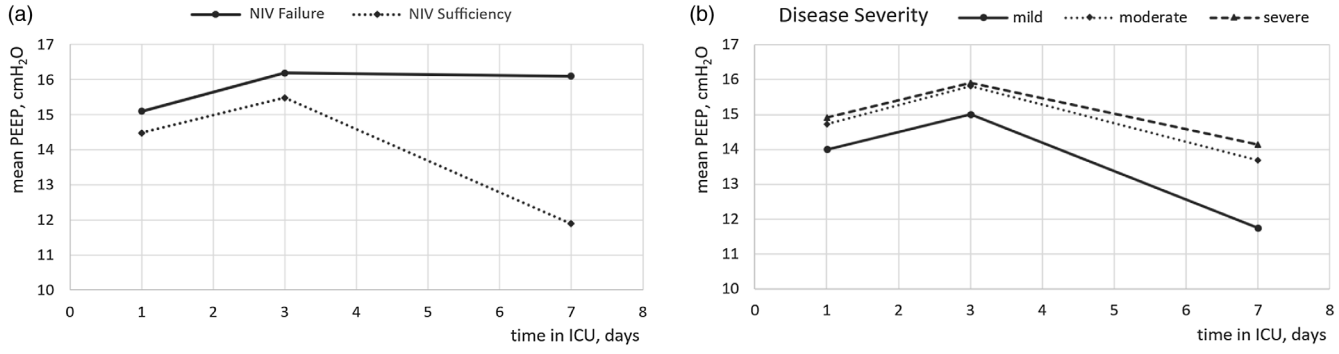

Figure 1. The difference in PEEP levels administered throughout the first week: (a) based on NIV failure was statistically significant ($P < 0.001$); (b) based on disease severity was not significant ($P = 0.911$).

on Days 3 ($P = 0.015$) and 7 ($P < 0.001$) compared to patients who required intubation.

Subcutaneous emphysema ($P = 0.002$), pneumomediastinum ($P = 0.021$), and pneumothorax ($P = 0.019$) all occurred more frequently in patients who required intubation.

Discharge from ICU and Survival

In total, 61 (64.21%) patients were discharged from ICU; ICU mortality was 35.79%. A total of 46 patients died during their stay in the hospital; hospital mortality was 48.42%. Patients who were intubated had a lower chance of survival ($P < 0.001$); only 6

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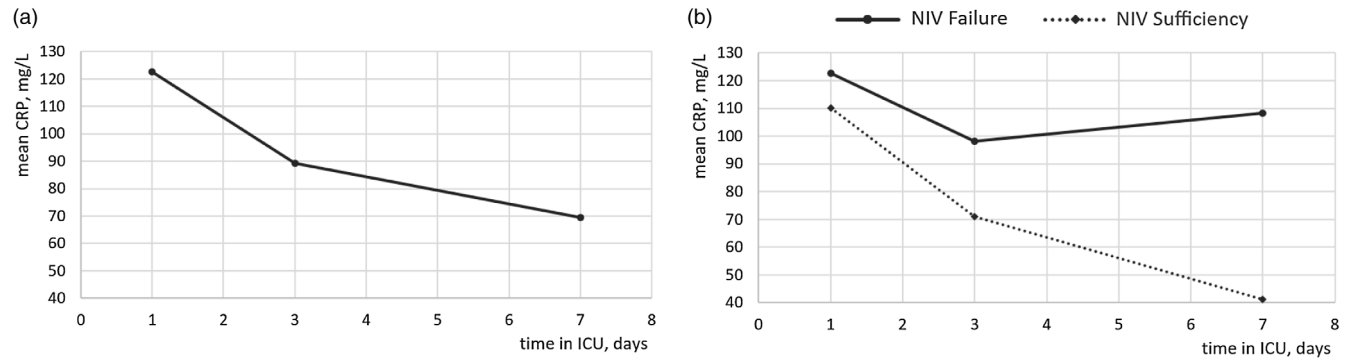

Figure 2. Change in CRP plasma concentration during the first week in the ICU: (a) a statistically significant decrease was visible ($P < 0.001$); (b) difference in CRP dynamic based on NIV failure.

(14.63%) of them survived. Out of 54 patients who were solely on NIV, 43 (79.63%) survived. Patients with moderate or severe ARDS had a lower chance of discharge from ICU ($P = 0.009$) and a lower hospital survival rate ($P = 0.009$) compared to patients with mild ARDS.

Discussion

In this study, NIV was a sufficient means of ventilation for 54 (56.84%) patients; 41 (43.16%) patients required a switch to IMV. The likelihood of NIV failure was significantly higher in patients with moderate or severe ARDS. However, even in patients with severe ARDS, 51.22% of patients could be kept on NIV. This is comparable to the study by Jog et al., which investigated the treatment of COVID-19 patients with severe ARDS (P/F < 150) with HFNO and/or NIV due to unavailability of IMV and reported that 35.9% of such patients managed to avoid intubation.[25] Mortality in patients who required a switch to IMV was 87.5%. The most prominent factors leading to NIV failure in this study were increased work of breathing and ventilator asynchrony, impaired consciousness, and hemodynamic disorder. This is in line with other studies as reported by Radovanovic et al. who determined that the major factors for a switch to IMV were decreased levels of consciousness, exhaustion, refractory hypoxemia, sepsis, and hemodynamic instability.[26]

ICU mortality of the patients in this study was 35.79%. That is comparable to the pooled ICU mortality (28.3%) reported by Chang et al.[27] The hospital mortality in this study was 48.42%; however, for the patient group that was only treated with NIV, hospital mortality was only half of that at 20.37%; and the ICU mortality for that group was only 3.70%. The patient group that required IMV had a hospital mortality of 85.37% with an ICU mortality of 77.50%. These results are in correspondence with the results from Jurjević et al. (their reported hospital mortality was 16% vs 79%).[22] On the other hand, Menzella et al. reported no difference in mortality between the 2 patient groups.[28] The largest difference in the dynamic of monitored respiratory and laboratory parameters between the 2 patient groups was visible between the first and third days of the ICU stay. By Day 3 a significantly larger decrease in PEEP was observed in patients for whom NIV was sufficient means of oxygenation for the entirety of their stay in the ICU compared to patients who required a switch to IMV. A significant improvement in PaO_2, P/F ratio, and HACOR score by Day 3 was also observed in the same patient group. Onkar et al. reported a significant difference in P/F ratio between NIV-sufficient and failed NIV group after only 24 hours of ventilation.[29]

Another observation made by Jurjević et al. was that with PEEP values from 15 to 20 cmH_2O patients felt comfortable and breathed easier while their oxygenation improved.[22] While patient comfort was not one of the defined outcomes in this study, as per our protocol, clinical signs as well as a subjective feeling of comfortable breathing were both taken into consideration when adjusting the PEEP levels. Patient comfort was measured using the Likert scale. Results of this study were compared to the study conducted by Bellani et al., which had the largest cohort of patients with COVID-19 treated with NIV as first-line treatment; aside from slightly higher mean PEEP values and FiO_2 set at a slightly lower level in this study, the rest of the respiratory parameters were in correspondence with Bellani et al.'s results.[30]

In the cases of a few of the patients in this study, COVID-19 ARDS was complicated by pneumothorax, pneumomediastinum or subcutaneous emphysema, which could be due to elevated PEEP, but also a consequence of increased work of breathing.[31] Often reported complications in other studies investigating CPAP/NIV in patients with COVID-19-related ARDS included pulmonary embolisms, renal failure, cerebrovascular accident, heart failure, septic shock, arrhythmia, ventilator-associated pneumonia, and myocardial infarction.[26] CPAP-related complications such as pneumothorax were found to be uncommon. However, in those studies, applied PEEP levels did not exceed 10 cmH_2O.

The limitations of this study are that it is retrospective, it lacks a control group that would have been treated by lower PEEP values which would allow a direct comparison of outcomes between the 2 PEEP treatment modalities, and the occurrence of some of the collected parameters (eg, complications) was too low to reach statistical significance. In addition, the study lacks measurements of plateau pressure, driving pressure, airway closing and opening pressure, airway occlusion pressure, and transpulmonary pressure that was due to the diversity of the ventilatory equipment used and lack of human and financial resources.

Conclusion

This is a retrospective cohort study exploring the efficacy and safety of NIV with a high $PEEP/FiO_2$ strategy in patients with AHRF due to COVID-19. Out of 95 patients, for 56.84% of them, NIV was a sufficient means of ventilation. NIV failure was higher in patients with moderate or severe ARDS. Hospital mortality was

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48.42%, but when analyzing only the NIV–treated group, the mortality dropped to 20.37%. Patients who did not require intubation showed a significant decrease in PEEP, improved oxygenation parameters, and HACOR score by Day 3 compared to those requiring intubation. The dynamic changes between the 2 patient groups were most pronounced between the first and third days of ICU stay.

In summary, this study suggests that NIV can be effective in managing COVID-19 patients, but the decision to use NIV should take into consideration the severity of ARDS. The study highlights the need for further research with controlled designs and comprehensive measurements to better understand the optimal ventilation strategies for COVID-19 patients in the ICU.

Author contributions. All authors contributed to the study's conception and design. Material preparation, data collection, and analysis were performed by Nikica Karković, Ivan Jurković, Romana Perković, and Zvonimir Popović. The first draft of the manuscript was written by Lovro Hrvoić, Gloria Mamić, and Nikolina Džaja, and all authors commented on previous versions of the manuscript. The final manuscript was reviewed and edited by Ivan Šitum, Daniel Lovrić, and Lovro Hrvoić. All authors read and approved the final manuscript.

Competing interests. The authors report no conflicts of interest.

Ethical standards. This study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Approval was granted by the Ethics Committee of the University Hospital Centre Zagreb (class: 8.1–22/156-3: no.: 02/013-JG).

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