

# To Determine the Efficacy of HFNC Therapy against Conventional Oxygen Delivery Devices in Acute Respiratory Failure - A Systematic Review

Subhadeep Pal

DDT, B. Sc. RT, M. Sc. RT, SIHS (SIU), FNIV

**Abstract:** *To assess and to evaluate the impact, effectiveness and efficacy of HFNC therapy on functional and subjective respiratory parameters in patients with acute hypoxic respiratory failure in comparison to non-invasive ventilation and conventional oxygen delivery devices in acute respiratory failure and my objective is to conclude (1) appraise available evidence with regard to the utility of HFNC in neonatal, pediatric, and adult patients with ARF (2) review the physiology of HFNC; (3) describe available HFNC systems and (4) review ongoing and planned trials studying the utility of HFNC in various clinical settings.*

**Keywords:** HFNC, AHRF, PEEP, FIO<sub>2</sub>, dysnea, nasal cannula, ICU

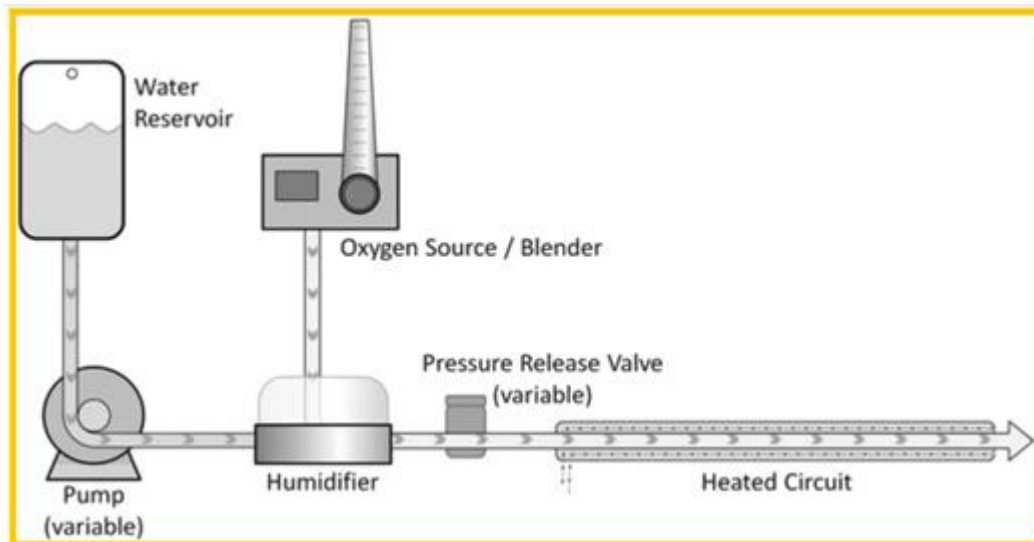
## 1. Introduction

Oxygen is the commonest drug prescribed in hospitals. The inhaled concentration is altered by the administered oxygen flow rate, the characteristics of the delivery device and the patient's respiratory pattern. For hypoxemic respiratory failure, the frontline treatment is supplemental oxygen. In 1967 "acute respiratory distress" was recognized and reported for the first time in the medical literature, and PEEP was considered to be effective for improving oxygenation. Since then, despite having well-known adverse effects, mechanical ventilation with an endotracheal tube (invasive ventilation) has no doubt saved many patients. During the 1990s, physicians began to prescribe non-invasive ventilation (NIV) to support patients with acute respiratory failure. Acute respiratory failure (ARF) is a common and life-threatening medical emergency in patients admitted to hospitals. It is caused by a variety of diseases, including heart failure, pneumonia, and exacerbations of chronic obstructive pulmonary disease. Many patients with ARF require oxygen therapy. The devices for oxygen therapy include unassisted oxygen delivery devices and assisted ventilation devices. Unassisted oxygen therapy is also called conventional oxygen therapy (COT). It is the main supportive treatment administered to patients with ARF and is usually delivered with nasal prongs or facemasks. Assisted ventilation devices that are commonly used in hospitals include noninvasive ventilation (NIV, e. g., continuous positive airway pressure and biphasic positive airway pressure) and invasive mechanical ventilation (IMV). Previous studies have shown that avoiding IMV significantly decreases the risk of death. Therefore, choosing an optimal oxygen therapy device is very important for

reducing the rates of IMV and mortality while also ensuring patients' safety and comfort.

Since then, NIV has been found to be superior to invasive ventilation for patients with COPD exacerbations and acute cardiogenic pulmonary Edema, in those patients who are immunocompromised and in acute respiratory failure.

In the 2000s, high-flow nasal cannula (HFNC) therapy gained attention as an alternative means of respiratory support for patients who were critically ill and was attractive because it was even less invasive. Initially, there was controversy as to whether it was as good as NIV for treating acute hypoxemic respiratory failure. Analyses of the results of recent clinical trials, however, show that, at least it is not inferior to NIV. A typical HFNC system consists of a flow generator, active heated humidifier, single-limb heated circuit, and nasal cannula. According to the monitored oxygen concentration, FIO<sub>2</sub> can be titrated with flows up to 60 L/min. The differences between NIV and HFNC are the interfaces as well as consistent pressure versus the ability to provide different inspiratory and expiratory pressures. Although NIV interfaces add to the anatomic dead space, HFNC delivery actually decreases dead space. Because HFNC is an open system, it does not actively enhance tidal volume; however, it does improve alveolar ventilation by washing out anatomic dead space. The simplicity and excellent patient tolerance of the system is attractive, and, owing to these advantages, the use of HFNC for adults who are critically ill has been dramatically increasing. HFNC may make it easier to initiate earlier respiratory support, and the device has the potential to decrease the necessity or duration of mechanical ventilation



## 2. Methodology

In this review we have we have discussed about the use of HFNC machine and its use and efficacy against other conventional in the patients suffering with acute respiratory failure. Articles published in the year between 2016 to 2021 in PubMed database were searched and reviewed. Various articles regarding the topic have been studied but only seven articles from different author have been included in this review. The collected data and the reports assessed the quality of each study. Randomized controlled trials that compared HFNC therapy with COT in patients with ARF were included. the references of the following articles have also been furnished in the review.

## 3. Results

In the Systematic review of publications that evaluated HFNC in critically ill subjects with or at risk for acute respiratory failure and performed a meta-analysis comparing HFNC with noninvasive ventilation (NIV) and with standard

oxygen therapy regarding major outcomes: incidence of invasive mechanical ventilation and ICU mortality. The review was limited to adult subjects, and only original peer-reviewed randomized controlled trials were selected. Exclusion criteria were observational studies and quasi-experimental trials and patients with a do-not-intubate order in the emergency room or in the general ward. A total of 9 studies were included.

### HFNC and Invasive Mechanical Ventilation:

HFNC demonstrated outcomes similar to NIV with respect to the need for invasive mechanical ventilation in a meta-analysis of 3 trials (OR 0.83, 95% CI 0.57–1.20,  $P = .31$ ,  $I^2 = 22\%$ ) with a low heterogeneity among studies (fig 1). Similar outcomes to conventional oxygen therapy were also observed (OR 0.49, 95% CI 0.22–1.08,  $P = .17$ ,  $I^2 = 37\%$ ) in a moderate heterogeneity meta-analysis of 5 trials (fig 2) of hypoxemic respiratory failure in medical (3 trials, one in immunosuppressed subjects), surgical (one study), and post-procedure (one study) subjects.

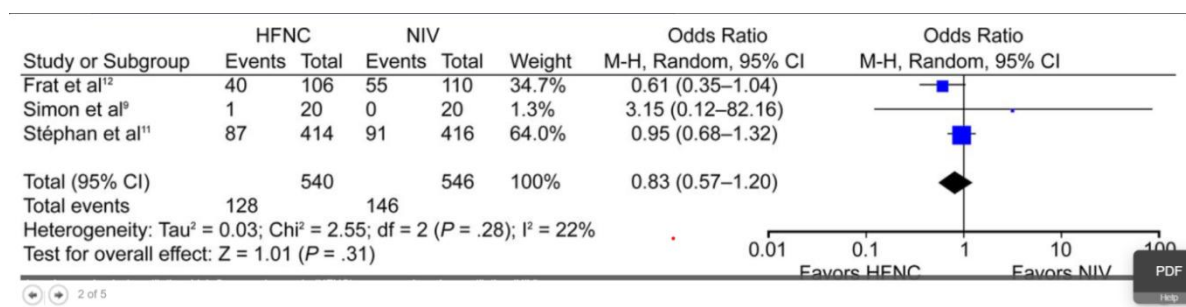


Figure 1

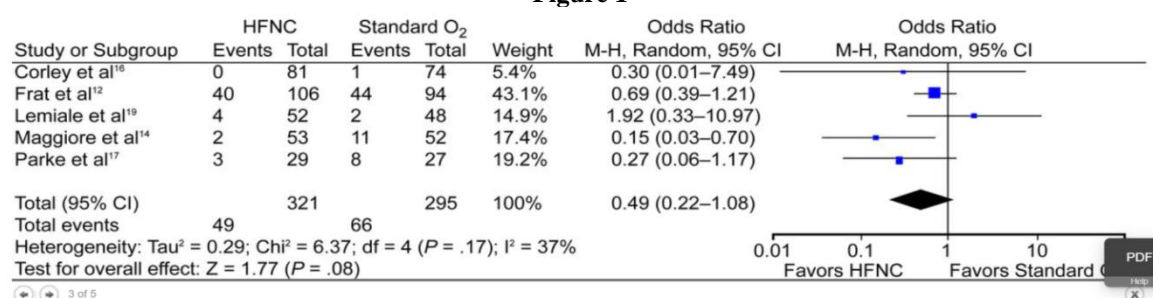


Figure 2

### HFNC and Mortality

Two studies compared HFNC and NIV mortality in hypoxemic respiratory failure, and there was no difference between groups in their meta-analysis (OR 0.72, 95% CI

0.23–2.21,  $P = .56$ ,  $I^2 = 83\%$ ) (fig 3); that meta-analysis also showed no difference between groups in the comparison of HFNC and standard oxygen therapy (OR 0.69, 95% CI 0.33–1.42,  $P = .29$ ,  $I^2 = 11\%$ ) (fig 4).

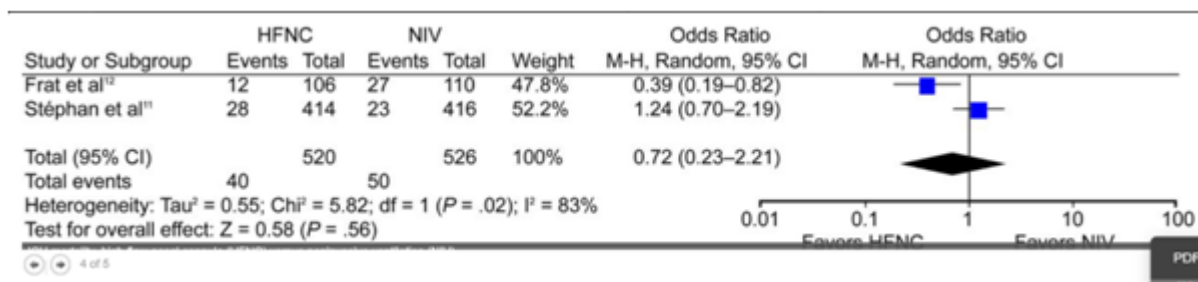


Figure 3

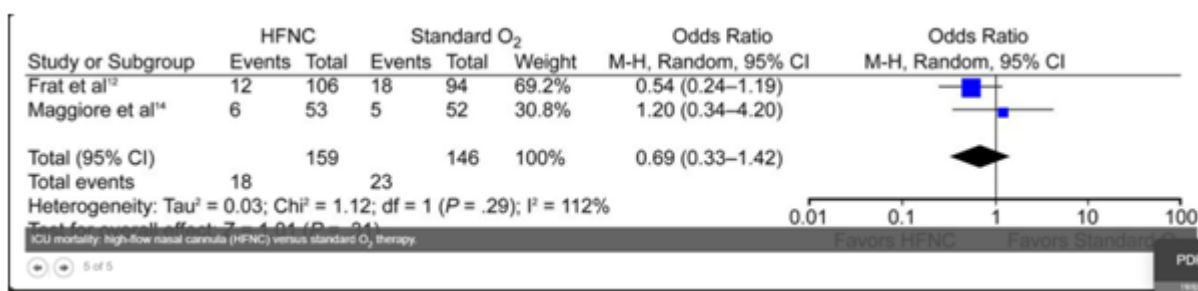


Figure 4

HFNC can be a useful alternative that has been concluded in many studies with increased patient comfort and reductions in dyspnea scores. Inspired gases in HFNC are warmed and humidified, improving patient comfort and possibly reducing airway inflammation, leading to improved drainage of respiratory secretions and additionally, the high flows match the high spontaneous inspiratory flows generated by patients with dyspnea, reducing mixing of room air and permitting delivery of more reliable FIO<sub>2</sub>. A reduction in tachypnea also should occur by flushing out anatomical dead space in the upper airway by high oxygen concentration.

Despite several physiological advantages of HFNC, such as constant FIO<sub>2</sub> during peak inspiratory flow, improvements in oxygenation, washout of the nasopharyngeal dead space, reducing the work of breathing, generation of flow-dependent PEEP, and an increase in end-expiratory lung volume, its use is not free of limitations, such as those that have been established in postextubation postoperative cardiac surgery patients with body mass index  $\geq 30$  kg/m<sup>2</sup>, in whom HFNC did not improve atelectasis, when a low level of PEEP (no more than 3–4 cm H<sub>2</sub>O) provided by HFNC should not be sufficient. It should be noted that prolonged HFNC use ( $\geq 48$  h) is associated with sequential failure and delayed intubation and may increase ICU mortality. Acute respiratory failure is not a unique physiopathologic model, and HFNC is not appropriate in all cases.

In a patient with hypoxemia alone, oxygen therapy is often sufficient to correct the condition. In contrast, although HFNC may normalize oxygen saturation, it may not be sufficient to correct the underlying disturbance when there is a ventilation-to-perfusion ratio mismatch or in the context of alveolar hypoventilation, when a reduction in the work of breathing is necessary with PEEP and inspiratory pressure

support. The data on oxygenation improvement suggest that HFNC could be superior to standard oxygen therapy but inferior to NIV.

Very few studies have compared the clinical effects of HFNC devices with COT devices, as HFNC is a simple system with clinical effects mainly dependent on flow, oxygen concentration, and temperature setting. Generally, end-inspiratory lung volume increases as flow increases and greater flow also washes out more anatomic dead space.

For patients with acute hypoxemic respiratory failure, the HFNC gas temperature may affect comfort: at equal flows, sometimes it is also evident that lowering the temperature to 31°C can be more comfortable than 37°C. Patients with more-severe hypoxemia find higher flows more comfortable. Although the functional differences between various HFNC systems are minor, it is essential to prevent rainout in the inspiratory circuit to avoid adverse clinical events. Another HFNC drawback in the clinical setting is noise. This needs to be successfully addressed to provide optimal care for patients. Thereby we can say that it can be actually be used in firstline treatment of acute hypoxemic respiratory failure in respect to other COT.

Coronavirus disease 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) prompts a wide range of clinical courses, from asymptomatic to the need for intensive care. However, respiratory support is the basis of treatment in acute respiratory failure. Non-Invasive Ventilation (NIMV), High Flow Nasal Cannula (HFNC) and Invasive Mechanical Ventilation (IMV) options are available for providing this respiratory support based on the patient's clinical condition,

and these applications are known to provide clinical benefits in SARS-CoV2

This study was planned retrospectively in five cohort intensive care units for COVID-19. Data of patients over 18 years of age who were followed-up and treated in intensive care unit for acute respiratory failure due to Covid 19 pneumonia between March 15th, 2020, and May 30th, 2020, were retroactively reviewed. The study included patients admitted to the intensive care unit with acute respiratory failure due to Covid-19 pneumonia who underwent conventional oxygen therapy (COT) by reservoir mask or HFNC.

Covid-19 was diagnosed with PCR (Polymerase Chain Reaction) test. The diagnosis of pneumonia was made through clinical findings and the appearance of multifocal ground-glass opacities that had consolidated on computed tomography. Acute respiratory failure was defined as having a P/F (Partial oxygen pressure/Fraction of oxygen saturation) ratio of less than 300 despite conventional oxygen therapy with a reservoir mask of 6 lt/min.

Although all patients with acute respiratory failure who were admitted to the hospital were candidates for HFNC treatment, the number of applications in the same period was well above the capacity of both beds and devices.

The study was divided into two groups. The data of patients who underwent HFNC were included in the first group1, and the data of patients who underwent COT with reservoir mask were included in group 2.

In Group 1, during HFNC treatment, the flow air temperature was 31–37 degrees, the flow rate was 30–60 lt/min, and the FiO2 delivered was in the range of 40–90% with target SpO2 range of > 93%. Treatment was applied continuously at the beginning; intermittent application was started after P/F > 250 and clinical well-being occurred.

Group 2, COT was applied with reservoir mask with a flow rate of 6–15 lt/min with SpO2 value of > 93%. FiO2 (%) =  $21 + 4 \times \text{flow rate (liter/min)}$  formulation was used for the calculation in patients receiving COT.

From the study we come to know that HFNC is the nasal delivery of heated and humidified air to the patient with high flow (20–70 lt / min) and more stable oxygen support (Fio2: 21–100%). Physiologically; It provides improvement in acute respiratory failure such as mild and moderate ards by increasing airway pressure, end-expiratory lung volume, oxygenation, and the rate of carbon dioxide clearance of gas content in the dead space. Patient self-inflicted lung injury, which may develop as a result of excessive breathing effort of the patient, is prevented by decreasing respiratory work and rate. In addition, HFNC has been shown to reduce the need for intubation when compared to conventional methods such as nasal cannula or mask. Consequently, by preventing intubation, the complications caused by sedation, long intensive care unit (ICU) stay or invasive mechanical ventilation will decrease.

But although it has drawbacks, HFNC application has a similar risk of contamination among aerosol-generating procedures with conventional oxygen masks. In addition, compared with typical ARDS, it was observed that respiratory mechanics are more protected and lung compliance is higher in acute respiratory failure due to covid-19, but there is a pulmonary thrombotic damage associated with increased d-dimer levels.

Considering all these factors HFNC takes up a pivotal role in clinical practice, The application of HFNC provides the desired concentration of oxygen by heating and moistening it with high flow. These features are its most important advantages compared to COT. It also has lower transpulmonary pressures compared to NIV and IMV and causes less lung damage. Because transpulmonary pressure, which is the sum of the pressure applied to the airway by the ventilator and the pleural pressure created by the patient's spontaneous respiratory effort, is the main cause of lung stress.

The use of HFNC in hypoxic respiratory failure has shown better patient comfort, decreased respiratory distress, regressed tachypnea, better oxygenation, and decreased intubation requirement have been found. However, significant differences in mortality have not been detected. According to the current information, mortality in COVID-19 patients with critical illness was 49%, and as high as 50–90% in the presence of IMV. Here we conclude that the need for intubation was less in the patient group who underwent HFNC compared to the patient group who underwent COT. Therefore, we think that the cumulative effect of both less intubation need and better oxygenation in patients with HFNC has positive results on mortality. Oxygen therapy with HFNC in patients with acute respiratory failure due to COVID-19 pneumonia reduces short-term mortality, the need for intubation, and improves oxygenation compared with COT. HFNC is an important and safe alternative treatment for acute hypoxic respiratory failure due to pneumonia secondary to COVID-19.

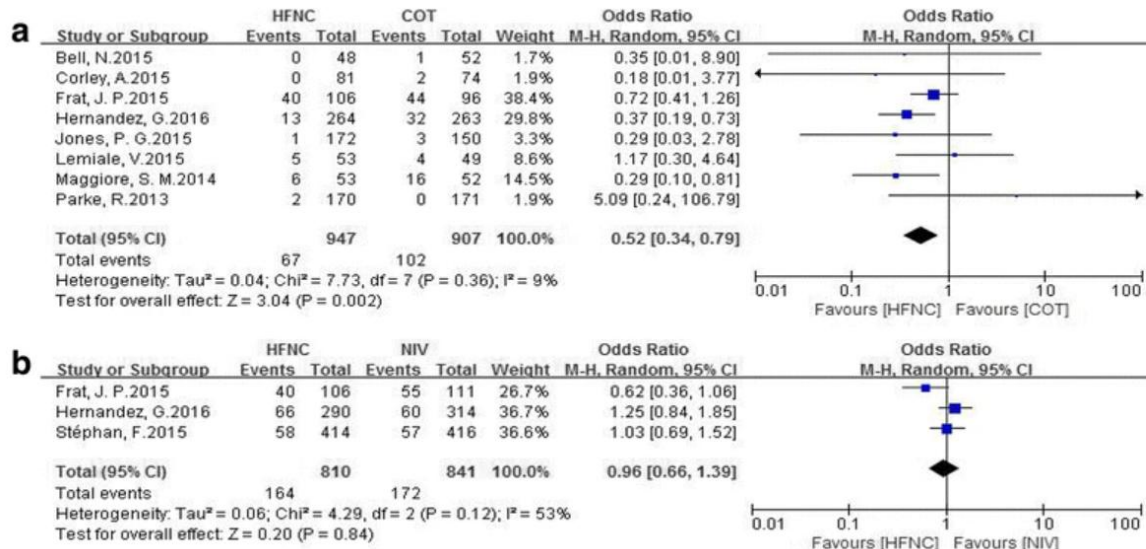
In this review of the literature that was conducted from the electronic databases from inception up to 20 October 2016, 601 articles that were screened. Only randomized clinical trials comparing HFNC with COT or HFNC with NIV were included. The intubation rate was the primary outcome; secondary outcomes included the mechanical ventilation rate, the rate of escalation of respiratory support and mortality. They have done subgroup analysis to assess possible influences of the oxygen therapy system on clinical outcomes, which allowed them to explore the possible causes of the heterogeneity. In the comparison of HFNC to COT, the first tried to find out whether there was a different treatment effect of the oxygen therapy system in patients with post-extubation acute respiration failure (ARF) and patients with ARF that occurred for other reasons. Second, we assessed the effect of trials that allowed COT to escalate to HFNC versus those studies that did not. Moreover, they also compared the results of RCTs with patients from single-centre studies versus patients from multi-centre studies.



**Primary outcomes**

Compared to COT, HFNC was associated with a significant reduction in the intubation rate (OR 0.52, 95% CI 0.34 to 0.79,  $P=0.002$ ; M-H random;  $n=1854$ ; heterogeneity  $I^2=9\%$ ,  $P=0.36$ ) (Fig.5). No difference was found in the

intubation rates between HFNC and NIV therapy (OR 0.96, 95% CI 0.66 to 1.39,  $P=0.84$ ; M-H random;  $n=1651$ ; heterogeneity  $I^2=53\%$ ,  $P=0.12$ ).

**Figure 5**

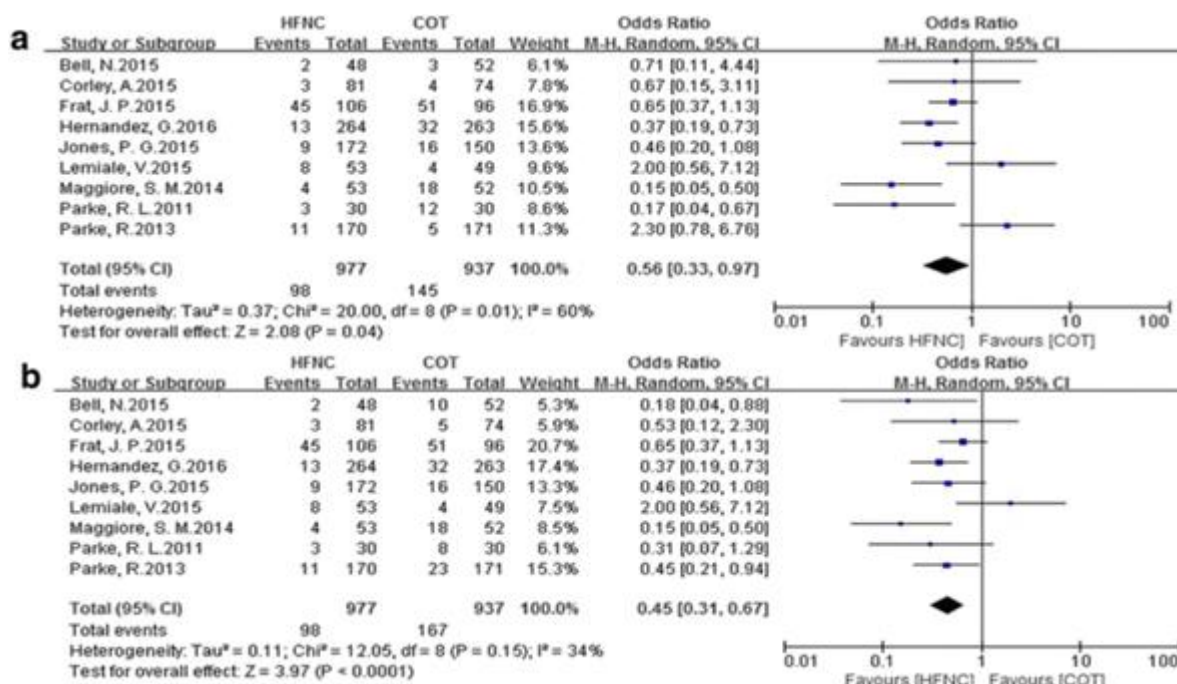
Comparison of intubation rates. a High-flow nasal cannula oxygen (HFNC) versus conventional oxygen therapy (COT). b HFNC versus noninvasive ventilation (NIV). CI confidence interval.

**Secondary outcomes**

Nine RCTs that recruited 1914 patients showed that the use of HFNC significantly reduced the mechanical ventilation rate (OR 0.56, 95% CI 0.33 to 0.97,  $P=0.04$ ), and the heterogeneity was moderate with  $I^2=60\%$  for heterogeneity ( $P=0.01$ , M-H random) (Fig.6).

The overall rate of escalation of respiratory support was also significantly lower in the HFNC group when compared with the COT group (OR 0.45, 95% CI 0.31 to 0.67,  $P<0.00001$ ), and the heterogeneity was low with  $I^2=34\%$  for heterogeneity ( $P=0.15$ , M-H random) (Fig.6).

Only five RCTs expressed data on mortality, and there was no difference between HFNC and COT therapies (OR 1.01, 95% CI 0.67 to 1.53,  $P=0.96$ ; M-H random;  $n=1497$ ; heterogeneity  $I^2=0\%$ ,  $P=0.52$ ) (Fig.6)



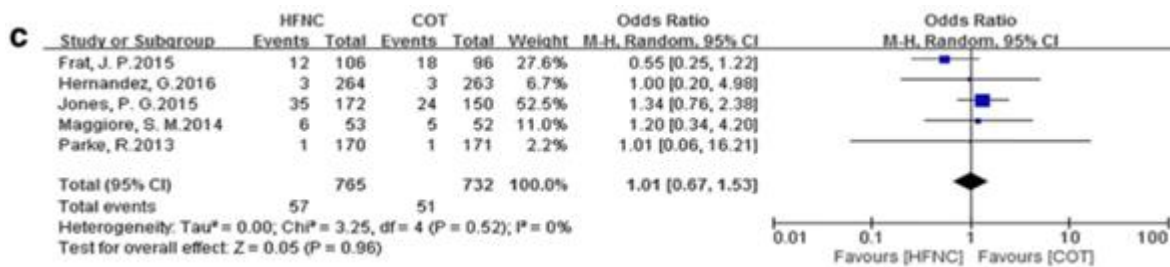


Figure 6

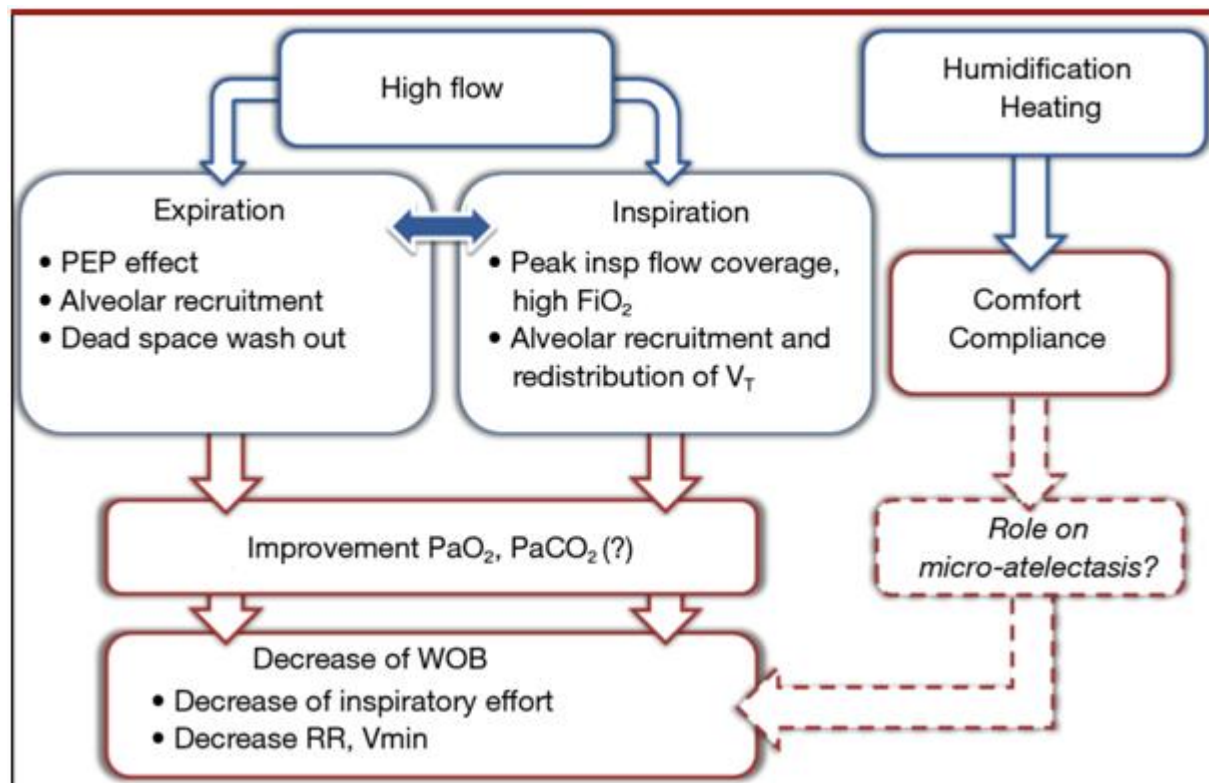
Comparison of secondary outcomes in patients who received high-flow nasal cannula oxygen (HFNC) compared to conventional oxygen therapy (COT). a Effect on the rate of mechanical ventilation. b Effect on the rate of escalation of respiratory support. c Effect on mortality. CI confidence interval

So the main finding of the study was that HFNC significantly reduced the rate of intubation, mechanical ventilation and escalation of respiratory support compared with COT in adult patients with respiratory failure, but there was no difference in mortality. On the other hand, when compared to NIV, no significant difference in intubation rate, escalation of respiratory support rate or mortality was detected. The following points can be concluded from these extensive study that HFNC has several advantages when compared to conventional oxygen therapy (COT): (1) the high-flow rates match the patient's inspiratory flow rates, which creates a positive pressure effect and reduces the anatomic dead space; (2) HFNC can deliver a predictable and constant  $FiO_2$ ; (3) HFNC can increase the partial arterial pressure of oxygen ( $PaO_2$ ) / $FiO_2$  ratio, which reduces the entrainment of room air and the dilution of oxygen (4) the heated and humidified gas that is inhaled can improve mucociliary motion and sputum clearance; and (5) there is reduced upper airway resistance, reduced work of breathing and improvement in thoraco-abdominal synchrony. Based on the above advantages, several studies found that HFNC could improve comfort level, increase oxygenation and decrease the dyspnea score in adult patients.

Hypoxemic ARF is characterized by severe acute hypoxemia ( $PaO_2/FiO_2$  ratio  $<300$ ) and causes a high respiratory drive reflected by clinical signs of respiratory distress. This drive results in highly labored breathing, especially during inspiration. The blood gas pattern is hallmarked by hyperventilation and hypocapnia. Consequently, occurrence of hypercapnia is a sign of impending respiratory muscle fatigue that must be considered as a serious complication. The peak inspiratory flow generated by patients with ARF is a mean 30–40 L/min, and can exceed 60 and even reach 120 L/min in more severe patients, which is substantially higher than the flow rates of standard oxygen delivery systems. As a result, inhaled oxygen is mixed with room air, thereby reducing the

$FiO_2$  delivered to the patient, which does not exceed 0.7 with standard oxygen systems

HFNC can deliver high  $FiO_2$  compared to other oxygen delivery systems, through a higher flow rate, up to 70 L/min, which in most cases exceeds the patient peak inspiratory flow rate. Evaluated performance of oxygen delivery devices in healthy subjects by measuring  $FiO_2$  using a standard mask, a non-rebreathing mask and HFNC. With a standard mask,  $FiO_2$  was less than 0.6 despite a flow of 12 L/min, and dropped below 0.5 when ARF was simulated by thoracic contention. Although the non-rebreathing mask avoided such a  $FiO_2$  drop during simulated ARF, the highest  $FiO_2$  obtained was less than 0.7, even with a flow rate of 15 L/min. By comparison,  $FiO_2$  reached 0.85 using HFNC set with a flow rate of 40 L/min. Nonetheless, HFNC is likely to perform better during ARF than traditional oxygen supplementation with high  $FiO_2$  more reliably delivered. Indeed, HFNC may also generate a low level of positive pressure in the upper airway directly proportional to the gas flow delivered, thereby possibly improving oxygenation. However, due to air leakage the pressure levels are quite variable. The large nasal prongs could create some nasal obstruction, while continuously delivered high flow causes resistance during expiration, thereby generating positive pressure. Consequently, positive pressure is markedly reduced when the patient opens his mouth. Parke et al. measured nasopharyngeal pressure in postoperative patients at different levels of flow using HFNC. The pressure recorded during spontaneous breathing on HFNC correlated linearly with administered flow-rate and was significantly higher when subjects breathed with their mouths closed: exceeding 3 cmH<sub>2</sub>O with a gas flow rate of 50 L/min with mouth closed, and less than 2 cmH<sub>2</sub>O with mouth open. This low positive airway pressure generates a PEEP effect including alveolar recruitment that might also improve gas exchange. physiological increased end-expiratory lung volume was found with HFNC, suggesting alveolar recruitment induced by PEEP effect. In ARF, it is found that during inspiration tidal volume did not change under HFNC after starting with standard oxygen, suggesting homogeneous distribution of tidal volume, i. e., better distribution of lung densities, suggesting less regional lung strain with HFNC.



The success of non-invasive strategies also depends on tolerance and patient compliance. Despite a high oxygen flow rate, HFNC seems to be better tolerated than NIV and standard oxygen. The heated humidifier of HFNC provides the same physiological conditions as those found in alveoli with absolute humidity of 44 mg/L of water. Standard oxygen through face mask provides non-humidified or under-humidified cold gas that dries the upper airway and leads to reduced patient comfort, even when a bubble humidifier is used.

HFNC seems to be a good alternative to standard oxygen and NIV as treatment for patients with hypoxemic ARF. Its good tolerance, physiological effects including high  $\text{FiO}_2$ , PEEP effect and dead space washout lead to decreased work of breathing and probably avoid lung strain.

Respiratory support is applied to maintain adequate oxygenation and alveolar ventilation, and the first-line treatment for hypoxemic respiratory failure is supplemental oxygen. During spontaneous breathing, inspired air passes through the nose, pharynx, larynx, and trachea. Due to the great ability of the human nose and upper airway to warm and humidify inspired gas, on the way down to the alveoli, inspired air is warmed up to body temperature and fully saturated with water vapor. The nose and upper airway are also excellent radiators: During natural breathing, even when the ambient air is cold and dry, they are capable of maintaining temperature in the oropharyngeal space. Supplemental oxygen, however, is not usually humidified when administered at low flow. Bubble humidifiers are sometimes used for humidifying medical gas delivered to spontaneously breathing patients, but the absolute humidity of the emergent gas remains low.

Dry or poorly humidified medical gas may elicit patient complaints, such as dry nose, dry throat, and nasal pain, and consequent poor tolerance of oxygen therapy

HFNC is considered to deliver well-conditioned gas to patients. As an open system with constant flow, HFNC is able to deliver a constant amount of vapor. Humidification is influenced by many factors, and only when HFNC flow is higher than the inspiratory flow of a patient with optimally positioned nasal prongs is it reasonable to expect that the patient is inspiring well-conditioned gas. During spontaneous breathing, however, VT and inspiratory flow varies, and, if HFNC flow is less than patient inspiratory flow, the patient will inspire atmospheric air. When HFNC flow is sufficiently high, the absolute humidity of inspired gas is unlikely to be a problem. Even so, we should bear in mind that HFNC devices usually incorporate a heated humidifier into the mechanical ventilation system, and the capability of such systems to create adequate vapor for high flow.

HFNC devices usually incorporate a heated circuit to avoid losing vapor in condensation, although some condensation is inevitable. When patients receiving nasal CPAP complain of symptoms in the nose and pharynx, heated humidification may be applied to reduce the adverse effects of ventilation; once this is done, condensation may accumulate in the circuit, and subsequent spraying of water droplets into the nostril may disturb sleep.

The breathing pattern of the patient, the delivered flow of HFNC, and the type of delivery device can influence humidification during HFNC. As always, the position of HFNC nasal prongs is also important.



HFNC oxygen delivery has already proved its value as an effective mode of noninvasive ventilatory support and has been gaining attention as a simple and well-tolerated alternative means of respiratory support for critically ill patients. Physicians have been using it for a wide variety of underlying diseases and conditions. It seems to be effective for treating hypercapnic respiratory failure and mild to moderate hypoxemic respiratory failure.

Evidence suggests that HFNC is an effective modality for early treatment of adults with respiratory failure associated with diverse underlying diseases.

Acute respiratory failure (ARF) is a common complication in hospitalized patients. The causes of ARF include pneumonia, cardiogenic pulmonary edema (CPE), and chronic obstructive pulmonary disease (COPD). Although oxygen therapy using conventional devices is usually prescribed for patients with ARF, many patients require advanced respiratory support. Invasive mechanical ventilation (IMV) is traditionally used in such patients. However, with recent recognition of ventilator-associated adverse events, alternatives to IMV for providing respiratory support are desired.

High-flow nasal cannula oxygen therapy (HFNC) is an alternative to IMV that was recently introduced to treat ARF. It provides some physiological effects, such as some extent of expiratory positive airway pressure (EPAP) and a washout effect on CO<sub>2</sub> in the upper airway. A previous study showed that HFNC could decrease the need for positive airway ventilation, including NIV.

Patients with hypercapnic respiratory failure are also frequently treated with NIV, especially patients with COPD exacerbation or CPE. In addition to pressure support in BPAP, the improved respiratory mechanics provided by EPAP can improve ventilation and reduce PaCO<sub>2</sub>. Although HFNC can also reduce PaCO<sub>2</sub> through a washout effect on the upper airway, there is limited evidence for the effectiveness of HFNC in hypercapnic patients.

High-flow nasal cannula oxygen therapy was reported to decrease the work of breathing and minute ventilation without increasing tidal volume, probably due to its washout effect on the upper airway. Therefore, HFNC might be associated with less risk of aggravating lung injury due to excessive lung expansion, as compared with NIV. Another possible reason is that both approaches have different effects on airway secretion. Management of airway secretion is important, especially in patients with pneumonia. Generally, excessive secretion is a risk factor for NIV failure, and it was reported that NIV could not improve sputum clearance. By contrast, HFNC was reported to improve airway clearance owing to the humidified air. Therefore, HFNC might be more suitable for patients with excessive secretion.

HFNC was associated with lower risk of 30-day mortality in patients with pneumonia or patients without hypercapnia, but a greater risk of treatment failure in patients with CPE or hypoxemia.

## 4. Conclusion

In conclusion, after reviewing all the articles that we have selected in our study, we conclude that the HFNC (high flow nasal cannula) as a new effective modality in delivering supplemental oxygen to the patients at high flow rate in respect to other conventional oxygen delivery devices, it has the capability of delivering up to 100% humidified and heated oxygen at a flow rate of up to 60 liters per minute. All settings are controlled independently allowing for greater confidence in the delivery of supplemental oxygen in addition to greater control over the delivery of FiO<sub>2</sub>, there are several benefits to using a high-flow nasal cannula that we have found out to be promising is mentioned below.

Basically, there are 5 physiologic mechanisms that are believed to be responsible for the efficacy of high-flow nasal cannula are:

- Physiological dead space washout of waste gasses including carbon dioxide (CO<sub>2</sub>)
- Decreased respiratory rate
- Positive end-expiratory pressure
- Increased tidal volume
- Increased end-expiratory volume

High Flow nasal cannula has many clinical applications. Some of the potential areas of clinical application where it is evolving with evidence are as follows

- Acute Hypoxemic Respiratory Failure
- Post-Surgical Respiratory Failure
- Acute Heart Failure /Pulmonary edema
- Hypercapnic Respiratory Failure, COPD
- Pre & Post extubation Oxygenation
- Obstructive Sleep Apnea
- Use in the emergency department
- Delaying intubation of patient

Acute hypoxemic respiratory failure (AHRF) occurs due to intrapulmonary shunting of blood because of airspace collapse or filling. It is usually refractory to supplemental oxygen. This occurs when there is an increase in alveolar-capillary hydrostatic pressure, increased alveolar-capillary permeability, blood due to hemorrhage, and/or fluid because of an inflammatory condition such as pneumonia. As previously discussed, high-flow nasal cannula therapy provides PEEP. It is established that although high-flow nasal cannula did not reduce the rate of intubation among immunocompetent patients with non-hypercapnic hypoxic respiratory failure, patients who received high-flow nasal cannula therapy experienced reduced mortality, both in the intensive care unit (ICU) and at 90-days. The results also depicted an increase in ventilator-free days, degree of comfort, reduced dyspnea severity, and a decreased respiratory rate. No significant adverse effects link to high flow nasal cannula were noticed.

Physiologically, the ability to independently control FIO<sub>2</sub> and oxygen flow in NIV and high-flow nasal cannula renders a clear advantage over regular oxygen therapy in patients with acute hypoxic respiratory failure, prone to hypercapnia. High-flow nasal cannula certainly provides a



more comfortable alternative in patients who struggle with tolerating an NIV modality.

Like many other medical interventions, there are limitations and drawbacks to the high-flow nasal cannula. One of the primary drawbacks is the expense for care relative to low flow nasal cannula, increased complexity and training to initiate care, decreased mobility, a risk for ineffective sealing of nasal prongs or the passageways leading to leaking of air and loss of the positive airway pressure effect, a potential to delay intubation, and the potential to inappropriately delay of end-of-life decisions. Furthermore, potential risk factors to noninvasive ventilation apply to a limited extent in the use of high-flow nasal cannula as well. That includes patients with alteration of consciousness, facial injury, excessive secretion with the risk of aspiration, and hemodynamic instability, other problems that can be considered are huge consumption of medical oxygen, sound that the machine provides can be a problematic or traumatizing to the patient, and like other oxygen delivery devices it can spread aerosol and that is considered as potential risk in situation like covid.

Although it is a new modality in the medical domain few concrete studies are done, more studies are required to fulfill all the criteria to establish it as a best noninvasive mechanism to deliver high flow oxygen against conventional proved modalities of oxygen delivery.

## References

- Fig (1, 2, 3, 4)-<https://doi.org/10.4187/respcare.04831>  
Fig (5, 6)-[10.1186/s13054-017-1760-8](https://doi.org/10.1186/s13054-017-1760-8)
- [1] Nedel, W. L., Deutschendorf, C., & Moraes Rodrigues Filho, E. (2017, January 1). High-flow nasal cannula in critically ill subjects with or at risk for respiratory failure: A systematic review and meta-analysis. *Respiratory Care*. American Association for Respiratory Care. <https://doi.org/10.4187/respcare.04831>
  - [2] Nishimura, M. (2019). High-flow nasal cannula oxygen therapy devices. *Respiratory Care*, 64 (6), 735–742. <https://doi.org/10.4187/respcare.06718>
  - [3] Sayan, İ., Altınay, M., Çınar, A. S., Türk, H. Ş., Peker, N., Şahin, K., ... Demir, G. D. (2021). Impact of HFNC application on mortality and intensive care length of stay in acute respiratory failure secondary to COVID-19 pneumonia. *Heart and Lung*, 50 (3), 425–429.
  - [4] Zhao, H., Wang, H., Sun, F., Lyu, S., & An, Y. (2017). High-flow nasal cannula oxygen therapy is superior to conventional oxygen therapy but not to noninvasive mechanical ventilation on intubation rate: A systematic review and meta-analysis. *Critical Care*, 21 (1), 8
  - [5] Frat, J. P., Coudroy, R., Marjanovic, N., & Thille, A. W. (2017, July 1). High-flow nasal oxygen therapy and noninvasive ventilation in the management of acute hypoxemic respiratory failure. *Annals of Translational Medicine*. AME Publishing Company. <https://doi.org/10.21037/atm.2017.06.52>
  - [6] Nishimura, M. (2016). High-flow nasal cannula oxygen therapy in adults: Physiological benefits, indication, clinical benefits, and adverse effects. *Respiratory Care*, 61 (4), 529–541. <https://doi.org/10.4187/respcare.04577>

- [7] Koga, Y., Kaneda, K., Fujii, N., Tanaka, R., Miyauchi, T., Fujita, M., ... Tsuruta, R. (2020). Comparison of high-flow nasal cannula oxygen therapy and non-invasive ventilation as first-line therapy in respiratory failure: a multicenter retrospective study. *Acute Medicine & Surgery*, 7 (1).