

**Impact of High Flow Nasal Canula Oxygen Therapy on Intensive Care Unit with Acute Respiratory Failure: A Prospective Observation Study**Pankaj Kumar<sup>1</sup>, Vikash Kumar<sup>2</sup>, Alok Kumar Bharti<sup>3</sup>, Aditya Prakash<sup>4</sup><sup>1</sup>Senior Resident, Department of Anaesthesiology and Critical Care, IGIMS, Patna<sup>2</sup>Senior Resident, Department of Anaesthesiology, GMC, Purnea<sup>3</sup>Associate Professor, Department of Anaesthesiology, IGIMS, Patna<sup>4</sup>Associate Professor, Department of Anaesthesiology, MM College Hospital, Palamu

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**Abstract**

Although though high-flow nasal cannula treatment has been available for some time, there are still a lot of individuals who aren't familiar with how to use the equipment correctly. Before the new treatment is implemented, there should be seminars organized for the professionals working in the hospital, including respiratory therapists, nurses, and others. The patient will have an easier time breathing if the flow is high because it will flush out excess CO<sub>2</sub> and wash away any stale air that may be in the lungs, which will allow for improved oxygenation. Because of the influence of positive end-expiratory pressure and the clearance of mucus through vapours created by hot water, the alveoli are able to expand to their full size. This is possible because to both of these factors. A specialized nasal cannula is used in order to provide high flow nasal oxygen, also known as HFNO. This method is capable of delivering a flow rate of up to 70 l/min while maintaining a FiO<sub>2</sub> value that is very close to 100%. While its usage is well-established in critical care for patients who can breathe on their own, new applications in anesthesia are now being researched as a part of this field. THRIVE (Transnasal Humidified Rapid Insufflation Ventilatory Exchange) and STRIVE Hi (Spontaneous Respiration utilizing IntraVenous anaesthesia and High-flow nasal oxygen) research suggest its usage in this sector. When a patient is receiving high-flow nasal cannula treatment, the best possible outcome may be achieved via the collaboration of a multidisciplinary team that includes a respiratory therapist, a clinical or critical care nurse, and a medical physician. The potential for patients to have beneficial impacts on their health would be significantly enhanced. We investigated intubation rates, long-term outcomes after HFNC, as well as the variables that are connected to long-term functional impairment in this prospective study that was conducted at a single center. We hypothesised that HFNC would provide the patient adequate time to recover from AHRF and avoid intubation as it delivers a high oxygen concentration and minimises the amount of dead space. Antiviral medication in combination with steroid treatment has the potential to provide the best results in this particular scenario.

**Keyword:** HFNC, Acute Respiratory Failure.

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**Introduction**

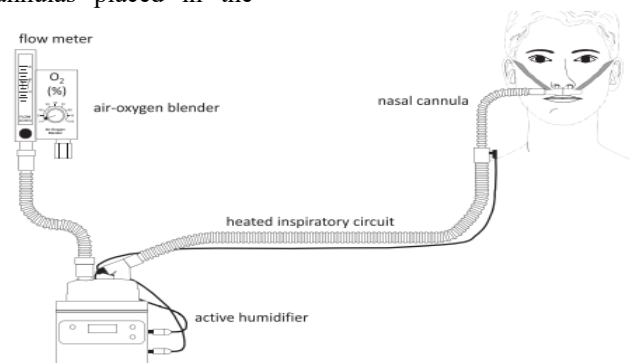
The patient need optimal breathing and oxygenation levels in order to benefit from respiratory support, which is why this assistance is provided. In this context, ensuring adequate ventilation of the alveoli is very necessary in order to expel the carbon dioxide that is produced within the human body. [1] At the present, minute ventilation is controlled during invasive or noninvasive ventilatory support in order to give proper alveolar ventilation. This is done in order to ensure enough oxygenation of the lungs. Because it improves inspiratory tidal volume (VT) while maintaining appropriate alveolar ventilation, noninvasive ventilation (NIV) has become the primary modality of choice for delivering respiratory support to patients

experiencing an acute exacerbation of chronic obstructive pulmonary disease (COPD). Unfortunatously, non-invasive ventilation (NIV) cannot be used in some conditions owing to inadequate mask tolerance. The provision of oxygen to critically sick patients via the use of high-flow nasal cannulas (HFNC), also known as nasocannulas, has recently come to the attention of medical professionals as a feasible alternative method of providing respiratory support. An air and oxygen blender, an active heated humidifier, a single heated circuit, and a nasal cannula are the components that make up this apparatus. At the air/oxygen blender, the inspiratory fraction of

oxygen (FIO<sub>2</sub>) may be adjusted to be anywhere between 0.21 and 1.0 at flow rates of up to 60 L/min.

Before it is distributed via the heated circuit, the gas passes through the active humidifier, which causes it to become heated and humidified (Figure 1). The user interface of the NIV and the HFNC is another important distinction between the two versions. The amount of anatomical dead space that is created by NIV interfaces is increased, but the amount of space that is occupied by dead tissue is reduced by HFNC interfaces. It is impossible for HFNC to actively improve VT since neither the inspiratory push nor the expiratory pull are effective in such an open circuit. In spite of this, it helps people with COPD by first reducing the amount of physical dead space and then enhancing the airflow in the alveoli.

It has been recommended that individuals who are hypoxemic should begin treatment with the use of supplementary oxygen. Cannulas placed in the



Device for administering oxygen via the nasal cannula at a high flow rate. The flow rate of a 0.21 to 1.0 FI O<sub>2</sub> air/oxygen blender is 60 liters per minute. A single-limb heated inspiratory circuit is heated by a gas that has been heated by an active humidifier. Large nasal cannulas provide therapeutic gas that has been warmed and humidified. (2017), Laurent Papazian and Amanda Corley.

The normal flow rate of oxygen is limited to 15 L/min by most systems. Patients suffering from respiratory failure have inspiratory fluxes ranging from 30 to 100 L/min. Because of the significant disparity between the patient's own inspiratory flow and the flow that is provided, FIO<sub>2</sub> is unreliable and subpar. Patients suffering from hypoxia are gravitating toward HFNC oxygen treatment. The vast majority of the data has been published in the field of neonatology [4]. HFNC gives physiological advantages over normal oxygen delivery methods. The number of severely sick patients treated with it has gone up. It addresses a variety of medical conditions. There are no clinical investigations that are dependable, big, or controlled. Mini-CPAP, transnasal insufflation, nasal high flow, nasal high-flow ventilation, high-flow treatment, and high-flow nasal cannula oxygen therapy are some of the names that have been given to this method in the scientific

patient's nose and face masks are the two most common ways that oxygen is delivered to patients.

These devices have a range of limits, which may limit the effectiveness of the oxygen delivery and the patient's tolerance for these restrictions. Complaints of a dry nose, dry throat, and soreness in the nasal passages are typical when the flow of oxygen is insufficient. This is because, in the majority of instances, the oxygen is not humidified at these levels. Patients have reported that they feel uncomfortable when the absolute humidity is low, despite the fact that bubble humidifiers are widely used to humidify air that is provided to patients who are spontaneously breathing [2,3]. A poor tolerance to oxygen treatment may be the result of inadequate heating and humidification of the surrounding environment.

literature. The research examines the physiological impacts of HFNC as well as its therapeutic applications.

### The Definition of Acute Hypoxemic Respiratory Failure and Its Characteristics

Acute hypoxemic respiratory failure, also known as de novo respiratory failure, is characterized by a reduction in gas exchange as a result of component failure within the respiratory system. Hypoxemic acute respiratory failure explains it (ARF). A ventilation-perfusion mismatch, a shunt, or impaired diffusion may all lead to hypoxemia. Lung failure causes it. A patient is considered to have hypoxemic acute respiratory failure (ARF) if their PaO<sub>2</sub> is below 60 mmHg while they are breathing room air. This notion cannot be applied in intensive care units (ICUs), which are hospitals that primarily treat patients using oxygen. The PaO<sub>2</sub>/FiO<sub>2</sub> ratio is defined by the majority of clinical studies. These studies either directly measure or infer FiO<sub>2</sub> levels. A PaO<sub>2</sub>/FiO<sub>2</sub> ratio of less than 300 mmHg, which is similar to a PaO<sub>2</sub> of less than 60 mmHg in ambient air, or more than 200 mmHg for severe instances is considered to be hypoxemia. Nevertheless, the definition of hypoxemia differs from study to study.

In order to detect acute respiratory failure, an increased respiratory rate, respiratory muscle tiredness, and thoracoabdominal asynchrony are all possible diagnostic tools (ARF).

The rates of intubation and death were found to range anywhere from 30% to 51% and 8% to 36%, respectively, among the various studies. Due to the lack of a universally accepted criteria for hypoxemic acute respiratory failure (ARF).

[5,6] It is related with a worse prognosis to have severe hypoxemic ARF, which is defined as a  $\text{PaO}_2/\text{FiO}_2$  that is less than 200 mmHg and a respiratory rate that is more than 25 breaths per minute. In recent experiments, these severity criteria were used in order to evaluate different oxygenation strategies. [7,8] Since the prognoses of hypoxemic ARF patients are dependent on the amount of oxygen that they are deprived of, further research is required. To identify hypoxemic acute respiratory failure, one should look at the  $\text{PaO}_2/\text{FiO}_2$  ratio, the respiratory rate, and any relevant clinical data (ARF). The researchers need to recruit trial-consistent persons to assist the bedside physicians.

#### **There are several reasons why de novo and acute hypoxic respiratory failure may occur**

The diagnosis of hypoxemic acute respiratory failure is made when there is no evidence of chronic lung disease or cardiogenic pulmonary emphysema, therefore excluding the possibility of acute-on-chronic respiratory failure.

[9] There are a number of factors that may lead to hypoxemic acute respiratory failure (ARF), but pneumonia is the most common cause. Hypoxemia persists despite the use of positive pressure ventilation in patients who have acute respiratory distress syndrome (ARDS), which is a subtype of hypoxemic acute respiratory failure (ARF). Patients with ARDS also have bilateral lung infiltrates that are not cardiogenic. ARDS is an abbreviation for "acute respiratory distress syndrome." The Berlin classification has the same risk variables as the de novo respiratory failure classification. Pneumonia and stomach aspiration are two examples of risk factors that might either be direct or indirect (pancreatitis, extrapulmonary sepsis, and polytrauma). [30] In addition to infectious pneumonia, ARDS may be brought on by immunological conditions such connective tissue disorders and vasculitis, as well as by drug-induced or malignant lung diseases. ARDS-mimicking agents are the causes for this. [10] Is it possible to grade acute hypoxemic respiratory failure?

Hypoxemia and other organ failures, including shock or altered consciousness, are most often associated with the prognosis of acute respiratory failure (ARF). [11,12–14] The use of the ARDS category based on the  $\text{PaO}_2/\text{FiO}_2$  ratio—mild (300

mmHg), moderate (200–300 mmHg), and severe (100 mmHg)—raises doubts regarding the accuracy of the ratio computation in freely breathing persons in patients who have hypoxemic acute respiratory failure (ARF). A PEEP of at least 5 cmH<sub>2</sub>O is required for ARDS to be identified in a patient, and the patient must also have bilateral lung infiltrates visible on chest imaging. Hypoxia cannot be explained by cardiac failure, nor can it be caused by an overflow of fluid. [15]

A post hoc analysis of two prospective studies including 127 spontaneously breathing persons with hypoxemic acute respiratory distress syndrome (ARFS) and bilateral lung infiltrates indicated that the  $\text{PaO}_2/\text{FiO}_2$  ratio correctly categorized the severity of these conditions. This ratio was obtained using regular oxygen and 24 hours after NIV administration (set with a PEEP level of 5 cmH<sub>2</sub>O). [16] 87% of hypoxemic patients with bilateral lung infiltrates who were treated with standard oxygen had the right  $\text{PaO}_2/\text{FiO}_2$  ratio assessed by standard oxygen. After receiving NIV, the remaining 13% of patients achieved  $\text{PaO}_2/\text{FiO}_2$  ratios of more than 300 mmHg, which meant that ARDS was no longer present in their cases. After the implementation of NIV, the percentage of patients with mild or moderate ARDS on regular oxygen did not change, whereas the number of patients with severe ARDS did decrease. During periods of spontaneous breathing, calculating the  $\text{PaO}_2/\text{FiO}_2$  ratio might be challenging. The calculations can only go so far. In a study involving many centers, hypoxemic ARF patients who were receiving oxygen analysis with a non-rebreathing mask at a flow rate of 15 liters per minute had a mean fraction of inspired oxygen ( $\text{FiO}_2$ ) of 65%. While this method is more precise than flow/ $\text{FiO}_2$  conversion tables, it is still just an approximation and may be challenging to implement in real-world settings. The formula  $\text{FiO}_2 (\%) = 21 \text{ oxygen flow (L/min)} \times \text{three}$  was used in order to evaluate a method that is more straightforward and usable and makes use of standard oxygen while wearing a mask. [17]

The  $\text{FiO}_2$  measurement, the 3% formula, the 4% formula, and the conversion table all produce a value for  $\text{FiO}_2$  that is less than 6%, 65 that is less than 13%, 75 that is less than 8%, and 95 that is less than 0%. [18] In addition, the  $\text{PaO}_2/\text{FiO}_2$  ratio was computed in the most exact manner by using the 3% method to determine the value of  $\text{FiO}_2$ . 143 56 mmHg while using the 3% formula, and 140 63 mmHg when using  $\text{FiO}_2$ . A non-invasive method for diagnosing ARDS is possible by using ratios of pulse oximetry saturation ( $\text{SpO}_2/\text{FiO}_2$  (S/F) that are at least 97%. [18] Rice et al. [18] suggested using this method to stay away from incorrect ARDS diagnoses. There is a correlation between the ratio of  $\text{SpO}_2/\text{FiO}_2$  and the ratio of  $\text{PaO}_2/\text{FiO}_2$  as shown by the equation: ( $\text{PaO}_2/\text{FiO}_2$ ). As a result, the cutoff

points for the SpO<sub>2</sub>/FiO<sub>2</sub> ratio were determined to be 235 and 315, which corresponded to values of 200 and 300 PaO<sub>2</sub>/FiO<sub>2</sub>, respectively. As a result of the possibility of incorrectly identifying patients with a FiO<sub>2</sub> of 1 as having a SpO<sub>2</sub> of 100%, the SpO<sub>2</sub>/FiO<sub>2</sub> ratio was not included in the Berlin criteria of ARDS. Berlin, Germany, is responsible for developing the Berlin definition of ARDS. As a result, hypoxemic acute respiratory failure (ARF) may be classified by monitoring the PaO<sub>2</sub>/FiO<sub>2</sub> ratio, calculating FiO<sub>2</sub> using the 3% technique under standard oxygen, and classifying the severity similarly to ARDS. Despite this, there are no PaO<sub>2</sub>/FiO<sub>2</sub> ratio-based epidemiologic studies available to evaluate the prognosis of hypoxemic ARF. Clinical criteria and readings of the PaO<sub>2</sub>/FiO<sub>2</sub> ratio can be used to diagnose hypoxemic acute respiratory failure (Hypoxemic ARF). This helps standardize participants in clinical trials that aim to identify the most effective non-invasive oxygen delivery system that will reduce the need for intubation and boost survival rates.

### Objective of the Study

To improve the data used to direct noninvasive oxygenation/ventilation and targeted invasive mechanical ventilation.

This prospective, single-center, observational study included consecutive adult patients with COVID-19 pneumonia who were treated with a high-flow nasal cannula.

To test this treatment on individuals with acute respiratory failure.

### Materials and Methods

The prospective observational research at General Hospital evaluated COVID-19 pneumonia HFNC therapy. Six months following discharge, hospitalized individuals granted permission via telephone to assess their daily lives by completing preselected questions (Table S1).

From September 2020 to May 2021, our hospital enrolled all ICU COVID-19 pneumonia patients over 18 years old. SARS-CoV-2-associated pneumonia was verified by hypoxic respiratory failure requiring oxygen supplementation, opacities on chest radiographs, and a positive polymerase chain reaction from a nasopharyngeal or anterior nasal swab. PaO<sub>2</sub>/FiO<sub>2</sub> 200 mmHg or SpO<sub>2</sub> 90% with a partial/non-rebreather mask at flow 15 L/min was considered "failure of the traditional oxygen delivery" (Table S2). Two-hour surveillance of individuals with HFNC. The ICU staff intubated depending on the patient's condition.

Our research did not include patients who received HFNC for less than 12 hours, solely as end-of-life care, or who did not choose to be intubated and resuscitated upon hospital admission.

The documentation of demographics, symptoms, hospitalization, and ICU admission. During 24 hours of HFNC therapy, our team monitored hemodynamic parameters, respiratory rate, FiO<sub>2</sub>, SpO<sub>2</sub>, and ROX score every 2 hours. Before HFNC, the SpO<sub>2</sub>/FiO<sub>2</sub> ratio determined the respiratory component of the SOFA score [19].

ROX is SpO<sub>2</sub>/FiO<sub>2</sub>/RR [20]. Blood gas in the arteries was measured. The intubation time, respiratory system compliance (CRS), and PaO<sub>2</sub>/FiO<sub>2</sub> ratio of intubated individuals were measured at intubation and after 24 hours. When HFNC therapy started, we received EMR lab results. We selected the closest result close to 8:00 a.m. The Supplemental Material contains procedures.

Intubation and mechanical ventilation have to be the primary outcomes. Hospital and ICU stay, HFNC therapy, mechanical ventilation, and clinical indicators during HFNC treatment and intubation were secondary outcomes. Telephone discussions with patients and medical records gave mortality and functional results at six months. After obtaining patient permission, an English or Spanish questionnaire (MGB-IRB # 2021P002892) was administered to measure persistent COVID-19 symptoms, oxygen supplementation, and independence in daily activities (Table S1) [21].

48 hours before to HFNC therapy, frontal (portable) chest radiographs were taken to evaluate lung parenchymal involvement. The pulmonary x-ray severity (PXS) score (numbers ranging from 0 to 24, with higher values indicating more severe lung abnormalities) was automatically generated from radiographs using a validated convolutional Siamese neural, network-based method [22]. Using frontal chest radiograph pixel data, the deep learning method computes the severity of consolidative lung disease. This score corresponds to some radiologists' manual COVID-19 illness severity ratings [23]. As described in the literature, chest radiography was used to determine PXS values.

Comparing baseline metrics, respiratory mechanics, and hemodynamic data between HFNC success and failure using parametric or nonparametric two-sample tests. Shapiro-Wilk established the normality of the distribution. The t-test/Wilcoxon rank-sum and chi-square tests contrasted categorical/categorical and continuous/categorical groups. After intubation, outcomes and explanatory factors were investigated using logistic regression. A linear mixed model with fixed effects on time (hours) and intubation status and random effects on patients was used to compare repeated assessments of HFNC therapy.

Six months following hospital admission, we utilized multivariable modeling to identify characteristics associated with a new functional restriction (inability to ascend 1–2 flights of stairs).

We developed six criteria [24] based on research and clinical practice. Consideration was given to demographic characteristics (age, body mass index, gender), co-morbidities (diabetes, asthma), and clinical aspects (hospitalization intubation). Age and BMI were uninterrupted. The dependent variable in a multivariate logistic regression model with six covariates as independent variables was functional restriction. Estimated odds ratios with 95% confidence intervals (CI). Spss performed data quality evaluation, statistical analysis, and visualization. 0.05 was statistically significant.

### Data analysis and Result

#### HFNC Short-Term Intubation Outcomes

187 people received HFNC treatment during the study. The analysis excluded 26 palliative air hunger patients who received HFNC. Eight non-intubated HFNC patients were excluded. HFNC treated 30 (20%) of the remaining 153 patients without intubation. Everyone survived. HFNC intubated 123 (80%). 100 of 123 (81%) HFNC and intubation failures occurred within 48 h. (Supplement). 45 intubated patients died (37%). 1. Hospitals killed 29.4%. (45 out of 153). 108 survived hospitalisation

(30 in the HFNC success group, 78 in the HFNC failure group).

#### Long-Term Examination Analysis

All discharged patients died (Table 1). 70/90 patients (73%) completed the 6-month follow-up. 20 patients rejected, died, or were unreachable after hospital discharge. Four 6-month-olds perished (three in the HFNC failure group and one in the HFNC success group). 32% died at 6 months (29 out of 90). Out-of-hospital mortality was under 4% at 6 months. One in two responders returned to work after discharge, but endotracheal intubated patients took longer (7 vs. 12 days,  $p = 0.03$ ). (1). Sixty percent of HFNC success patients reported new problems after discharge, compared to 81% of failure patients. At 6 months, both groups required oxygen. Groups had similar hospital readmission. Half of responders showed new motor or sensory deficiencies, although both groups had equal rates (Table 1).

50% of males and 18.2% of women reported new functional capacity restrictions (OR = 4.65, 95% CI [1.28, 20.6]). (2). Moreover, this new limitation increased 2.5-fold with each 10 kg/m<sup>2</sup> BMI increase (OR = 2.63, 95% CI [1.14, 6.76]).

**Table 1: This new limitation was unrelated to age, asthma, diabetes, or hospital intubation.6-month follow-up. Nasal cannula.**

	All Focuses	Success	Failure	p
Long term survey				
Discharge from hospital alive, n	90	30	60	
Alive at 6-month follow-up, n (%discharged)	100(86)	20 (90)	69 (92)	0.90
Age deceased, years Median (IQR)	66.8 (52–72)	62	67 (52–76)	

**Table 2 (a): Job before hospital and back to work**

	All Focuses	Success	Failure	p
Job before hospital, tot	72	24	49	
Y, n (%)	39 (50)	14 (50)	24 (46)	0.29
Back to work, tot	35	10	20	
Y, n (%)	20 (55)	15 (70)	19 (60)	0.50
Days back, tot	20	0	15	
Median (IQR)		35 (20–65)	80 (40–150)	0.03

**Table 2 (b):**

	All Subjects	Success	Failure	p
New problem after discharge, tot	80	23	54	
Y, n (%)	58 (72)	14 (59)	45 (80)	0.048
Quality of life equal similar, tot	77	24	56	
Y, n (%)	30 (41)	13 (49)	20 (37)	0.31
Able to walk 1–2 flight of stairs, tot	78	25	57	
Y, n (%)	30 (32)	16 (58)	15 (9)	0.06
Any new medications, (tot)	45	44	65	
Y, n (%)	48 (55)	15 (45)	30 (62)	0.14

**Table 2 (c):**

	All Focuses	Success	Failure	p
New oxygen supplementation, tot	83	244	56	
Y, n (%)	14 (17)	4 (13)	12 (19)	0.51
Breathing problem, tot	77	25	53	
Y, n (%)	36 (47)	12 (47)	25 (47)	0.98
Sensory loss, tot	71	25	47	
Y, n (%)	33 (47)	8 (37)	24 (52)	0.71
Motor deficit, tot	75	25	51	
Y, n (%)	37 (48)	12 (45)	26 (55)	0.74
Hospital redmission, tot	88	27	62	
Y, n (%)	30 (34)	9 (30)	20 (35)	0.74
Medical reason, tot	30	9	20	
n (%)	24 (80)	7 (78)	21 (82)	0.72
Reintubated, tot	30	10	22	
n (%)	3 (8)	2 (14)	2 (6)	0.46

**HFNC Failure Predictors**

HFNC success 2 (1–2) days vs. failure 1 (0–3) days was the period between hospital admission and HFNC therapy. HFNC success group: 7 (5–10) days; failure group: 6 (3–8) days) from symptom

onset to hospitalisation. As seen in Table 3, efficient HFNC care lowered comorbidities, particularly diabetes mellitus. Despite the failure group's greater hypertension rates (p-value 0.06).

**Table 3: Factors associated with functional capacity restriction at 60 days in 79 HFNC-treated COVID-19 pneumonia survivors.**

Covariate	n/Total N	(%)	Non arranged		arranged	
			OR (95%CI)	p-Value	OR (95% CI)	p-Value
Age, years	-	-	0.77 (0.58, 0.95)	0.02	0.89 (0.63, 1.25) a	0.24

**Table 3(a): patient gender**

Covariate	N	Total N	(%)	Non arranged		arranged	
				OR (95% CI)	p-Value	OR (95% CI)	p-Value
M	23	46	(50.0)	4.50 (1.64, 13.93)	0.005	4.65 (1.28, 20.6)	0.03
F	6	33	(18.2)	Reference (1.00)		Reference (1.00)	

**Table 3(b): patient has Asthma**

Covariate	N	Total N	(%)	Non arranged		Arranged	
				OR (95%CI)	p-Value	OR (95%CI)	p-Value
Yes	3	18	(16.7)	0.27 (0.06, 0.93)	0.057	0.21 (0.03, 1.01)	0.07
no	25	59	(42.4)	Reference (1.00)		Reference (1.00)	

**Table 3(c): patient has Diabetes Mellitus and Intubation during hospitalization**

	Covariate	n	Total N	(%)	Non arranged		Arranged	
					OR (95%CI)	p-Value	OR (95%CI)	p-Value
Diabetes Mellitus	Yes	9	35	(25.7)	0.40 (0.15, 1.03)	0.06	0.34 (0.09, 1.10)	---
	no	20	43	(46.5)				
Intubation during hospitalization	Yes	16	54	(29.6)	0.40 (0.14, 1.03)	0.058	0.39 (0.11, 1.31)	0.13
	no	13	25	(52.0)				
a: age estimates in 10-year increments; b: body mass index estimates in 10 kg/m <sup>2</sup> increments.								

**Table 4: compares important demographics, comorbidities, vital signs, laboratory data, and x-ray findings between patients who successfully weaned off high-flow nasal cannula and those who failed and needed intubation. Data are usually presented as mean [SD], n [%], or median [interquartile range].**

Demographic information, body mass index and HFNC duration Subject, n (%)	% HFNC Success	% HFNC Failure	p
patient	(20.4) 35	(70.2) 80	
Age, y	60 ± 22	65 ± 15	0.23
Gender (female) n (%)	(40)10	(39) 45	0.4
Race, non-White, n (%)	(48)15	51)62	0.99
Ethnicity non-Hispanic, n (%)	(64)20	(60)73	0.76
Body mass index, kg/m <sup>2</sup>	28.6 (24.4–36.2)	30.7 (27.2–35.4)	0.45
HFNC duration, hours	69.6 (29.7–102)	13(4–29)	<0.01

**Table 4(a): Comorbidities**

Comorbidities	% HFNC Success	% HFNC Failure	p
No comorbid disease, n (%)	(20)6	6 (5)	<0.01
Asthma, n (%)	(20)6	23 (20)	0.98
COPD, n (%)	(17)5	14 (12)	0.52
Active cancer, n (%)	(20)6	20 (17)	0.74
HFrEF, n (%)	(7)2	10 (9)	0.71
Coronary artery disease, n (%)	(13)4	26 (23)	0.25

**Table 4(b): Vital signs and x-ray findings and Laboratory values**

Laboratory	HFNC rate		p	Signs and findings	HFNC rate		p
	% HFNC Success	% HFNC Failure			% HFNC Success	% HFNC Failure	
Hypertension, n (%)	(63) 19	94 (80)	0.06	Oxygen saturation,	93.7 (92–96)	93 (90–96)	0.78
Diabetes mellitus, n (%)	(27) 11	62 (53)	0.01	Respiratory rate, breaths/min	26.6 (22.6–31)	32 32 (26–38)	<0.01
Chronic kidney disease, n (%)	(17) 6	30 (26)	0.52	FiO <sub>2</sub> before HFNC (%)	89 (44–95)	85 (70–95)	0.02
Creatinine	0.88 (0.76–1)	2 (0.89–2.04)	<0.01	Heart rate, beats/min	84 ± 15	88 ± 25	0.29
Urea	23 (15–28)	20 (15–36)	0.19	Mean arterial pressure, mmHg	85 (82–102)	88 (81–98)	0.83
White blood cells	8.66 (5.86–11.54)	9.64 (6.73–12.84)	0.23	SpO <sub>2</sub> /FiO <sub>2</sub>	109 (103–204.6)	99 (88–130)	0.03
Platelets	295 (198–352)	232 (176–297)	0.09	Last SpO <sub>2</sub> /FiO <sub>2</sub> during HFNC	190 (140–227)	89 (94–136)	<0.01
Bilirubin	0.5 (0.4–0.7)	0.4 (0.5–0.7)	0.07	Pulmonary x-ray severity (PXS) score, severe (%)	10(34)	35 (40)	0.84
C-reactive protein	102.6 (70.7–245.3)	141.5 (74.6–211.5)	0.64	Modified SOFA Score	3 (4–6.64)	5 (4–7)	0.359

On chest x-rays taken 48 h following HFNC treatment, the two groups had similar PXS ratings. The ROX index increased with time and was greater in the HFNC success group 2 hours after treatment (median ROX index at 2 h 4.85 [3.65–6.73] vs. failure: 3.7 [3–4.9]; p 0.01). (Table 4).

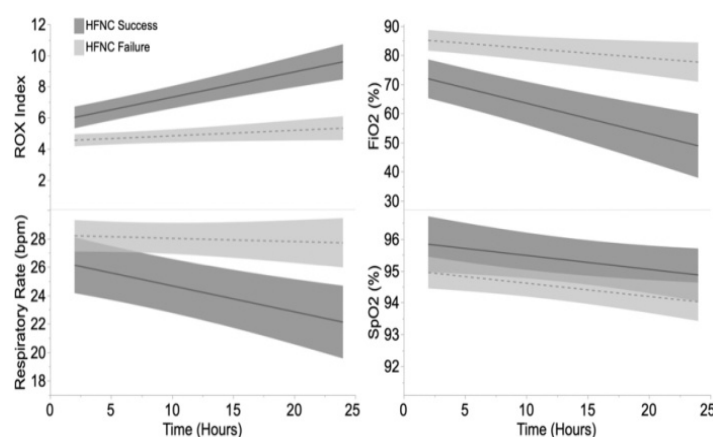


Figure 2 shows the ROX index, RR, FiO<sub>2</sub>, and SpO<sub>2</sub> under high-flow nasal cannula (HFNC) support. The continuous (HFNC success) and dotted (HFNC failure) lines show linear mixed model predictions.

Table 5: After initiating high-f low nasal cannula treatment, respiratory rate, SpO<sub>2</sub>, FiO<sub>2</sub>, and ROX index were measured at 2, 6, 12, and 24 hours. Here, data is medianed (interquartile range).

Variable	Time (h)	Success (n=30)	Failure (n=123)	p
Respiratory rate, breath/min	2	25 (22–33)	30 (23–35)	0.21
	6	25 (22–30)	27 (22–31)	0.29
	12	23 (20–25)	26 (23–31)	<0.01
	24	21 (19–28)	24 (20–31)	0.20
SpO <sub>2</sub> , %	2	96 (95–98)	96 (94–97)	0.23
	6	96 (94–98)	(92–97)	0.04
	12	95 (94–97)	(94–97)	0.77
	24	95 (94–97)	96 (93–97)	0.90
FiO <sub>2</sub> , %	2	69 (60–100)	100 (80–100)	<0.01
	6	60 (50–88)	85 (70–100)	<0.01
	12	55 (40–70)	80 (70–90)	<0.01
	24	50 (40–70)	75 (63–100)	<0.01
ROX Index	2	4.85 (3.65–6.73)	3.7 (3–4.9)	<0.01
	6	6.75 (4–7.88)	4.6 (3.3–5.65)	<0.01
	12	8.15 (5.78–10.65)	4.65 (3.78–5.95)	<0.01
	24	7.2 (6.1–10.38)	5 (3.23–6.95)	<0.01

## Discussion

In this single-center, prospective observational analysis, the technique used by our institution averted the intubation of twenty percent of the COVID-19 pneumonia and AHRF patients who were receiving HFNC. In addition, being male and having a high body mass index were risk factors for developing additional limits on daily living activities six months after being discharged from the hospital. The HFNC protocol ensured that treatment in the ICU was carried out efficiently and effectively. In the years prior to COVID-19, patients who did not react to oxygen therapy were intubated. Patients who may need invasive mechanical ventilation now have a more sophisticated respiratory alternative available to them thanks to the HFNC treatment.

Treatment with HFNC is beneficial for acute respiratory failure. The HFNC therapy, which is able to maintain a constant FiO<sub>2</sub> level, results in an increase in patient comfort as well as an

improvement in breathing and physiologic dead space [25,26]. Treatment for HFNC may eliminate the need for tracheostomy.

After six months, the survival rates of patients who had HFNC or tracheal intubation were comparable. According to these data as well, twenty percent of HFNC weaners were able to escape intubation without suffering lasting injury. This is a noteworthy addition to the field since it is the first research that has examined the long-term impact of HFNC usage on ADL independence six months after the patient has been discharged from the hospital. Long-term research on the effects of HFNC for COVID-19 pneumonia has not been conducted.

The most significant risk variables for long-term impacts at 6 months were found to be male sex and a higher BMI. After being discharged, a new restriction was more likely to manifest itself in males than in women. When males with COVID-19, the risk of severe illness and mortality is significantly increased [27].



According to the findings of our study, patients in critical care units who had a higher BMI at admission had a greater likelihood of developing a new restriction during the course of the follow-up period of six months. Patients diagnosed with COVID-19 who had a body mass index (BMI) of 30 or above were shown to have an increased risk of being hospitalized, being admitted to the intensive care unit (ICU), requiring invasive mechanical ventilation, and passing away [28].

Failures of HFNC were characterized by substantially increased respiratory rates, oxygen needs, and ROX index scores 12 and 24 hours after the start of HFNC (Table 4). The ROX index is used by bedside respiratory therapists in order to evaluate patients' levels of respiratory failure [29]. Researchers Prakash et al. who conducted a meta-analysis came to the conclusion that the ROX index score reliably forecasts HFNC failure. Within twenty-four hours, a ROX index score of five was considered to be the most successful indicator of HFNC performance. This particular meta-analysis takes into account eight separate research, totaling 1,302 participants. 4.65 was the median ROX index for HFNC failure in our study sample at 12 hours, whereas 8.15 represented HFNC success. When a patient arrives at the hospital, the ROX index may be used to determine whether or not they need substantial respiratory assistance or mechanical ventilation. Our findings suggest that other hospitals and medical centers might use our HFNC start-up procedure, which involves careful observation of the patient's vital signs as well as their ROX index.

Oxygenation levels were comparable in both survivors and non-survivors, but greater levels of respiratory system compliance were linked with an increased risk of death. The outcomes of our investigation were validated by a study using mechanical ventilation and individuals with acute respiratory distress syndrome. The respiratory disease may be predicted by the patient's respiratory compliance and their driving pressure [30]. The severity of hypoxemia may be estimated by non-survival respiratory and hemodynamic indicators including reversible vs irreversible atelectasis, cardiac output, and matching of ventilation and perfusion.

Our investigation is limited in scope. The limited applicability of our results is due to the prospective nature of our single-center analysis. Second, there was no randomization and no control group to compare the results to. Patients who have begun treatment for HFNC between September 2020 and May 2021 were eligible for eligibility. This single-center prospective trial did not involve randomization, but it did validate an HFNC procedure that reduced the number of patients who required intubation without worsening the length of stay (LOS), long-term neurological problems, or

quality of life, including activities related to work and family.

#### HFNC Patients Have More Treatment Triggers

To assess clinical HFNC therapy efficacy, one needs a standardised and quantitative procedure. Roca et al. created the ROX index as a simple bedside tool to predict HFNC therapy efficacy [31]. SaO<sub>2</sub>, FiO<sub>2</sub>, and respiratory rate comprise the ROX index. At every time point, HFNC was related with a higher ROX index score. Nevertheless, a ROX index value of 4.88 12 hours after HFNC treatment was substantially associated with therapy completion. Nevertheless, age-related respiratory rate fluctuations may make the ROX index less accurate for younger individuals [32]. The mean ROX index scores before and after treatment were not significantly different between the two groups.

Since most patients in these trials had a variety of reasons and did not have significant acute respiratory distress, few studies have examined risk factors for progression to non-invasive ventilation or intubation with mechanical ventilation. Kelly et al. defined children with higher critical illness as those who arrived to the pediatric emergency department with a triage respiratory rate greater than the 90th percentile for their age, an initial venous PCO<sub>2</sub> greater than 50 mm Hg, and a pH greater than 7.30. Acute bronchiolitis may prevent intubation after HFNC treatment [33]. Kamit et al. found that patients with a lower admission SpO<sub>2</sub>/FiO<sub>2</sub> ratio were more likely to fail HFNC. HFNC was more effective for patients with a S/F ratio of 200 or above 60 minutes into therapy [34]. Betters et al. found that increased FiO<sub>2</sub> demand, intubation, and cardiac comorbidities predicted HFNC failure [35]. In a retrospective analysis by Abboud et al. on children with viral bronchiolitis who failed HFNC (requiring intubation) and those who succeeded [36], increased respiratory rate and pCO<sub>2</sub> clearance predicted success. We found that a drop in the S/F ratio and a rise in FiO<sub>2</sub> at the onset and peak were early and probable signs of failure necessitating respiratory assistance. A lower S/F ratio indicates failure and needs more respiratory assistance. These results may help HFNC advocates decide whether to advance treatment to non-invasive ventilation or intubation with mechanical ventilation for children at high risk of failing HFNC therapy. Our results suggest that children at higher risk of failing HFNC therapy need more vigorous treatment.

#### Conclusions

According to the findings of our research, we found out that the requirement for the use of mechanical ventilation might be avoided in twenty percent of the patients who were given treatment, successfully weaned off of HFNC, and discharged from the hospital while they were still alive. This discovery was made after we discovered that the need for

mechanical ventilation might be avoided in twenty percent of the patients. This was found out when we found out that the need for mechanical ventilation may perhaps be avoided in twenty percent of the patients who were given therapy, successfully weaned off of HFNC, and released from the hospital. In spite of the fact that HFNC was shown to lower the intubation rates of COVID-19 pneumonia patients admitted to the ICU with AHRF, it is possible that any delay in intubation would have a detrimental effect on the patient's prognosis. This is because HFNC was shown to lower the intubation rates of COVID-19 pneumonia patients admitted to the ICU with AHRF. This is due to the fact that it was established that HFNC might lower the rates of intubation for COVID-19 pneumonia patients who were brought to the ICU with AHRF. It was shown that individuals with a higher body mass index (BMI) and male sex were at a greater risk for long-term functional impairment six months after being released from the hospital. [Citation needed] [Citation needed] Patients who have been treated in a hospital setting prior to participating in the research were considered for participation. The results of a second research also arrived at the same conclusion, which provided further support for the findings of the first study. The results of our study indicate that more work has to be done to enhance treatment and reduce the likelihood of unfavorable outcomes for those who are considered to be at risk.

## References

1. Laghi F, Tobin MJ. No Title. In: Principles and Practice of Mechanical Ventilation. McGraw-Hill; 2013:129–162.
2. Darreau C, Martino F, Saint-Martin M, et al. Use, timing and factors associated with tracheal intubation in septic shock: a prospective multicentric observational study. *Ann Intensive Care*. 2020;10(1):62.
3. Mascheroni D, Kolobow T, Fumagalli R, Moretti MP, Chen V, Buckhold D. Acute respiratory failure following pharmacologically induced hyperventilation: an experimental animal study. *Intensive Care Med*. 1988;15 (1):8–14.
4. Yoshida T, Uchiyama A, Matsuura N, Mashimo T, Fujino Y. The comparison of spontaneous breathing and muscle paralysis in two different severities of experimental lung injury. *Crit Care Med*. 2013;41(2):536–45.
5. Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med* 2015;372(23): 2185–96.
6. Lemiale V, Mokart D, Resche-Rigon M, Pène F, Mayaux J, Faucher E, et al. Effect of noninvasive ventilation vs oxygen therapy on mortality among immunocompromised patients with acute respiratory failure: a randomized clinical trial. *JAMA* 2015;314(16):1711–19.
7. Azoulay E, Lemiale V, Mokart D, Nseir S, Argaud L, Pène F, et al. Effect of high-flow nasal oxygen vs standard oxygen on 28-day mortality in immunocompromised patients with acute respiratory failure: the HIGH randomized clinical trial. *JAMA* 2018;320(20):2099–107.
8. Ospina-Tascón GA, Calderón-Tapia LE, García AF, Zarama V, Gómez-Álvarez F, Álvarez-Saa T, et al. Effect of high-flow oxygen therapy vs conventional oxygen therapy on invasive mechanical ventilation and clinical recovery in patients with severe COVID-19: a randomized clinical trial. *JAMA* 2021;326(21): 2161–71.
9. Grieco DL, Menga LS, Cesarano M, Rosà T, Spadaro S, Bitondo MM, et al. Effect of helmet noninvasive ventilation vs high-flow nasal oxygen on days free of respiratory support in patients with COVID-19 and moderate to severe hypoxemic respiratory failure: the HENIVOT randomized clinical trial. *JAMA* 2021;325(17):1731–43.
10. Ehrmann S, Li J, Ibarra-Estrada M, Perez Y, Pavlov I, McNicholas B, et al. Awake prone positioning for COVID-19 acute hypoxaemic respiratory failure: a randomised, controlled, multinational, open-label meta-trial. *Lancet Respir Med* 2021;9(12):1387–95.
11. Perkins GD, Ji C, Connolly BA, Couper K, Lall R, Baillie JK, et al. Effect of noninvasive respiratory strategies on intubation or mortality among patients with acute hypoxemic respiratory failure and COVID-19: the RECOVERY-RS randomized clinical trial. *JAMA* 2022; 327(6):546–58.
12. Demoule A, Chevret S, Carlucci A, Kouatchet A, Jaber S, Meziani F, et al. Changing use of noninvasive ventilation in critically ill patients: trends over 15 years in francophone countries. *Intensive Care Med* 2016;42(1):82–92.
13. Ferguson ND, Fan E, Camporota L, Antonelli M, Anzueto A, Beale R, et al. The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material. *Intensive Care Med* 2012;38(10):1573–82.
14. Gibelin A, Parrot A, Maitre B, Brun-Buisson C, Mekontso Dessap A, Far-toukh M, et al. Acute respiratory distress syndrome mimickers lacking common risk factors of the Berlin definition. *Intensive Care Med* 2016;42(2):164–72.
15. Frat JP, Ragot S, Coudroy R, Constantin JM, Girault C, Prat G, et al. Predictors of intubation in patients with acute hypoxemic respiratory failure treated with a noninvasive oxygenation strategy. *Crit Care Med* 2018;46(2):208–15.
16. Antonelli M, Conti G, Moro ML, Esquinas A, Gonzalez-Diaz G, Confalonieri M, et al. Predictors of failure of noninvasive positive pressure ventilation in patients with acute hypoxemic

- respiratory failure: a multi-center study. *Intensive Care Med* 2001;27(11):1718–28.
17. Bellani G, Laffey JG, Pham T, Madotto F, Fan E, Brochard L, et al. Noninvasive ventilation of patients with acute respiratory distress syndrome. Insights from the LUNG SAFE study. *Am J Respir Crit Care Med* 2017;195(1):67–77.
  18. Coudroy R, Frat JP, Boissier F, Contou D, Robert R, Thille AW. Early identification of acute respiratory distress syndrome in the absence of positive pressure ventilation: implications for revision of the Berlin criteria for acute respiratory distress syndrome. *Crit Care Med* 2018;46(4):540–6.
  19. Coudroy R, Frat JP, Girault C, Thille AW. Reliability of methods to estimate the fraction of inspired oxygen in patients with acute respiratory failure breathing through non-rebreather reservoir bag oxygen mask. *Thorax* 2020;75(9):805–7.
  20. Rice TW, Wheeler AP, Bernard GR, Hayden DL, Schoenfeld DA, Ware LB, et al. Comparison of the SpO<sub>2</sub>/FIO<sub>2</sub> ratio and the PaO<sub>2</sub>/FIO<sub>2</sub> ratio in patients with acute lung injury or ARDS. *Chest* 2007;132(2):410–17.
  21. Dreyfuss D, Saumon G. Role of tidal volume, FRC, and end-inspiratory volume in the development of pulmonary edema following mechanical ventilation. *Am Rev Respir Dis* 1993;148(5):
  22. Grasselli G, Pesenti A, Cecconi M. Critical care utilization for the COVID19 outbreak in Lombardy, Italy. *JAMA*. 2020;323(16):1545.
  23. Babcock CI, Franco R, Bunting L, et al. Co-Ventilating Patients During a Critical Ventilator Shortage: A Method for Implementation From the Washington DC COVID-19 Co-Ventilation Task Force.
  24. Ferrando C, Mellado-Artigas R, Gea A, et al. Patient characteristics, clinical course and factors associated to ICU mortality in critically ill patients infected with SARS-CoV-2 in Spain: A prospective, cohort, multicentre study. *Rev Esp Anestesiol Reanim*. 2020.
  25. Agarwal A, Basmaji J, Muttalib F, et al. High-flow nasal cannula for acute hypoxemic respiratory failure in patients with COVID-19: systematic reviews of effectiveness and its risks of aerosolization, dispersion, and infection transmission. *Can J Anesth*. 2020;67(9):1217–48.
  26. Sudre, C.H.; Murray, B.; Varsavsky, T.; Graham, M.S.; Penfold, R.S.; Bowyer, R.C.; Pujol, J.C.; Klaser, K.; Antonelli, M.; Canas, L.S.; et al. Attributes and predictors of long COVID. *Nat. Med*. 2021, 27, 626–631.
  27. Roca, O.; Riera, J.; Torres, F.; Masclans, J.R. High-flow oxygen therapy in acute respiratory failure. *Respir. Care* 2010, 55, 408–413.
  28. Dysart, K.; Miller, T.L.; Wolfson, M.R.; Shaffer, T.H. Research in high flow therapy: Mechanisms of action. *Respir Med*. 2009, 103, 1400–1405.
  29. Booth, A.; Reed, A.B.; Ponzo, S.; Yassaee, A.; Aral, M.; Plans, D.; Labrique, A.; Mohan, D. Population risk factors for severe disease and mortality in COVID-19: A global systematic review and meta-analysis. *PLoS ONE* 2021, 16, e0247461.
  30. Kompaniyets, L.; Goodman, A.B.; Belay, B.; Freedman, D.S.; Sucusky, M.S.; Lange, S.J.; Gundlapalli, A.V.; Boehmer, T.K.; Blanck,
  31. H.M. Body Mass Index and Risk for COVID-19-Related Hospitalization, Intensive Care Unit Admission, Invasive Mechanical
  32. Ventilation, and Death-United States, March-December 2020. *MMWR Morb. Mortal. Wkly. Rep*. 2021, 70, 355–361.
  33. Chandel, A.; Patolia, S.; Brown, A.W.; Collins, A.C.; Sahjwani, D.; Khangoora, V.; Cameron, P.C.; Desai, M.; Kasarabada, A.; Kilcullen, J.K.; et al. High-Flow Nasal Cannula Therapy in COVID-19: Using the ROX Index to Predict Success. *Respir. Care* 2021, 66, 909–919.
  34. Prakash, J.; Bhattacharya, P.K.; Yadav, A.K.; Kumar, A.; Tudu, L.C.; Prasad, K. ROX index as a good predictor of high flow nasal cannula failure in COVID-19 patients with acute hypoxemic respiratory failure: A systematic review and meta-analysis. *J. Crit. Care* 2021, 66, 102–108.
  35. Amato, M.B.P.; Meade, M.O.; Slutsky, A.S.; Brochard, L.; Costa, E.L.V.; Schoenfeld, D.A.; Stewart, T.E.; Briel, M.; Talmor, D.S.; Mercat, A.; et al. Driving pressure and survival in the acute respiratory distress syndrome. *N. Engl. J. Med*. 2015, 372, 747–755.
  36. VanderWeele TJ, Hernán MA, Robins JM. Causal directed acyclic graphs and the direction of unmeasured confounding bias. *Epidemiology*. 2008;19(5):720–8.
  37. Sterne JAC, White IR, Carlin JB, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ*. 2009;338: b2393.
  38. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med*. 2009;28(25):3083–107.
  39. Marini JJ, Gattinoni L. Management of COVID-19 Respiratory Distress. *JAMA - J Am Med Assoc*. 2020;323(22):2329–30.
  40. Tobin MJ, Laghi F, Jubran A. Caution about early intubation and mechanical ventilation in COVID-19. *Ann Intensive Care*. 2020; 10(1): 78.
  41. Rola P, Farkas J, Spiegel R, et al. Rethinking the early intubation paradigm of COVID-19: Time to change gears? *Clin Exp Emerg Med*. 2020;7(2):78–80.

42. Demoule A, Vieillard Baron A, Darmon M, et al. High Flow Nasal Canula in Critically Ill Severe COVID-19 Patients. Am J Respir Crit Care Med. Published online August 6, 2020.

43. Demoule A, Vieillard Baron A, Darmon M, et al. High Flow Nasal Canula in Critically Ill Severe COVID-19 Patients. Am J Respir Crit Care Med. Published online August 6, 2020; rccm.202005–2007LE.