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IMPROVING OXYGENATION TRAJECTORIES IN COVID-19 ICU PATIENTS WITH NIV FAILURE DECLINING INTUBATION: EFFICACY OF MANDATORY-SPONTANEOUS HYBRID VENTILATION

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ABSTRACT

Background: Severe COVID-19 pneumonia often results in hypoxemic respiratory failure, particularly in patients with over 60% lung involvement. While non-invasive ventilation (NIV) offers supportive care without intubation, some patients fail to respond, and either they or their surrogates decline endotracheal intubation. This presents a clinical challenge, as escalating pressure in NIV may risk barotrauma. In response, a novel strategy combining mandatory ventilator-generated breaths with spontaneous respiratory efforts—termed hybrid ventilation—was proposed. **Aim:** To evaluate the efficacy of mandatory-spontaneous hybrid ventilation in improving oxygenation and clinical outcomes in NIV-failure COVID-19 patients who decline intubation. **Methods:** A prospective, randomized controlled trial was conducted on 100 COVID-19 patients with failed NIV and refusal of intubation. Patients were randomized into two groups: a control group receiving standard NIV and a study group receiving hybrid ventilation (NIV plus 8–10 machine-generated breathing cycles per minute). The primary outcome was the SpO_2/FiO_2 (S/F) ratio measured at baseline, 12 hours, and 24 hours. Secondary outcomes included hemodynamic stability and adverse effects. **Results:** Both groups had similar baseline characteristics. The study group showed significant improvement in the S/F ratio at 12 hours (0.91±0.01 vs. 0.87±0.01, $p<0.0001$) and 24 hours (0.92±0.05 vs. 0.88±0.04, $p<0.0001$) compared to controls. No adverse hemodynamic effects or complications were observed. **Conclusion:** Hybrid ventilation significantly improves oxygenation in COVID-19 ICU patients experiencing NIV failure and declining intubation, offering a safe and effective alternative to invasive ventilation in this critical subset of patients.

KEYWORDS: COVID-19, Non-Invasive Ventilation (NIV), Hybrid Ventilation, Oxygenation, ICU, SpO_2/FiO_2 Ratio, Intubation Refusal, Respiratory Failure, Mandatory Breaths, Randomized Controlled Trial.

INTRODUCTION

Coronavirus Disease 2019 (COVID-19), caused by the SARS-CoV-2 virus, has posed significant global health challenges, particularly due to its ability to cause severe respiratory illness requiring intensive care support. Critically ill COVID-19 patients are often characterized by extensive pulmonary involvement, typically evident on imaging as ground-glass opacities and consolidation, leading to hypoxemic respiratory failure and acute respiratory distress syndrome (ARDS). These patients frequently exhibit symptoms such as severe dyspnea, air hunger, and respiratory fatigue, which can progress to generalized exhaustion and clinical deterioration if not managed effectively.

Non-Invasive Ventilation (NIV) is a preferred method of ventilatory support in patients with respiratory failure who are not yet candidates for intubation. It delivers positive airway pressure through a tightly fitted facial or oronasal mask, assisting patients' spontaneous breathing efforts without the need for invasive airway access. The success of NIV hinges on the patient's respiratory drive and effort. However, in some patients, particularly those with more than 60% lung involvement and severe hypoxemia (SpO_2/FiO_2 ≤148), NIV alone may prove

insufficient. These cases are classified as NIV failure and typically warrant escalation to invasive mechanical ventilation (IMV).[1,2] In certain clinical scenarios, patients or their surrogates may decline endotracheal intubation due to personal, cultural, or prognostic concerns. Managing such patients presents an ethical and clinical dilemma, as increasing NIV pressures to compensate may result in adverse effects such as barotrauma (e.g., pneumothorax or emphysema).[3] To address this challenge, the concept of hybrid ventilation was introduced—combining NIV with mandatory machine-generated ventilator breaths. This approach aims to supplement spontaneous efforts with controlled mechanical support, enhancing alveolar recruitment, reducing the work of breathing (WOB), and improving gas exchange.[4] Previous research has supported the role of synchronized ventilation strategies in ARDS to optimize oxygenation while maintaining patient comfort and minimizing ventilator-induced lung injury.[5] In the context of COVID-19, where conventional approaches are sometimes limited by patient preferences or resource constraints, hybrid ventilation emerges as a promising alternative. By maintaining non-invasive support while providing partial mechanical assistance, this method may bridge the gap for patient's ineligible for IMV. This study investigates the efficacy and safety of hybrid ventilation in improving oxygenation in COVID-19 ICU patients with failed NIV and surrogate refusal of intubation, aiming to provide evidence-based guidance for this critical and vulnerable subgroup.

METHOD

This study was designed as a prospective, parallel-group, randomized controlled trial conducted in the ICU of Imam Al-Hussein Medical and Educational City in Karbala, Iraq. It aimed to assess the efficacy of mandatory-spontaneous hybrid ventilation in improving oxygenation among COVID-19 patients who had failed non-invasive ventilation (NIV) and refused endotracheal intubation.

A total of 100 patients, aged 50–75 years, with confirmed COVID-19 and more than 60% lung involvement on CT scan were enrolled. All patients demonstrated NIV failure, defined as persistent hypoxemia with a SpO_2/FiO_2 (S/F) ratio ≤148 despite receiving FiO_2 ≥60% and PEEP between 5–10 cmH_2O for at least two hours. Additionally, each patient had documented refusal of intubation by a legal surrogate.

Participants were randomly allocated into two groups:

- **Group A (Control group):** Received standard NIV using spontaneous breathing with adjusted FiO_2 and PEEP.
- **Group B (Study group):** Received hybrid ventilation—standard NIV plus 8–10 machine-generated mandatory breathing cycles per minute, superimposed onto the patient's own spontaneous efforts.

Baseline demographic and clinical data including age, gender, weight, heart rate, mean arterial pressure (MAP), temperature, and initial S/F ratio were recorded (Phase 1). After the intervention, S/F ratios and vital signs were reassessed at 12 hours (Phase 2) and again at 24 hours (Phase 3).

Continuous monitoring included ECG, SpO_2, non-invasive blood pressure, and ventilator parameters (FiO_2, PEEP, and inspiratory pressure). Patients were excluded if they were already intubated, under 18 years of age, had NIV mask intolerance, severe comorbidities such as shock, or structural lung diseases.[1,6,7] The primary outcome was the change in S/F ratio over 24 hours. Secondary outcomes included hemodynamic stability and adverse events such as barotrauma or intolerance to the intervention.

RESULTS

Table 1 shows that the control and study groups were well-matched at baseline in terms of demographics and vital signs, including age, gender distribution, body weight, height, mean arterial pressure (MAP), temperature, heart rate, and S/F ratio. All p-values were >0.05, indicating no statistically significant differences between the groups before the intervention. This confirms successful randomization and comparable starting conditions.

Table 1: Phase 1 Clinical Baseline Data.

Parameter	Control Group	Study Group	p-value
Age	60.5 ± 6.2	61.2 ± 6.8	>0.05
Gender (M/F)	30/20	28/22	>0.05
Weight (kg)	78.3 ± 12.5	79.1 ± 11.8	>0.05
Height (cm)	170.2 ± 8.3	171.4 ± 7.6	>0.05
MAP	92.7 ± 10.1	93.1 ± 9.8	>0.05
Temperature	37.0 ± 0.5	37.1 ± 0.6	>0.05
Heart Rate	88.5 ± 7.1	87.2 ± 8.4	>0.05
S/F Ratio	0.87 ± 0.01	0.87 ± 0.01	>0.05

At 12 hours after the intervention, the **study group receiving hybrid ventilation** showed a **significantly higher S/F ratio (0.91 vs. 0.87, p<0.0001)**, indicating improved oxygenation. Additionally, **lower PEEP and FiO_2 requirements** in the study group suggest better lung compliance and gas exchange efficiency. Hemodynamic parameters (MAP, temperature, heart rate) remained stable with **no significant difference**,

indicating **clinical safety** of the intervention. As in table 2.

Table 2: Phase 2 Clinical Data Statistics (12 hours' post-intervention)

Parameter	Control Group	Study Group	p-value
S/F Ratio	0.87	0.91	<0.0001
PEEP	5.6	3.7	<0.0001
FiO2	0.87	0.91	<0.0001
MAP	93.21	91.98	0.547
Temperature	37.21	37.09	0.293
HR	89.51	90.13	0.692

Table 3: Phase 3 Clinical Data Statistics (24 hours' post-intervention): At 24 hours, the oxygenation benefit persisted, with the study group maintaining a significantly improved S/F ratio (0.92 vs. 0.88, $p<0.0001$). PEEP and FiO_2 remained significantly lower in the hybrid group, further supporting the efficacy of hybrid ventilation. Vital signs remained similar across groups, reinforcing continued safety and tolerance of the hybrid method.

Table 3: Phase 3 Clinical Data Statistics (24 hours post-intervention).

Parameter	Control Group	Study Group	p-value
S/F Ratio	0.88	0.92	<0.0001
PEEP	5.7	3.6	<0.0001
FiO2	0.88	0.92	<0.0001
MAP	93.11	93.09	0.992
Temperature	37.13	36.97	0.463
HR	85.6	87.7	0.346

Table 4: S/F Ratio Progression Over Time: This table highlights the temporal improvement in oxygenation in the study group. While both groups started with the same baseline S/F ratio (0.87), only the study group improved significantly at 12 and 24 hours, while the control group showed minimal change. The difference became statistically significant after the first 12 hours and continued to increase by 24 hours, confirming the positive impact of hybrid ventilation on oxygenation trajectories.

Table 4: S/F Ratio Progression Over Time.

Time Point	Control Group S/F Ratio	Study Group S/F Ratio	p-value
Baseline	0.87	0.87	>0.05
12 hours	0.87	0.91	<0.0001
24 hours	0.88	0.92	<0.0001

The temporal trajectory of oxygenation, quantified by the S/F ratio, demonstrated a statistically significant improvement ($p < 0.0001$) in the study group receiving hybrid ventilation (mandatory machine-generated breathing cycles + spontaneous efforts). At 12 hours, the study group achieved an S/F ratio of 0.91 ± 0.01versus 0.87 ± 0.01 in controls; by 24 hours, this divergence widened to 0.92 ± 0.05 (study) versus 0.88 ± 0.04 (control). Hemodynamic and thermoregulatory parameters (MAP, heart rate, temperature) remained stable in both groups ($p > 0.05$), underscoring the intervention's safety. The progressive rise in S/F ratio reflects sustained enhancement of gas exchange, supporting the efficacy of mandatory cycle augmentation in mitigating hypoxemia among NIV-failure patients declining intubation. As in fig 1.

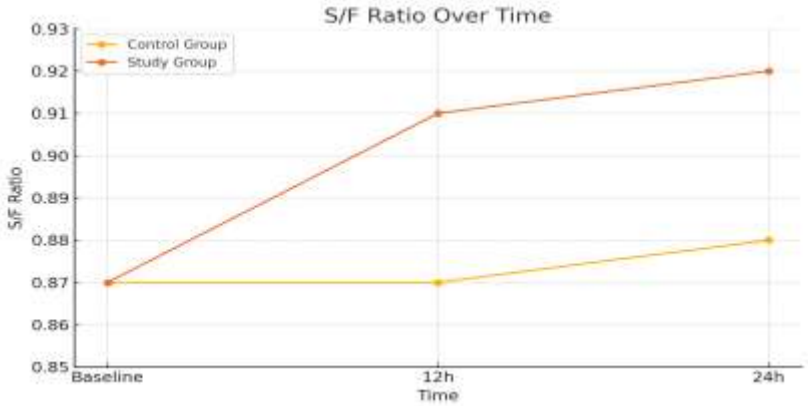

Fig. 1: S/F Ratio Infograph Interpretation.

DISCUSSION

This randomized controlled trial demonstrates that the use of mandatory-spontaneous hybrid ventilation significantly improves oxygenation in COVID-19 ICU patients with non-invasive ventilation (NIV) failure who decline endotracheal intubation. The intervention group, which received 8–10 ventilator-generated mandatory cycles alongside spontaneous efforts, exhibited a significant improvement in SpO_2/FiO_2 (S/F) ratio at both 12 and 24 hours' post-intervention, compared to the control group receiving standard NIV. These findings suggest that hybrid ventilation is not only effective but also safe, as there were no adverse effects on hemodynamic parameters such as mean arterial pressure (MAP), heart rate, or temperature during the study period. The likely mechanism behind the improved oxygenation involves enhanced alveolar recruitment and reduced work of breathing. The addition of mandatory breaths supports patients whose respiratory muscles are fatigued, thereby promoting better ventilation-perfusion matching and gas exchange without the risks associated with invasive mechanical ventilation (IMV).[8] This approach aligns with prior studies that highlight the importance of maintaining patient-ventilator synchrony to improve outcomes in acute respiratory distress syndrome (ARDS).[9] Moreover, the results of this study show a greater oxygenation benefit than those typically seen with high-flow nasal cannula (HFNC) or NIV alone in similar patient populations, suggesting a unique role for hybrid ventilation as a bridge therapy. Grieco et al. reported only modest improvements in S/F ratios with HFNC in severe COVID-19 cases, whereas the present study demonstrates a sustained increase to 0.91 and 0.92 at 12 and 24 hours, respectively.[10] Ethically, hybrid ventilation addresses a growing need to respect patient autonomy while still providing beneficial respiratory support. In patients or families who refuse intubation—whether for prognostic, personal, or cultural reasons—clinicians are often left with limited options. Hybrid ventilation offers a middle ground, supporting oxygenation and survival without violating patient preferences. This approach adheres to the ethical principles of beneficence and non-maleficence while honoring autonomy.[11]

Despite its promising results, the study has limitations. The single-center design may limit generalizability, and the short 24-hour observation period does not capture long-term outcomes such as mortality, length of ICU stays, or quality of life. Additionally, the study was not blinded, which may introduce performance or observer bias. Future multicenter trials with longer follow-up periods are essential to validate these findings and explore long-term clinical benefits.

CONCLUSION

Mandatory cycles and noninvasive ventilation (NIV) comprise hybrid ventilation, substantially enhanced oxygenation in patients with NIV failure COVID-19 patients who are declining intubation.

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