

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

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

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Short Running Title: Decision Day

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

NIV - Non-Invasive Ventilation

ARDS - Acute Respiratory Distress Syndrome

ICU – Intensive care unit

FRC – functional residual capacity

P-SILI – patient self-inflicted lung injury

CPAP – continuous positive airway pressure

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 [1,2,3]. 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]. We wanted to investigate the efficacy and safety 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 is out of most 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.

RESULTS

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 nonsignificant in the first week. Also, logistic regression of HACOR ($R^2=0,328, p<0,001$), Horowitz index (PaO₂/FiO₂) ($R^2=0,334, p<0,001$), 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

Results suggest there is high chance of NIV failure if on day 3, there is Horowitz index 150 mmHg or lower, with PEEP levels higher than 16 cmH₂O, and maintained or increased PEEP level in first 3 day of respiratory support (figure 2). NIV failure is defined as insufficient level of 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. 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

NIV with high PEEP was a safe option for the initial respiratory treatment of all patients despite the severity of acute respiratory distress syndrome (ARDS). For some patients, it was also shown to be the only necessary form of oxygen supplementation throughout the entirety of their stay in the ICU. Our data shows there is a definitive time when we need to evaluate and escalate respiratory support to IMV, and that day is day 3 of non-invasive respiratory support.

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CONFLICT OF INTEREST

Authors don't have any financial interest or any conflict of interest.

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.. All authors have read and agreed to the published version of the manuscript.”

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FIGURES

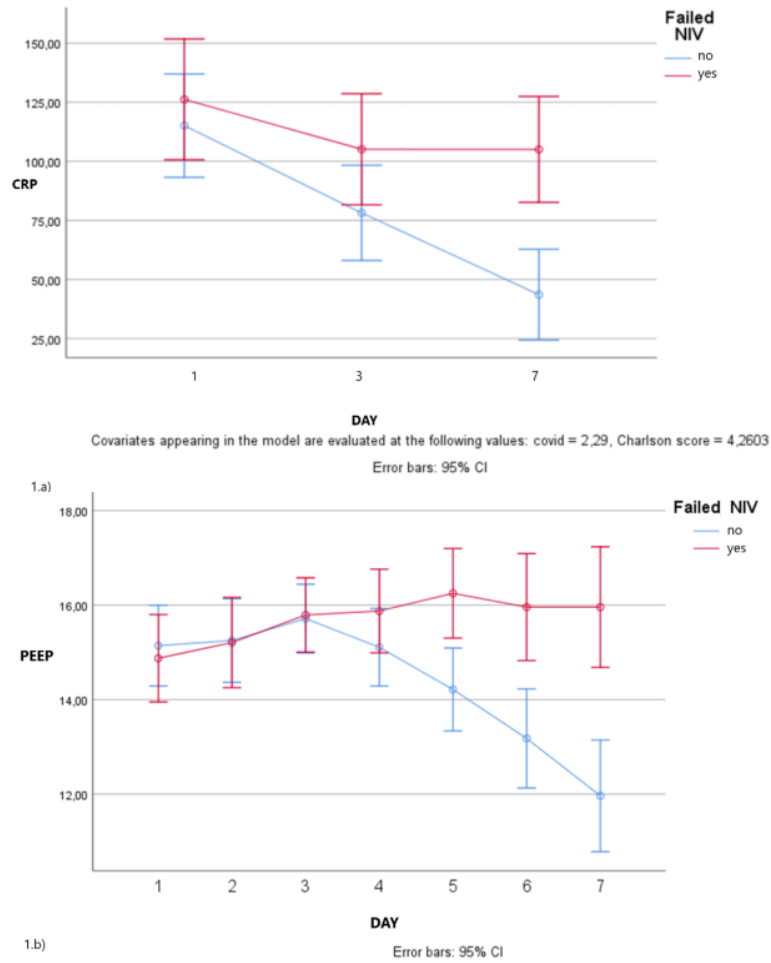


Figure 1. a) CRP levels over time b) PEEP levels over times in failed and non failed group

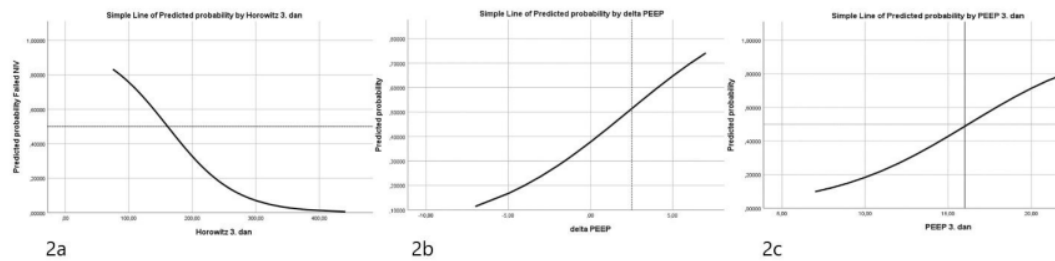


Figure 2. Predicted probability of failing NIV respiratory support in relationship with a) Horowitz index, b) change of PEEP, c) PEEP level on day 3.