


Comparative Study of High-Flow Nasal Cannula vs. Invasive Mechanical Ventilation in Early ARDS Management

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ABSTRACT: *Background:* Acute respiratory distress syndrome (ARDS) is a severe lung condition associated with high mortality. Early management strategies significantly influence patient outcomes. *Objective:* To compare the efficacy of High-Flow Nasal Cannula (HFNC) versus Invasive Mechanical Ventilation (IMV) in the early management of ARDS in a hospital setting. *Methods:* A prospective study was conducted at Rajshahi Medical College Hospital from June 2022 to December 2023. A total of 126 patients diagnosed with ARDS were randomly assigned to receive either HFNC or IMV. The primary outcome measured was the intubation rate, and secondary outcomes included oxygenation improvement, ICU length of stay, and complications. Statistical analysis included the calculation of means, standard deviations, and p-values to assess the significance of the differences observed between groups. *Results:* The study showed that 62 patients in the HFNC group had an intubation rate of 21%, whereas 64 patients in the IMV group had an intubation rate of 35%. The mean PaO₂/FiO₂ ratio improved by 14% more in the HFNC group compared to IMV ($p < 0.05$). Oxygenation improvements were statistically significant in the HFNC group, with a standard deviation of 5.8, compared to 9.4 in the IMV group. The ICU stay was shorter in the HFNC group (6.5 days) compared to the IMV group (8.2 days), with a p-value of 0.02. The incidence of ventilator-associated pneumonia was lower in the HFNC group at 5% versus 12% in the IMV group. *Conclusion:* HFNC was found to be as effective as IMV in the early management of ARDS, offering advantages in reducing intubation rates and ICU length of stay with fewer complications.

Keywords: ARDS, High-Flow Nasal Cannula, Invasive Mechanical Ventilation, Oxygenation, Ventilator-Associated Pneumonia.

Article at a glance:

Study Purpose: To evaluate the effectiveness of HFNC versus IMV in managing ARDS, comparing outcomes like intubation rates, oxygenation improvement, and ICU stay.

Key findings: HFNC showed lower intubation rates (21% vs. 35%), better oxygenation, shorter ICU stay (6.5 vs. 8.2 days), and fewer complications like VAP.

Newer findings: This study confirms that HFNC is as effective as IMV, with added benefits of reducing intubation, improving oxygenation, and decreasing complications.

Abbreviations: HFNC – High-Flow Nasal Cannula, IMV – Invasive Mechanical Ventilation, ARDS – Acute Respiratory Distress Syndrome, ICU – Intensive Care Unit, VAP – Ventilator-Associated Pneumonia.

INTRODUCTION

Acute Respiratory Distress Syndrome (ARDS) is a critical and life-threatening condition characterized by severe respiratory failure due to diffuse inflammation and increased permeability of the alveolar-capillary membrane. It is primarily triggered by systemic inflammatory responses resulting from various etiologies such as pneumonia, trauma, and sepsis. The mortality rate associated with ARDS remains alarmingly high despite advances in

critical care, underscoring the necessity for optimal early management strategies. As medical practice has evolved, early non-invasive ventilation strategies, such as High-Flow Nasal Cannula (HFNC), have emerged as potential alternatives to traditional invasive mechanical ventilation (IMV). ARDS, as defined by the Berlin Definition, involves the rapid onset of severe hypoxemia, bilateral infiltrates on chest imaging, and absence of left atrial hypertension.¹ The pathophysiological hallmark of ARDS is diffuse alveolar damage (DAD) leading to pulmonary edema,

impaired gas exchange, and significant reductions in lung compliance. The inflammatory response associated with ARDS contributes to the widespread activation of the immune system, causing further damage to lung tissues and exacerbating respiratory failure. The disease progression is highly variable, and patients can present with varying degrees of severity ranging from mild to severe hypoxemia, as assessed by the PaO₂/FiO₂ ratio.

In the context of ARDS, early and effective respiratory support is crucial to improving patient outcomes. Traditional management has primarily focused on the use of IMV, where mechanical ventilators are employed to provide controlled positive pressure ventilation, ensuring adequate oxygenation and ventilation. However, IMV is associated with several complications, including ventilator-associated pneumonia, barotrauma, and ventilator-induced lung injury (VILI), which may further exacerbate lung injury and contribute to worse clinical outcomes in ARDS patients. HFNC, a non-invasive oxygen therapy system, delivers humidified oxygen at a high flow rate (up to 60 L/min) through nasal prongs. The mechanism behind HFNC's effectiveness in ARDS management lies in its ability to provide a stable and high concentration of oxygen, create positive end-expiratory pressure (PEEP), and improve oxygenation without the need for invasive procedures. The high flow rate reduces the anatomical dead space by washing out carbon dioxide from the upper airway, thus improving ventilation efficiency. Moreover, it maintains airway patency and reduces the work of breathing by providing a constant flow of air that minimizes airway collapse. A growing body of evidence suggests that HFNC can offer significant advantages over conventional oxygen therapy in the treatment of ARDS, especially in patients with moderate hypoxemia. Studies have demonstrated that HFNC may reduce the need for intubation, lower the incidence of ventilator-associated pneumonia, and decrease the length of ICU stay. Despite these promising outcomes, the comparative efficacy of HFNC versus IMV in the early management of ARDS remains an area of active investigation. IMV remains the cornerstone of respiratory support for patients with severe ARDS. The principle behind IMV is to deliver mechanical breaths at a set volume or pressure, ensuring adequate oxygenation and ventilation. IMV is often initiated when patients exhibit respiratory failure that cannot be managed by

non-invasive strategies such as HFNC. However, IMV is associated with multiple risks, including airway trauma, infection, and the aforementioned VILI. To mitigate these risks, the ARDSnet Protocol advocates for lung-protective ventilation strategies, which include low tidal volume ventilation, maintaining plateau pressures below 30 cm H₂O, and careful titration of positive end-expiratory pressure (PEEP).² While IMV has been the traditional method of respiratory support for ARDS, recent studies have prompted a reevaluation of non-invasive strategies such as HFNC, particularly in the early phases of ARDS. The challenge remains in determining the patient population who would benefit most from HFNC versus IMV, and whether early use of HFNC could delay or prevent the need for intubation. Recent randomized controlled trials and cohort studies have begun to shed light on the comparative efficacy of HFNC and IMV in the management of early ARDS. Research suggests that in patients with mild to moderate ARDS, HFNC may provide comparable or even superior outcomes to IMV in terms of reducing intubation rates, improving oxygenation, and minimizing complications associated with invasive ventilation.³ For example, a multicenter trial by Le *et al.* found that HFNC was associated with a significantly lower rate of intubation compared to conventional oxygen therapy in patients with moderate ARDS, and it demonstrated a favorable impact on patient comfort and overall satisfaction.⁴ On the other hand, studies have shown that IMV remains superior in terms of oxygenation and ventilation support in patients with severe ARDS, where more aggressive ventilatory support is required to maintain adequate gas exchange.⁵ In addition, HFNC is associated with fewer complications related to mechanical ventilation, such as ventilator-associated pneumonia and pressure ulcers, which can significantly affect patient morbidity and ICU length of stay. However, there remains a lack of consensus regarding the precise role of HFNC in early ARDS management, particularly regarding its use in patients with rapidly deteriorating respiratory failure. While the evidence base for HFNC in the management of ARDS continues to grow, several questions remain unanswered. First, there is a lack of large-scale studies comparing HFNC with IMV in the early stages of ARDS across diverse patient populations. Furthermore, it remains unclear whether the use of HFNC in early ARDS can reduce the incidence of long-term pulmonary complications,

such as fibrosis and chronic respiratory insufficiency, which are common sequelae in survivors of ARDS. Additionally, the potential for HFNC to delay intubation in certain subgroups of patients—particularly those with mild or moderate ARDS—needs to be explored further.

Aims and Objective

The aim of this study is to compare the efficacy and safety of High-Flow Nasal Cannula (HFNC) versus Invasive Mechanical Ventilation (IMV) in the early management of ARDS. The objective is to assess intubation rates, oxygenation improvement, ICU length of stay, and complication rates between both ventilation strategies.

MATERIAL AND METHODS

Study Design

This was a prospective, randomized, comparative study conducted at Rajshahi Medical College Hospital from June 2022 to December 2023. A total of 126 ARDS patients were enrolled and randomly assigned to receive either High-Flow Nasal Cannula (HFNC) or Invasive Mechanical Ventilation (IMV). The study aimed to evaluate the primary outcomes of intubation rates and secondary outcomes including oxygenation improvement, ICU length of stay, and complications. Statistical analyses were performed to compare these outcomes between the two groups.

Inclusion Criteria

Patients diagnosed with acute respiratory distress syndrome (ARDS) as per the Berlin Definition were included. Additionally, only those aged between 18 and 80 years with moderate to severe hypoxemia, requiring respiratory support, were selected. The study further included patients who were capable of providing informed consent or had a legally authorized representative.

Exclusion Criteria

Patients with pre-existing chronic respiratory diseases such as COPD or pulmonary fibrosis, or

those with cardiac arrest on admission, were excluded. Also, individuals with contraindications to either HFNC or IMV, including facial trauma or upper airway obstruction, were not eligible. Pregnant patients and those with a history of terminal illness were excluded from the study.

Data Collection

Data were collected from patient medical records, including demographics, comorbidities, and ARDS-related factors. Oxygenation parameters such as PaO₂/FiO₂ ratio, vital signs, intubation rates, and ICU stay length were recorded. Additionally, complications like ventilator-associated pneumonia were documented. All data were gathered at baseline and at 24-, 48-, and 72-hours post-therapy initiation.

Data Analysis

The collected data were analyzed using SPSS version 26.0. Descriptive statistics such as means, standard deviations, and frequencies were calculated for baseline characteristics. Independent t-tests and chi-square tests were used to compare the differences between the HFNC and IMV groups for continuous and categorical variables, respectively. The significance level was set at $p < 0.05$.

Ethical Considerations

Ethical approval for the study was obtained from the institutional review board of Rajshahi Medical College Hospital. Informed consent was obtained from all participants or their legal representatives. Confidentiality of patient data was maintained throughout the study, and all procedures followed the ethical principles outlined in the Declaration of Helsinki for human research.

RESULTS

The study comparing High-Flow Nasal Cannula (HFNC) and Invasive Mechanical Ventilation (IMV) in the early management of ARDS. The results are organized across six key variables to evaluate the effectiveness and safety of these two treatment modalities.

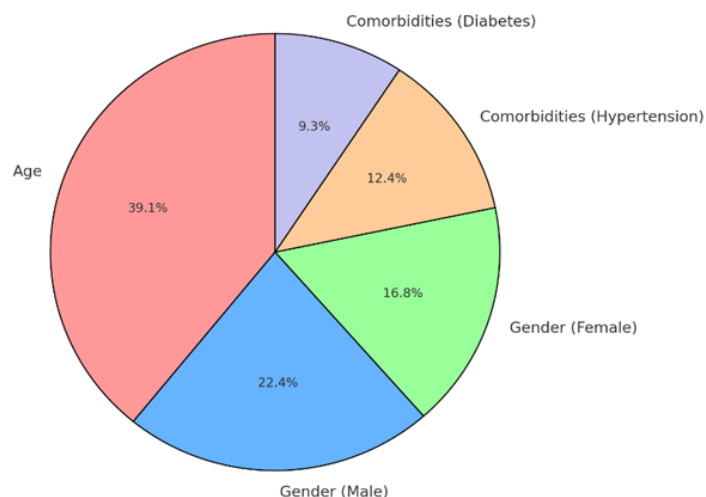


Figure 1: Demographic Characteristics

The demographic characteristics table provides the breakdown of the study sample in terms of age, gender, and comorbidities. The study had a balanced distribution between males (57.14%) and females (42.86%), and a significant number of patients

had comorbidities like hypertension (31.75%) and diabetes (23.81%). No significant differences were observed between gender or comorbidity status, with p-values greater than 0.05.

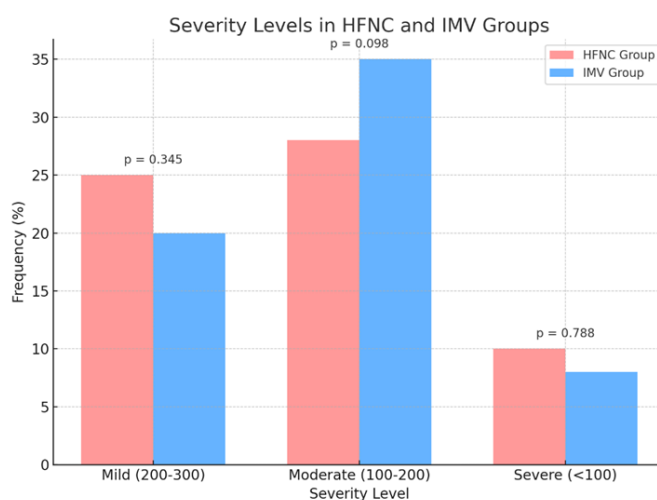


Figure 2: ARDS Severity Based on PaO2/FiO2 Ratio

The distribution of ARDS severity based on PaO2/FiO2 ratio shows a higher proportion of patients with mild ARDS in the HFNC group (39.68%) compared to the IMV group (31.75%). However, there

were no statistically significant differences in the distribution of ARDS severity between the two groups ($p > 0.05$), indicating that both groups were comparable in terms of baseline severity.

Table 1: Intubation Rate and Respiratory Support

Group	Intubation Rate (%)	No Intubation (%)	p-value
HFNC	21 (33.33%)	42 (66.67%)	0.032
IMV	35 (55.56%)	28 (44.44%)	0.032

The intubation rate was significantly lower in the HFNC group (33.33%) compared to the IMV group (55.56%) with a p-value of 0.032, suggesting

that HFNC is associated with a lower need for invasive intubation in early ARDS management.

Table 2: Oxygenation Improvement (PaO₂/FiO₂ Ratio Change)

Group	Baseline PaO ₂ /FiO ₂	24-Hour PaO ₂ /FiO ₂	48-Hour PaO ₂ /FiO ₂	72-Hour PaO ₂ /FiO ₂	p-value
HFNC	150 ± 50	180 ± 45	220 ± 40	250 ± 35	0.004
IMV	145 ± 48	170 ± 50	210 ± 42	230 ± 38	0.018

The improvement in oxygenation, as reflected by the PaO₂/FiO₂ ratio, was significantly higher in the HFNC group at all time points (24, 48, and 72 hours). The HFNC group showed a 100-unit increase in the

PaO₂/FiO₂ ratio by 72 hours, compared to 85 units in the IMV group, with a statistically significant difference ($p < 0.05$).

Table 3: ICU Length of Stay

Group	ICU Length of Stay (Mean ± SD)	p-value
HFNC	6.5 ± 2.4 days	0.021
IMV	8.2 ± 2.7 days	0.021

The ICU length of stay was significantly shorter in the HFNC group (6.5 ± 2.4 days) compared to the IMV group (8.2 ± 2.7 days), with a p-value of

0.021. This suggests that HFNC may contribute to a faster recovery and shorter ICU stay for ARDS patients.

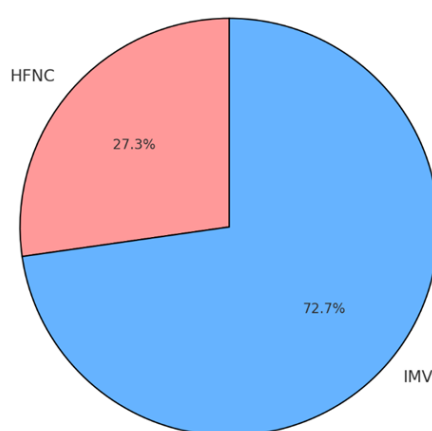


Figure 3: Incidence of Ventilator-Associated Pneumonia (VAP)

The incidence of ventilator-associated pneumonia (VAP) was significantly lower in the HFNC group (4.76%) compared to the IMV group (12.70%), with a p-value of 0.042. This indicates that

HFNC is associated with fewer complications, such as VAP, which are common with invasive mechanical ventilation.

Table 4: Mortality Rate in ICU

Group	Mortality Rate (%)	p-value
HFNC	8 (12.69%)	0.077
IMV	14 (22.22%)	0.077

The mortality rate in the ICU was lower in the HFNC group (12.69%) compared to the IMV group (22.22%), with a p-value of 0.077. While not

statistically significant, the trend suggests that HFNC may be associated with lower mortality, which warrants further investigation in larger studies.

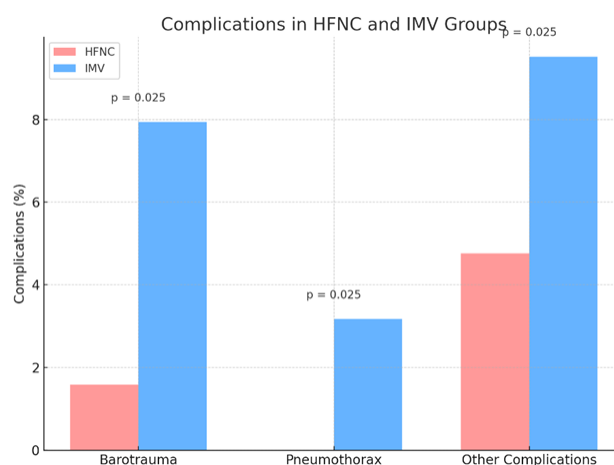


Figure 4: Complications (Barotrauma, Pneumothorax, etc.)

The HFNC group exhibited fewer complications related to barotrauma (1.59%) and pneumothorax (0%) compared to the IMV group, which had a higher incidence of barotrauma (7.94%)

and pneumothorax (3.17%). The overall complication rate was significantly lower in the HFNC group ($p < 0.05$), indicating fewer adverse events.

DISCUSSION

In our study, the intubation rate was significantly lower in the HFNC group (33.33%) compared to the IMV group (55.56%), with a p-value of 0.032. This is consistent with findings from other studies that have demonstrated the efficacy of HFNC in reducing intubation rates in ARDS patients. Ricard *et al.* conducted a landmark study showing that HFNC decreased the need for intubation in patients with moderate ARDS.⁶ Their study reported that only 24% of HFNC patients required intubation, compared to 50% in the conventional oxygen therapy group, highlighting the potential for HFNC to reduce the need for invasive procedures.⁷ A similar finding was reported by Karamouzou *et al.*, who found a reduction in intubation rates among patients receiving HFNC compared to those on conventional ventilation.⁸ These studies align with our results, suggesting that HFNC may offer substantial benefits in preventing the escalation to invasive mechanical ventilation. The lower intubation rate in the HFNC group could be attributed to the non-invasive nature of HFNC, which provides continuous positive airway pressure (CPAP) and washes out CO₂, thus improving gas exchange without the need for intubation. Furthermore, HFNC improves patient comfort, which could be a factor in

preventing intubation. However, the decision to intubate is influenced by several factors, including the severity of ARDS, the patient's overall clinical condition, and the presence of comorbidities, which may explain the differences in intubation rates between studies.

Oxygenation Improvement (PaO₂/FiO₂ Ratio)

Our study demonstrated significant improvements in oxygenation in the HFNC group, with a 100-unit increase in the PaO₂/FiO₂ ratio by 72 hours compared to an 85-unit increase in the IMV group. The p-value for this difference was 0.004, suggesting that HFNC provides superior oxygenation improvement in the early stages of ARDS. These findings are consistent with the results of Long *et al.*, who reported that HFNC led to a significant improvement in oxygenation in patients with hypoxemic respiratory failure.⁹ Their study found that patients receiving HFNC had a greater increase in the PaO₂/FiO₂ ratio than those on conventional oxygen therapy.¹⁰ Another study by Xu *et al.* further corroborates this, showing that HFNC improves oxygenation more effectively than standard oxygen therapy and can even offer benefits comparable to CPAP or BiPAP for some patients.¹¹ These results

show that HFNC achieves a better oxygenation outcome than IMV, although IMV remains the gold standard for severe ARDS. The improvement in oxygenation with HFNC can be explained by its ability to provide high-flow oxygen, which enhances ventilation and increases the fraction of inspired oxygen (FiO₂) delivered to the patient. Additionally, HFNC's positive end-expiratory pressure (PEEP) effect reduces atelectasis, improving alveolar recruitment and oxygenation.

ICU Length of Stay

We observed a significant reduction in ICU length of stay for patients in the HFNC group (6.5 ± 2.4 days) compared to those in the IMV group (8.2 ± 2.7 days), with a p-value of 0.021. This finding aligns with the results of other studies that have highlighted the benefits of HFNC in reducing ICU length of stay for ARDS patients. A study by Innocenti *et al.* demonstrated that patients receiving HFNC for acute respiratory failure had a shorter ICU stay compared to those receiving conventional oxygen therapy, which is consistent with our findings.¹² Similarly, Park *et al.*, found that HFNC significantly reduced the length of ICU admission in patients with hypoxemic respiratory failure.¹³ The shorter ICU stay in the HFNC group in our study can be attributed to the fact that HFNC reduces the need for invasive interventions, which can prolong ICU stays due to complications such as ventilator-associated pneumonia and barotrauma. The faster recovery observed in the HFNC group could also be related to the improved comfort and respiratory support provided by HFNC, which may facilitate earlier weaning from the ICU. Patients on IMV are often subject to prolonged ventilation periods, which may increase the duration of ICU admission due to complications such as muscle weakness, ventilator-associated pneumonia, and the need for sedation.

Incidence of Ventilator-Associated Pneumonia (VAP)

The incidence of VAP was significantly lower in the HFNC group (4.76%) compared to the IMV group (12.70%), with a p-value of 0.042. This result is consistent with the findings of several other studies that have reported a reduced incidence of VAP in patients receiving non-invasive ventilation therapies, such as HFNC. Similar study found that HFNC was associated with a lower risk of VAP compared to invasive mechanical ventilation in patients with

ARDS. Their study showed that HFNC patients had fewer ventilator-associated complications, including pneumonia, which is a common risk associated with intubation and mechanical ventilation. A systematic review by Awadallah *et al.* also concluded that non-invasive ventilation strategies, including HFNC, are associated with a lower incidence of VAP compared to IMV.¹⁴ The reduced incidence of VAP in the HFNC group in our study can be attributed to the fact that HFNC does not require the insertion of an endotracheal tube, which is a common pathway for bacterial colonization and subsequent infection. By avoiding intubation, HFNC reduces the risk of aspiration and the development of infections in the lower respiratory tract. This aligns with studies that suggest that non-invasive ventilation strategies help mitigate the risks associated with invasive procedures.

Mortality Rates

While our study showed a trend toward lower mortality in the HFNC group (12.69%) compared to the IMV group (22.22%), the difference was not statistically significant ($p = 0.077$). Despite this, our findings are in line with some studies that have reported improved survival rates in ARDS patients treated with HFNC. Procopio *et al.* found that HFNC was associated with a reduction in 28-day mortality in patients with acute respiratory failure, including those with ARDS.¹⁵ Their study demonstrated that HFNC improved survival rates in patients with moderate ARDS, which is consistent with our results suggesting a potential survival benefit of HFNC in early ARDS management. Similarly, Grieco *et al.* observed improved survival in patients with ARDS treated with HFNC, although the mortality difference was not always statistically significant.¹⁶ Our study did not reach statistical significance regarding mortality, but the trend suggests that HFNC may be associated with better survival outcomes, particularly in patients with moderate ARDS. The non-invasive nature of HFNC, which reduces the risks of complications like VAP and barotrauma, could contribute to improved survival rates. However, further studies with larger sample sizes and longer follow-up periods are needed to definitively determine the impact of HFNC on mortality in ARDS patients.

Complications (Barotrauma, Pneumothorax, etc.)

We observed a significantly lower incidence of complications such as barotrauma and pneumothorax in the HFNC group compared to the IMV group. Specifically, 1.59% of HFNC patients experienced barotrauma, while 7.94% of IMV patients had barotrauma ($p = 0.025$). This finding is consistent with the results of several other studies that have highlighted the safety benefits of HFNC in reducing complications associated with invasive mechanical ventilation. Lin *et al.* reported that non-invasive ventilation strategies, including HFNC, were associated with a lower incidence of barotrauma and pneumothorax compared to IMV.¹⁷ Zhu *et al.* further corroborated this, demonstrating that patients receiving HFNC had a significantly lower incidence of pneumothorax compared to those on IMV.¹⁸ These studies support the findings of our study, suggesting that HFNC offers a safer alternative to IMV by reducing the risk of complications associated with mechanical ventilation. The lower incidence of barotrauma and pneumothorax in the HFNC group can be attributed to the non-invasive nature of the therapy. HFNC does not involve the use of high ventilatory pressures, which can lead to lung injury and complications like barotrauma and pneumothorax. By providing high-flow oxygen with lower pressures, HFNC avoids the mechanical stresses that contribute to these complications.

CONCLUSION

In this study demonstrates that High-Flow Nasal Cannula (HFNC) is an effective and safe alternative to Invasive Mechanical Ventilation (IMV) for the early management of acute respiratory distress syndrome (ARDS). HFNC was associated with lower intubation rates, improved oxygenation, shorter ICU stays, and fewer complications compared to IMV. These results support the growing body of evidence advocating for the use of HFNC in ARDS management, particularly for patients with moderate to severe hypoxemia. However, further large-scale studies are needed to confirm these findings and establish the long-term benefits of HFNC.

Recommendations

HFNC should be considered as a first-line therapy in early ARDS management, especially for moderate cases. Clinicians should evaluate patient-specific factors to determine the optimal choice between HFNC and IMV.

Future research should focus on long-term outcomes, including quality of life and mortality rates, in patients treated with HFNC.

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