

Decision day – A retrospective analysis of COVID-19 patients treated with high PEEP non-invasive ventilation

Ivan ŠITUM¹, Ante ERCEG¹, Anja MANDARIĆ¹, Nikolina DŽAJA¹, Glorija MAMIĆ¹, Daniel LOVRIĆ²

¹Department of Anesthesiology and ICU, University Hospital Centre, Zagreb, Croatia

²Department of Cardiovascular Diseases, University Hospital Centre, Zagreb, Croatia

Ivan Šitum **ORCID ID:** 0000-0002-4113-2400

Ante Erceg **ORCID ID:** 0000-0003-4321-7050

Anja Mandarić **ORCID ID:** 0000-0002-0344-9028

Nikolina Džaja **ORCID ID:** 0000-0003-4779-3573

Glorija Mamić **ORCID ID:** 0000-0001-6505-3021

Daniel Lovrić **ORCID ID:** 0000-0002-5052-6559

ABSTRACT

Background and objectives. This retrospective analysis investigates the effect of high levels of Positive End-Expiratory Pressure (PEEP) during Non-Invasive Ventilation (NIV) in patients with COVID 19 Acute Respiratory Distress Syndrome (ARDS).

Materials and methods. In the University Hospital Center Zagreb from October 2021 to February 2022, the study analyzed data from 97 patients who received NIV for acute respiratory support during ICU stay. The effect of NIV on survival, the length of stay in the ICU as well as the duration of the support itself was investigated.

Results. Results show that despite low mortality in patients with NIV support, mortality is quite high in patients who required intubation. There is also a divergence of the respiratory support level parameter after the 3rd day on NIV, which suggests that moment as pivotal for assessing the continuation of NIV support.

Conclusions. The results show that high level PEEP is a viable option for starting respiratory support in ARDS, but also the importance of timely assessment to optimize patient outcomes.

Keywords: ARDS, COVID-19, non-invasive ventilation, PEEP

Abbreviations:

PEEP – Positive End-Expiratory Pressure

ICU – Intensive care unit

CPAP – continuous positive airway

NIV – Non-Invasive Ventilation

FRC – functional residual capacity

pressure

ARDS – Acute Respiratory Distress Syndrome

P-SILI – patient self-inflicted lung injury

IMV – invasive mechanical ventilation

INTRODUCTION

During the time of COVID pandemic medical wards were overwhelmed with patients in need of ventilator

support. Non-invasive mechanical ventilation was a good alternative to intubation because of its lesser invasiveness, fewer infectious complications, and the ability to support a bigger turnover of patients [1-3].

Corresponding author:

Ivan Šitum

E-mail: ivsitum@gmail.com

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RESULTS

Also, high PEEP was found to improve oxygenation, increase functional residual capacity (FRC) and reduce atelectotrauma [4]. 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 [5]. The adoption of high PEEP in NIV for COVID-19 patients is supported by emerging data suggesting that optimized airway pressures can significantly affect respiratory outcomes. By utilizing non-invasive methods, healthcare facilities could potentially ease the burden on ICU capacities and lower the morbidity associated with invasive ventilation methods. Moreover, the capability to swiftly modify ventilation settings and perform close monitoring provided a dynamic and effective response to the rapidly evolving health crisis.

This study aims to assess the efficacy of high PEEP NIV in treating COVID-19 induced ARDS, pinpointing critical junctures for intervention to prevent the need for invasive ventilation of non-invasive ventilation (NIV) with high positive end-expiratory pressure (PEEP) without pressure support (CPAP) in the treatment of patients with COVID-19-related acute respiratory distress syndrome (ARDS). It very important to timely identify patients who will fail NIV, to monitor and daily reevaluate, and timely transition to invasive mechanical ventilation [6].

MATERIALS AND METHODS

This is a retrospective cohort study with data collected from 97 patients who were administered NIV as part of their treatment in the COVID intensive care unit (ICU) at University Hospital Centre Zagreb during a period between October 2021 and February 2022. The definite outcome was survival; the effects of NIV and various respiratory and inflammatory parameters on discharge from ICU, number of days spent in ICU, and hospital were also investigated. Data were analyzed with IBM SPSS version 25. Continuous variables were presented as mean (SD) 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 One-way and Two-way repeated measures ANOVA. The non-normal distributed data were compared using the Mann-Whitney U test, Wilcoxon signed rank test, and Friedman test. Logistic and linear regression was used to assess the connection between parameters. A p-value of less than 0.05 was considered statistically significant.

The patients' mean age was $67 \pm 11,6$ years, mean Charlson comorbidity index was $4,23 \pm 2,15$. High PEEP NIV by total or full-face mask was applied in all 97 patients. NIV has been kept on throughout the ICU stay in 55 (56.7%) patients, while 42 (43.3%) patients required a switch to IMV. Overall ICU mortality was 35.5%, while ICU mortality of patients kept on NIV was 3.8%. The mean starting PEEP was $14,25 \pm 2,65$ and the mean CRP on day 1 was $115,58 \pm 67,27$. The observed trend in PEEP in the first week was slightly advancing to the PEEP level on day 3 and then evident divergence of PEEP levels after day 3 in failed (PEEP1 14.87, PEEP2 15.2, PEEP3 15.79, PEEP4 15.87, PEEP5 16.25, PEEP6 15.95, PEEP7 15.96) vs non failed group (PEEP1 15.14, PEEP2 15.25, PEEP3 15.71, PEEP4 15.1, PEEP5 14.21, PEEP6 13.18, PEEP7 11.96) (Figure 1b).

A non-parametric Friedman test of differences among repeated measures showed a Chi-square value of 15.31 which was significant ($p=0,018$). Also, the difference in trends in CRP between the same groups was significant, where the non-failed group had a trend of lower CRP (CRP1 113.85, CRP3 76.66, CRP7 41.22) vs failed group CRP that was stable (CRP1 127.93, CRP3 107.18, CRP7 108.22) (Figure 1a).

A non-parametric Friedman test of differences among repeated measures showed a Chi-square value of 37.47 which was significant ($p<0,001$). The difference in PCT and antibiotic use or positive cultures was non-significant in the first week. Also, logistic regression of HACOR ($R^2=0,328$, $p<0,001$), Horowitz index ($\text{PaO}_2/\text{FiO}_2$) ($R^2=0,334$, $p<0,001$), PEEP on day 3 ($R^2=0,143$, $p=0,004$) and change in PEEP ($R^2=0,106$, $p=0,012$) (delta PEEP, PEEP on day 3 minus PEEP on day 1) show predicted probability of failing NIV support.

DISCUSSION

Our findings suggest that high PEEP non-invasive ventilation is a promising initial management strategy for ARDS induced by COVID-19, particularly in settings overwhelmed by pandemic pressures. The data indicates that specific PEEP settings and their adjustments during the initial days of ventilation play a crucial role in determining the subsequent need for invasive ventilation. A notable observation from our study is the stratification of outcomes based on the PEEP adjustments within the first three days, suggesting a pivotal moment in the management of respiratory support. Results suggest there is a high chance of NIV failure if on day 3, there is Horowitz index 150 mmHg or lower, with PEEP levels higher than 16 cmH_2O , and maintained or increased PEEP level in first 3 days of respiratory support (figure 2). NIV failure is defined as insufficient level of

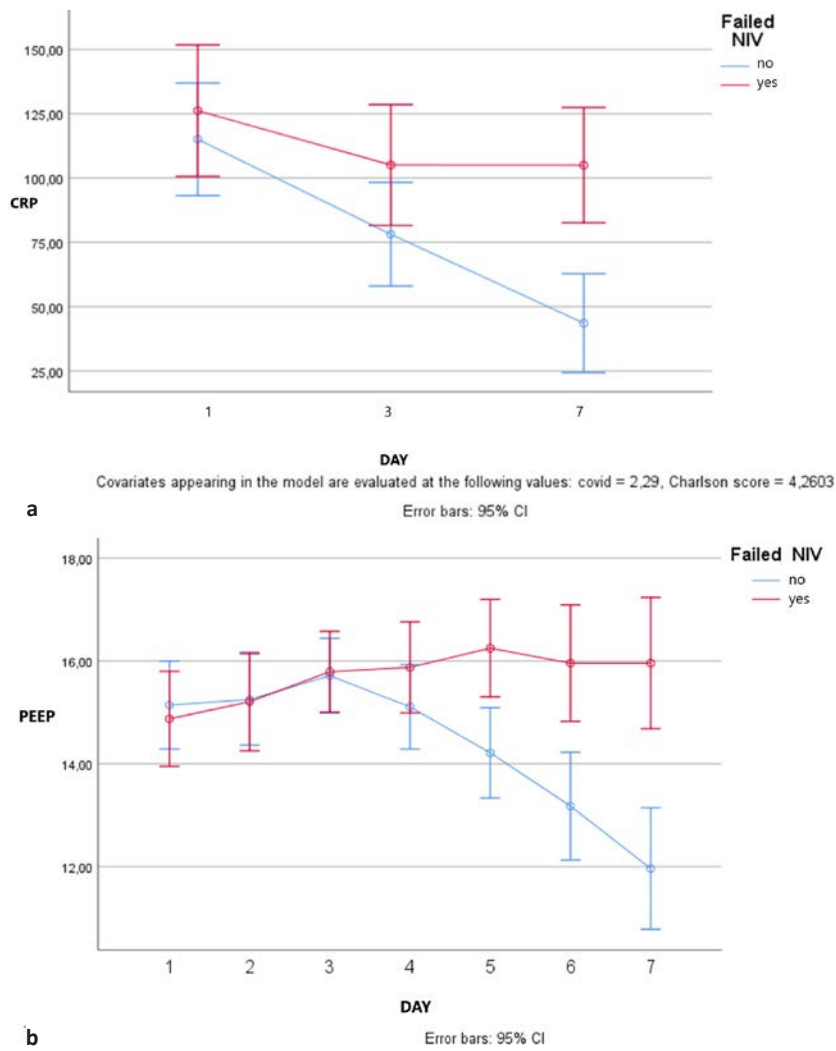


FIGURE 1. a) CRP levels over time b) PEEP levels over times in failed and non failed group

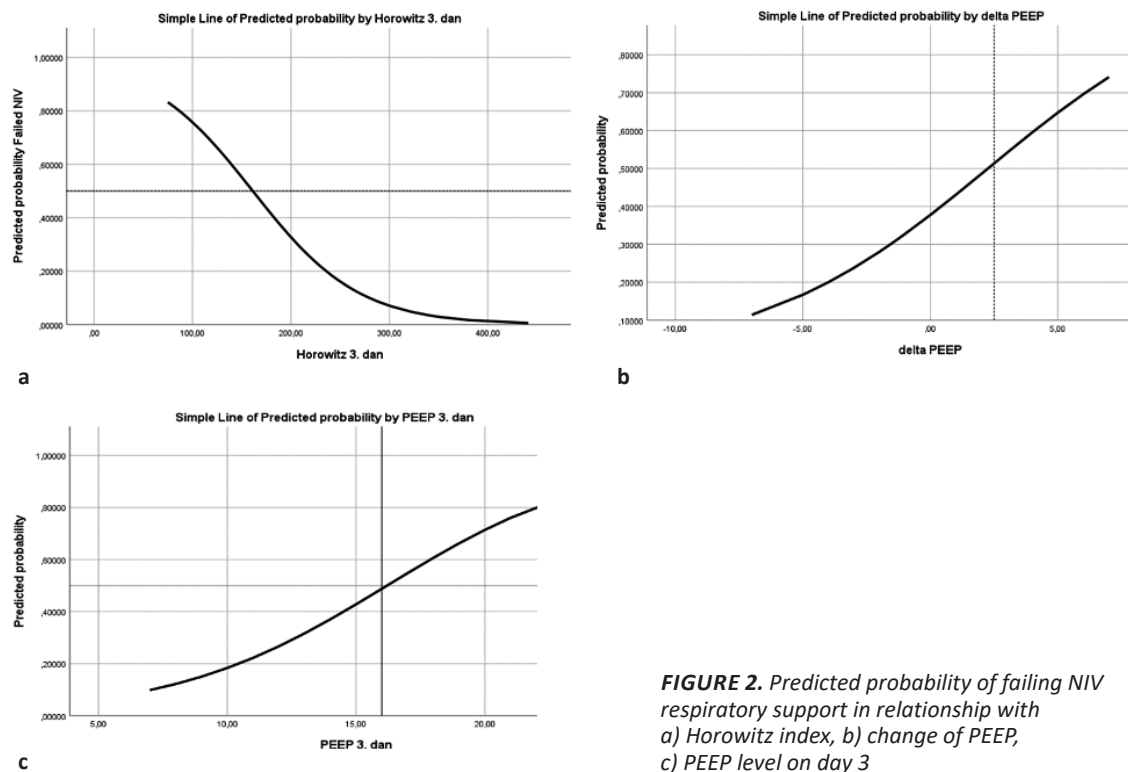


FIGURE 2. Predicted probability of failing NIV respiratory support in relationship with a) Horowitz index, b) change of PEEP, c) PEEP level on day 3

respiratory support and need for intubation and invasive mechanical ventilation. So, it is author's opinion that non-invasive mechanical ventilation is an excellent starting option for respiratory support in ARDS regardless of the severity of ARDS itself. Subsequent timely reevaluation and eventual progression to IMV is necessary regardless of the modality of respiratory support. Trends in the movement of PEEP, as well as other respiratory parameters, are good predictors of response to ARDS therapy, as well as the movement of inflammatory parameters. Moreover, the divergence in PEEP levels between the patients who continued with NIV successfully and those who failed indicates the necessity for individualized ventilation strategies. This highlights the importance of meticulous patient monitoring and timely adjustments based on the evolving clinical scenario. However, the challenge remains in the capacity constraints faced by healthcare systems during peaks of the pandemic, which could hinder the implementation of such tailored approaches. It underscores the need for robust healthcare infrastructure capable of adapting to significant pressures, ensuring that all patients receive optimal care tailored to their specific clinical needs. The shortcomings of this research lie in the incomplete monitoring of other respiratory parameters, which occurred due to overcrowding of the ICU and overworked health care personnel during the pandemic.

CONCLUSION

In conclusion, our study confirms that high PEEP non-invasive ventilation can be a safe and effective initial treatment modality for all patients with ARDS, regardless of the severity of their condition. It allows for significant flexibility in patient management, potentially reducing the need for invasive ventilation. Our analysis underscores the importance of the third day of NIV as a critical point for evaluating the need to escalate care. This finding is crucial for clinical practice, suggesting that timely interventions could prevent the progression to invasive ventilation, thus optimizing patient outcomes and resource utilization in critical care settings.

Author's contributions:

Conceptualization, I.Š. and D.L.; methodology, I.Š.; software, I.Š.; validation, I.Š., A.E., D.L.; formal analysis, I.Š.; investigation, I.Š, A.E., A.M.; resources, A.E., N.Dž.; G.M.; data curation, D.L.; writing – original draft preparation, I.Š., N.Dž.; G.M.; writing – review and editing, A.E., A.M., D.L.; visualization, I.Š.; supervision, D.L.; project administration, I.Š., A.M.; funding acquisition, I.Š, N.Dž.; G.M.
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