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# The Relationship Between the Type of Respiratory Support and Its Outcomes in Patients with COVID-19 Hospitalized in the Intensive Care Units

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**ABSTRACT**

*Given the unknown nature of the COVID-19 and the ambiguity surrounding the efficacy of various methods of treatment, the present study aimed to elucidate the correlation between the type of respiratory support administered and the resultant outcomes for patients with COVID-19 who were admitted to the intensive care units. In this retrospective cohort patients' records were categorized into two groups based on the type of respiratory support method employed: those who were solely intubated and those who received a combined mechanical ventilation approach utilizing an oxygen mask and intubation non-invasive ventilation plus intubation. The instrument used for collecting data comprised a form that encompassed demographic details alongside a history of pre-existing conditions and parameters pertinent to the patient's health status. A comprehensive examination of 260 files was conducted. Approximately 46% of the patients were categorized within the intubated group. The findings indicated that, the mean arterial oxygen levels were recorded at four distinct time points-upon hospital admission, upon ICU admission, prior to ventilator support, and following ventilator support- were statistically significant difference (P<0.001). The mean duration of hospitalization for the intubated group was markedly less than that of the group receiving NIV plus intubation (P < 0.001). The mean duration of being connected to a ventilator among the groups under investigation did not yield a statistically significant result. The analysis demonstrated no statistically significant difference in mortality rates between the two groups. Furthermore, examining survival curves revealed a statistically significant distinction between the two groups (P < 0.001). The results partially depend upon potential disparities in the effectiveness of invasive versus non-invasive methods. Consequently, further research in this domain appears imperative to corroborate a more robust endorsement for non-invasive techniques—attributable to their reduced side effects, user-friendliness, minimal training requirements, and broader clinical applicability.*

**Keywords: COVID-19; Non-invasive ventilation; Oxygen Therapy; Intubation; Respiratory Support**

## Introduction

COVID-19 typically presents with a cluster onset primarily impacting the respiratory system, with some patients experiencing rapid progression to acute respiratory distress syndrome (ARDS) [1]. Consequently, implementing timely and effective respiratory support strategies is crucial for achieving favorable clinical outcomes in critically ill patients. Respiratory support encompasses both invasive and noninvasive techniques. Advanced respiratory support includes oxygen supplementation, noninvasive ventilation (NIV), high-flow nasal cannula (HFNC), invasive mechanical ventilation (IMV), and extracorporeal membrane oxygenation (ECMO) for patients in the ICU exhibiting respiratory dysfunction [2].

Applying NIV to patients with acute respiratory failure enhances oxygenation levels, decreases the painful breathing process, and prevents endotracheal intubation (EI). The application of NIV for treating ARDS,

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however, is controversial. While NIV correlates with a decreased requirement for intermittent mandatory ventilation (IMV) and a lowered death rate in mild forms of ARDS, it is linked to an increased mortality rate in more severe cases of this condition. It is well-established that NIV mitigates complications associated with IMV, including pneumonia, sedative overdose, delirium, and ICU-acquired frailty. It has also been reported to benefit post-extubation respiratory care and support [3-5]. EI is frequently implemented as a therapeutic intervention for COVID-19 patients. It is employed in patients who are experiencing ARF and have not received NIV, thereby reducing the severity of pulmonary injury. Maintaining intubation for a long period could contribute to an exacerbation of respiratory insufficiency and, eventually, mortality [6].

Nasal intermittent positive pressure ventilation (NIPPV) is a noninvasive respiratory support technique that has gained extensive application, particularly in non-ICU environments, owing to the increased incidence of COVID-19-related acute hypoxemic respiratory failure (AHRF) surpassing the availability of ICU beds and ventilators. Research revealed a mortality rate of 69% among patients receiving NIV and 82% among those undergoing EI [9]. In addition, proportion of patients who responded to NIPPV treatment has been only 44% [10]. The previously mentioned studies regarding NIPPV in patients with acute respiratory failure have produced inconsistent results, and the efficacy of applying NIV on COVID-19 patients experiencing hypoxemic acute respiratory failure remains uncertain. Additional research is required to identify the most effective respiratory support technique for managing individuals with ARF.

COVID-19 complications are unusual, persistent, and rapidly developing, with limited scientific documentation and information. Consequently, gathering specialized insights about this condition and integrating them will significantly aid in advancing objectives and improving the overall pulmonary health of those afflicted with COVID-19. In light of the wide variety of invasive and non-invasive techniques available for respiratory support in patients requiring pulmonary assistance, particularly within critical care units during the acute phases of illnesses such as COVID-19, the present study was undertaken to explore and elucidate the impact of various respiratory support techniques as well as relationship between the type of respiratory support administered and the outcomes of the patients hospitalized in the ICUs.

## Materials and Methods

The present study is a retrospective cohort analysis. The research population comprised all COVID-19 patients admitted to the ICU of Shohada-ye Ashayer Educational and Medical Center in Khorramabad, Lorestan, Iran. All patients meeting the eligibility criteria for the research were identified and recruited using the full-count method from Sept 22, 2020, until the end of September 2021. The patients received treatment by NIV through masks, intubation, or a combination of both techniques. The inclusion criteria for selecting the subjects were individuals over 18 years old with a confirmed diagnosis of COVID-19. Patients with missing or unintelligible hospitalization file information, those who succumbed to other underlying conditions, or those who were referred or moved to different medical facilities were excluded from the study.

Having obtained approval from the ethics committee of Lorestan University of Medical Sciences (LUMS.REC.1400.324) and permission to collect samples, the researcher approached the aforementioned hospital's information technology (IT) unit and retrieved a list of all eligible patients from the hospital information system (HIS). The specified hospital/ medical center had three ICU wards allocated for treating COVID-19 patients, and sampling was conducted throughout all these wards. In the subsequent phase, the hospital's medical records were consulted to select and retrieve the files of eligible patients based on the type of respiratory support provided. The data were categorized into two groups:

intubation only and a combination of intubation with NIV.

The data collection tools utilized in this study comprised a demographic form including patient's age, gender, educational level, type of residency and a researcher-made checklist encompassing the history of pre-existing conditions and parameters relevant to the patient's status upon admission to the intensive care unit such as their vital signs, SpO2 levels, type of respiratory support device -either invasive (tracheal tube or tracheostomy) or non-invasive (NIV plus a continuous positive airway pressure (CPAP) mask-, duration of hospitalization and respiratory support, and discharge status (recovery or death). The items included in the checklist were derived from various sources and studies, serving as background and influential variables or as components pertinent to the inclusion criteria. Data analysis was conducted using SPSS version 25 software.

Initially, the normality of the data was assessed utilizing the Kolmogorov-Smirnov test. Independent t-tests and repeated measures ANOVA were employed to compare the two groups due to the normal distribution of the data. The non-parametric Wilcoxon and Friedman tests were employed for data exhibiting a non-normal distribution. In contrast, Fisher's exact test was utilized to compare qualitative variables between the two groups. To assess the relationship between the variables, the Cox proportional hazards model was employed, effectively controlling for confounding variables. Additionally, the Rock curve was utilized to ascertain the optimal model. The significance threshold was established at $P<0.05$.

## Results

The study comprised 260 patients diagnosed with COVID-19 who met the eligibility criteria for participation. Out of these, six patients were excluded from the study owing to incomplete or illegible data resulting from manual reporting, mortality attributable to underlying conditions, and the referral or transfer of patients to other facilities. Consequently, 260 records were subjected to analysis. Approximately 46% of the patients were categorized within the intubation group.

It was observed that 52.9% of the patients in the intubation group and 54.8% in the NIV plus intubation group were male, and over 60% of patients in the intubation group and more than 70% in the NIV plus intubation group had a documented history of infection. Additional demographic and clinical information are presented in Table (1). No statistically significant differences were noted among the study groups regarding gender, educational level, residential location, and pre-existing medical conditions.

The comparison of SpO2 levels in the study groups at four distinct time points: upon hospital admission (SpO2-1), upon ICU admission (SpO2-ICU), prior to ventilator support (SpO2–PRE-V), and following ventilator support (SpO2–POST-V) showed statistically significant changes ($P<0.001$) (Table 2 and Figure 1).

The analysis of the mean duration of hospitalization between the two groups, revealed that the mean duration of remaining hospitalized for the intubated group was markedly shorter than that the NIV plus intubation group ($P<0.001$). Conversely, there was no statistically significant difference in the mean duration of ventilator support between the two groups (Table 3). The mortality rate in both groups approached 100%, and the chi-square test results, revealed no statistically significant difference in mortality between the two groups. Nevertheless, the mean survival duration for the intubation and NIV plus intubation groups were 8.05 and 16.03 days, respectively.

Furthermore, regarding the observed survival curves employing the Kaplan-Meier method (Figure 2) alongside the outcomes of the Log rank test demonstrated a statistically significant disparity between the two groups($P<0.001$).

*Table1. Comparison of frequency distribution of demographic characteristics and history of pre-existing medical conditions of patients with COVID-19 (intubated and NIV plus intubation groups)*

| Variables | | Groups: Intubation (119) N(%) | NIV plus intubation (135) N(%) | *p* value |
|---|---|---|---|---|
| Gender | Female | 56(47.1) | 61(45.2) | 0.802 |
| | Male | 63(52.9) | 74(54.8) | |
| Educational level | Illiterate | 54(45.4) | 78(57.8) | 0.226 |
| | lower than high school diploma | 33(27.7) | 26(19.3) | |
| | High school diploma | 12(10.1) | 13(9.6) | |
| | Bachelor's degree and above | 20(16.8) | 18(13.3) | |
| Residential location | Urban | 97(81.8) | 104(77) | 0.440 |
| | Rural | 22(18.5) | 31(23) | |
| pre-existing medical conditions | Yes | 37(31.1) | 32(23.7) | 0.205 |
| | No | 82(68.9) | 103(76.3) | |

*Table 2. Mean and standard deviation of SpO2 levels at time points: SpO2-1, SpO2-ICU, SpO2–PRE-V, SpO2–POST -V*

| Variables | | Time points: $SpO_2$-1 | $SpO_2$-ICU | $SpO_2$–PRE-V | $SpO_2$–POST -V | *p* value |
|---|---|---|---|---|---|---|
| Groups | Intubation | 80.76(14.06) | 85.37(7.09) | 70.68(17.55) | 75.14(18.27) | □0.001 |
| | NIV plus intubation | 85.59(5.63) | 83.21(8.05) | 70.16(9.83) | 72.14(18.75) | □0.001 |
| | P value | 0.001 | 0.031 | 0.778 | 0.326 | |

*Table 3. Comparison of the mean duration of hospitalization and being connected to/supported by a ventilator between the two groups.*

| Duration | Group | Number | Mean (SD) | T-statistic | *p* value |
|---|---|---|---|---|---|
| Hospitalization in the ICU | Intubation | 119 | 7.83(10.04) | 6.389 | □0.001 |
| | NIV plus intubation | 135 | 15.84(9.90) | | |
| connected to/supported by ventilator | Intubation | 119 | 4.94(8.67) | -0.552 | 0.581 |
| | NIV plus intubation | 135 | 5.43(5.37) | | |

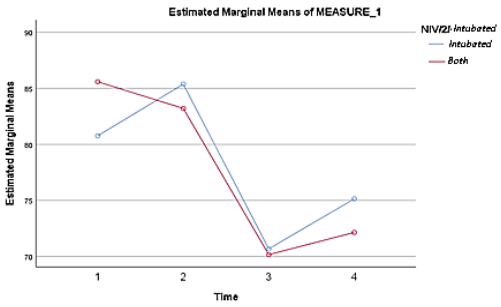


*Figure 1. The mean values of SpO2 in the intubation and NIV plus intubation groups at four distinct time points: SpO2-1, SpO2-ICU, SpO2–PRE V, SpO2–POST V.*

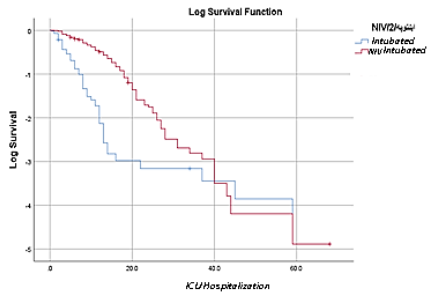


*Figure 2. A comparative analysis of survival curves between the intubated group and the NIV plus intubation group, employing the Kaplan-Meier methodology.*

The findings of the Cox proportional hazards regression, accompanied by 95% confidence intervals, are as follows. Upon controlling for factors such as gender, educational level, age, residential location, and pre-existing health conditions, the analysis revealed that individuals in the intubated group faced a significantly elevated mortality risk compared to those in the NIV plus intubation group. Furthermore, it can be inferred that mortality occurred more rapidly within the intubation group (HR=2.997, CI= 95% P<0.001, 2.523-3.985).

## Discussion

The findings indicated that regardless of the disparity in SpO2 levels among COVID-19 patients in the intubation and NIV plus intubation groups at four intervals, the mean duration of ventilator connection remained consistent across the examined groups. Boscolo et al. showed that COVID-19 patients admitted to the ICU who were promptly intubated did not vary in ventilator duration compared to those intubated following a period of NIV therapy [11]. Nonetheless, multiple research efforts have uncovered evidence which contradicts the previously stated conclusion [2, 12]. Therefore, it cannot be asserted that one method is more effective than the other, and further investigation in this area, considering various influencing factors, is necessary. On the other hand, the current study revealed that the remaining duration in the intubation group was markedly less than that observed in the NIV plus intubation group. The results of the study conducted by Dreher et al. [13] corroborate this finding, standing in contrast to the outcomes observed in the research by Windisch et al. It was argued that NIV holds the potential to delay or avoid the necessity for intubation and may be integrated as a lasting element within the ICUs [2].

Papoutsi et al. in a systematic review and meta-analysis stated that there were notable disparities in mortality rates between patients who underwent immediate intubation and those who were intubated following a period of NIV treatment [14]. Various studies have indicated mortality rates between 15 and 36% [15]. The elevated mortality rate observed in the current study could be attributed to the postponement of the treatment. In certain studies, over 80% of patients underwent intubation, indicating that intervention occurred before exacerbating respiratory symptoms and shortness of breath. The study by Daniel et al. examined and contrasted invasive intubation with non-invasive ventilation and reported an overall mortality rate of 77.5%. The mortality rates were 82% for the intubation group, 84% for the NIV plus intubation group, and 69% for the NIV alone group. Despite the markedly lower mortality rate observed with NIV in their study, the difference between the intubation and NIV plus intubation groups was not statistically significant [9]. Furthermore, the analysis of survival rates, the implementation of integrated approaches, and the careful selection of supportive strategies tailored to the patient's clinical status could impact the patient's survival duration. Initiating supportive treatment with an NIV mask and adjusting the treatment according to the patient's condition through intubation would probably enhance survival time compared to scenarios where intubation is performed from the beginning [16]. In this regard, patients with COVID-19 who received initial treatment with NIV exhibited the highest survival rate when compared to those who were intubated from the outset or those who underwent intubation following treatment with CPAP and NIV+CPAP [17]. The findings of the research conducted by Longhini et al. [7] also aligned with this perspective.

Among the current study's limitations, one must acknowledge the retrospective design, which restricts the opportunity to reassess the potentially distorted findings. Furthermore, the limited number of patients utilizing non-invasive ventilation compared to those requiring intubation, attributed to the unavailability of NIV masks during the research timeframe, constituted another constraint of this study. This situation compelled the researchers to amalgamate the independent NIV group with the combined NIV and intubation group. Consequently, this investigation should be replicated on a broader scale, incorporating data from additional medical centers.

## Conclusion

In summary, the findings of this study indicate that, despite the variations in SpO2 levels among COVID-19 patients across the four distinct time points, the mean duration of ventilator connection remained consistent. The length of hospitalization for the intubation group was notably less than that of the NIV

plus intubation group. Furthermore, the mortality rate in both study groups was nearly identical. Nevertheless, the mean survival duration in the NIV plus intubation group was extended, and the survival curves exhibited notable divergence. Furthermore, it was observed that subjects in the intubation group faced an elevated risk of mortality, and it can be asserted that death occurs more rapidly within this group. The variations noted in the outcomes of various studies underscore the intricate and obscure characteristics of the COVID-19 disease, necessitating additional inquiry and the incorporation of more comprehensive data. The findings of this research establish a foundation for undertaking subsequent investigations to assess the efficacy of applying NIV-based techniques. Consequently, it is imperative to pursue further investigation in this domain to substantiate a more compelling endorsement for the adoption of non-invasive techniques, which present reduced side effects, enhanced user-friendliness, minimal training prerequisites, and broader clinical applicability.

### Conflict of interests

The authors have no financial interest related to this article

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