Acute heart failure (AHF) is a life-threatening condition. The majority of patients come to the emergency room (ER) with pulmonary congestion and respiratory failure. Therefore, oxygen therapy is an essential modality in AHF apart from diuretics and improving hemodynamic. Non-invasive ventilation (NIV) is often required to reduce hypercapnia, acidosis, and respiratory rate in AHF. However, it is more invasive than conventional oxygen therapy. NIV is also less comfortable for patients and has limited use in the ER. The high-flow nasal oxygen (HFNO) is increasing in popularity during the COVID-19 pandemic. HFNO can deliver high flow oxygen with a constant fraction in patients with respiratory failure. Studies have reported the benefits of HFNO in acute heart failure. Therefore, HFNO may benefit and may be used as an alternative to acute heart failure patients who cannot tolerate NIV.

**Keywords:** Acute heart failure, High-flow nasal oxygen, Non-invasive ventilator, Oxygen therapy

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**INTRODUCTION**

Acute heart failure is the leading cause of patient morbidity and mortality. Shortness of breath is a cardinal symptom most often found in acute heart failure patients admitted to hospital. Cardiogenic pulmonary edema is a severe complication of acute heart failure and is the second most common cause of respiratory failure after pneumonia. Initial therapy for acute heart failure includes diuretics, vasodilators, and oxygen supplementation with a non-invasive ventilator (NIV) or mechanical ventilator. In patients with respiratory failure, conventional oxygen therapy is often ineffective. It is necessary to use continuous airway positive pressure (CPAP) or non-invasive positive pressure ventilation (NIPPV) to reduce hypercapnia, acidosis, and respiratory rate. This therapy can reduce the endotracheal intubation rate and the need for a ventilator, but it is more invasive than conventional oxygen therapy, is less comfortable for patients, and has limited use in the ER.

In recent years high-flow nasal oxygen (HFNO) has been safe and valuable in various clinical conditions. The popularity of HFNO is reaching its peak amid the COVID-19 pandemic, where there is an increasing need for ICUs and ventilators globally. HFNO is increasingly being used to prevent acute hypoxic respiratory failure patients from falling on a ventilator. HFNO is a less invasive oxygen therapy than NIPPV. HFNO can flow up to 60 liters of air per minute and is closer to the inspiratory flow requirements of respiratory failure patients than conventional oxygen therapy, which only flows a maximum of 15 liters per minute. HFNO also has various physiological benefits compared to conventional oxygen therapy.

There are no international guidelines that recommend HFNO as the first choice for cardiogenic pulmonary edema. However, studies on its benefits have been reported. This literature review was created to inform physicians about the benefits of HFNO therapy in patients with acute heart failure.

**Etiology of Acute Heart Failure:** About two-thirds of patients with acute heart failure have previously been diagnosed as chronic heart failure patients. On initial arrival in the ER, the patient showed worsening heart function. Myocardial ischemia, atrial fibrillation (AF), hypertension, infection, poor medication adherence, and excessive salt or alcohol consumption are all things that can cause acute worsening of chronic heart failure. In addition, about 50% of cases are associated with a decreased left ventricular ejection fraction. Cases associated with normal ejection fraction include patients with rapid AF or valve disease. Various etiologies and risk factors for acute heart failure are presented in Table 1 and Table 2.

**Table 1. Etiology and risk factors for acute heart failure.**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Population</th>
<th>Population characteristic</th>
<th>The main cause</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Fonarow et al., 2008)³</td>
<td>48.612</td>
<td>- Mean age 73 years</td>
<td>Multiple</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Percentage of women 52%</td>
<td>Infection of airway</td>
<td>12</td>
</tr>
</tbody>
</table>
Pathophysiology of Acute Heart Failure: Various cardiovascular or non-cardiovascular conditions result in acute heart failure through a single or a combination of pathogenesis mechanisms. The main sign of acute heart failure is congestion. Congestion is characterized by weight gain, peripheral edema, jugular vein distension, liver enlargement, hepatojugular reflux or ascites, and pulmonary congestion, characterized by shortness of breath and rhonchi. The two main mechanisms that cause congestion are fluid retention and fluid redistribution. In fluid retention, cardiac dysfunction causes a decrease in cardiac output (CO). Conversely, neurohormonal compensatory mechanisms will cause the release of aldosterone and vasopressin-arginine. The mechanism results in sodium and fluid retention in the kidneys. As a result, it causes congestion in the lungs and peripheral blood vessels. On the other hand, fluid redistribution occurs due to venous vasoconstriction. Venous vasoconstriction causes increased venous return and preload, whereas arterial constriction increases afterload. Both make left ventricular pressure increase, pulmonary capillary pressure increase, and pulmonary congestion occurs.

In the presence of cardiac dysfunction, several neurohormonal pathways, including the sympathetic nervous system, the renin-angiotensin-aldosterone system, and the arginine-vasopressin system, are activated to counteract the effects of heart failure to deliver oxygen to the periphery. Neurohormonal activation causes impaired sodium regulation and fluid accumulation. Tissue edema results from transudation from capillaries to interstitials due to excess drainage capacity of the lymphatic system.

Management of Acute Heart Failure: The initial management of acute heart failure should consist of 3 parts: triage, diagnosis, and initial therapy. Because acute heart failure is a life-threatening condition, current guidelines for managing acute heart failure recommend that initial diagnosis and therapy be carried out as soon as possible, especially 30-60 minutes from when the patient arrives at the hospital. Acute heart failure is a life-threatening pharmacological condition, so the process of diagnosing and administering pharmacological and non-pharmacological management must be carried out simultaneously and as early as possible. Patients with acute heart failure accompanied by hemodynamic disturbances (cardiogenic shock) or respiratory failure should receive circulatory support management and ventilatory assistance. The leading cause or precipitate causes the patient to fall in a condition of acute heart failure and administration of treatment according to that cause to prevent further deterioration.

Recommended Oxygen Therapy in Acute Heart Failure: In managing acute heart failure, apart from making the patient euvolemic with nitrates and loop diuretics, oxygen therapy is also an essential component in its management, especially in patients with hypoxemic respiratory failure. Oxygen can be given from conventional methods such as nasal oxygen, simple masks, non-rebreathing masks to NIV via CPAP or BiPAP, depending on the degree of severity. Oxygenation is given to patients with hypoxaemic conditions or respiratory distress with peripheral oxygen saturation (SpO2) of less than 90% or a partial arterial oxygen pressure (PaO2) of less than 60 mmHg (< 8.0 kPa). It is recommended to start...
oxygen therapy with a fraction of 40-60% and titrated until a \( \text{SpO}_2 \) reached above 90%, but caution should be exercised in patients with \( \text{CO}_2 \) retention.\(^{10}\)

Oxygen therapy can be given conventionally, but positive pressure ventilation (CPAP/BiPAP) can be given if hypoxemia still occurs. If the positive pressure ventilation does not improve, then transfer to the ICU for ventilator installation. A high dose of oxygen is recommended in patients with saturation below 90% and a \( \text{PaO}_2 \) below 60 mmHg.\(^{10}\) Giving oxygen therapy to patients with heart failure without hypoxemia should not be routinely given because it can cause hyperoxemia conditions.\(^{14}\) In patients with acute pulmonary edema, the use of NIV can improve respiratory distress, shortness of breath, respiratory rate, and acidosis. Despite the many benefits of NIV, its use is often inconvenient for patients, causing necrosis and thickening of the facial skin, conjunctivitis due to air leaking into the eyes, and the risk of aspiration in patients who vomit while using NIV. When compared with HFNO, the NIV had more facial skin damage and erythema.\(^{13}\)

**High-Flow Nasal Oxygen Therapy:** Traditionally, nasal oxygen therapy was delivered at a low flow rate through nasal oxygen. However, new nasal oxygen has emerged in recent years to deliver high-flow, moisturized oxygen to patients. The device is high-flow nasal oxygen (HFNO). HFNO can deliver oxygen at flow rates of up to 60 liters per minute. This device consists of oxygen connected to a humidifier and delivered through particular nasal oxygen. HFNO was initially used for preterm neonates and pediatric patients, but now HFNO has become one of the first-line therapies for patients with acute respiratory distress.\(^{15}\)

In the era of the COVID-19 pandemic, the popularity of HFNO is increasing. HFNO becomes a hypoxemia therapy amidst the limitations of ICUs and ventilators.\(^{16}\) The primary clinical manifestation of severe COVID-19 patients is hypoxemia accompanied by heavy breathing. Although NIV is known to have advantages in the presence of PEEP in patients with hypercapnia such as COPD, its efficiency is still low to reduce heavy breathing in severe COVID-19 patients. This occurs because the patient requires high inspiratory pressure, which causes air leakage in the NIV mask. The increased respiratory drive has also occurred in COVID-19 patients, requiring high airflow to meet the patient's respiratory needs.\(^{17}\) The survival sepsis campaign guidelines (SSC) recommend HFNO as a better therapy than conventional oxygen in hypoxemia COVID-19 patients.\(^{18}\)

**Physiological Effects of High-Flow Nasal Oxygen Therapy:** Various effects and advantages of HFNO have been reported. HFNO is more comfortable and tolerable to patients. Administration of conventional oxygen therapy delivers oxygen that is not humidified, drying the upper airway, affecting mucociliary clearance, creating atelectasis, and reducing patient comfort. In HFNO, the air has been pre-warmed so that it generally makes the patient comfortable, reduces tightness, and does not make the upper airway dry.\(^{15}\)

The peak inspiratory flow in patients with acute respiratory failure averages 30-40 liters per minute and can exceed 60 liters per minute in patients with severe sepsis. This airflow requirement is higher than standard oxygen therapy flow. Standard oxygen in patients with severe acute respiratory failure will cause the inhaled airflow to mix with room air so that the inhaled oxygen fraction will not reach 70%. In NIV, the oxygen fraction given can reach 100% if there is no air leak. However, the increase in airflow, higher in NIV, can cause leakage in face masks. HFNO can deliver high fraction oxygen and high flow rates of up to 60 liters per minute. It will meet the peak inspiratory flow requirements in respiratory failure patients.\(^{19}\) HFNO provides a constant high airflow so that there is no gas dilution, decreasing the oxygen fraction. The oxygen fraction in HFNO can also be adjusted from 21% to 100%.\(^{2}\)

Patients with acute respiratory distress usually have increased mucus secretion and require extra effort to spit it out. The efforts made by the patient will cause fatigue of the respiratory muscles, especially if the mucus is thick and cannot be coughed up. This is often seen in patients with NIV.\(^{15}\) In the provision of standard oxygen and NIV that flowed is dry and cold air. This air can cause mucociliary disorders, inflammation, and mucus retention.\(^{13}\) The water content of the mucus will affect the thickness of the sputum. Physiological humidification is essential in providing good respiratory epithelial function through sodium absorption and chloride secretion. Inspiratory air warmed to a temperature of 37°C Celsius promotes adequate mucosal function and improves mucus secretion. HFNO is an oxygen therapy device that provides warmed air. Some tools have user-adjustable temperature settings.\(^{15}\)

HFNO can also reduce the metabolic cost of breathing. Metabolic cost is the energy the body needs to warm the incoming air when breathing. The air will be warmed by the body to prevent bronchoconstriction due to cold effects, especially in tachypnoea and acute respiratory failure patients. HFNO will reduce
breathing and metabolic cost because the circulated air has been warmed by the tool.15

HFNO is an open system, while NIV is a closed system.2 HFNO can exert positive pressure on the upper airway, but the pressure varies (the pressure is higher when the mouth is closed). When the mouth is closed, the HFNO will provide an inspiratory pressure of 3 cm H2O, whereas if the mouth is open, it is less than 2 cm H2O at a flow of 60 liters per minute.19 This will increase the washout of the nasopharyngeal dead space. The ability to remove CO2 in the upper airway is an excess of HFNO due to high airflow. Various studies have shown HFNO to have the same PEEP effect as nasal CPAP.15 However, clinical studies show that the lower effect of PEEP HFNO only increases PaO2 without changing the PaO2/FiO2 ratio, whereas NIV increases both. This is because the presence of PEEP increases alveolar recruitment, which increases the PaO2/FiO2 ratio.19 PEEP causes the fluid in the alveoli to be pushed to the perivascular so that the surface of the alveoli can diffuse oxygen more.2

Use of the High-Flow Nasal Oxygen: Clinical practical guidelines issued by the European Society of Intensive Care Medicine state that administering HFNO in hypoxemic respiratory failure is a strong recommendation.5

HFNO therapy has many benefits, but doctors must remain vigilant about patient responses such as

Table 3. Comparison of HFNO and NIV in acute heart failure patients.13

<table>
<thead>
<tr>
<th>Advantage</th>
<th>HFNO</th>
<th>NIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>(I) The patient is more comfortable and can tolerate</td>
<td>(I) Can provide high PEEP</td>
<td>(II) Provide bilevel ventilation for type 2 respiratory failure patients</td>
</tr>
<tr>
<td>(II) There is no distraction when the patient eats and drinks</td>
<td>(III) Avoiding complications related to intubation</td>
<td>(IV) There is already much evidence on its use in acute heart failure</td>
</tr>
<tr>
<td>(III) Avoiding complications related to intubation</td>
<td>(IV) Easy to use and monitor</td>
<td></td>
</tr>
<tr>
<td>(V) Lowering metabolic costs</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Disadvantage                         |                                                                      |                                                                      |
|--------------------------------------|                                                                      |                                                                      |
| (I) Little evidence of benefit when high PEEP is required |                                                                      |                                                                      |
| (II) Useful only in type 1 respiratory failure, evidence is limited to type 2 respiratory failure |                                                                      |                                                                      |
| (III) Studies on acute heart failure are few |                                                                      |                                                                      |
| (II) The patient is uncomfortable |                                                                      |                                                                      |
| (III) Complications on the face such as erythema, skin necrosis, and risk of aspiration if the patient vomits |                                                                      |                                                                      |
| (IV) Patient non-compliance leads to treatment failure |                                                                      |                                                                      |

HFNO therapy can reduce shortness of breath in patients with acute heart failure. An RCT by Makdee et al. in 128 patients with cardiogenic pulmonary edema showed HFNO significantly decreased respiratory rate, decreased breathlessness.22 The study by Carratala et al. on HFNO saw significant improvements in comfort, oxygenation index, and respiratory rate at 1, 2, and 24 versus conventional oxygen (p <0.05).21

HFNO therapy improves the hemodynamics of patients with acute heart failure. The effect that CPAP has on HFNO can alter the hemodynamics of patients with heart failure. A study by Roca et al. on ten heart failure patients with NYHA class III administration of HFNO with flow rates of 20 L/min and 40 L/min showed that the inferior vena cava collapse index was lower than baseline 20% and 53%. The hemodynamic status increases due to intrathoracic pressure and
decreases cardiac preload. HFNO decreases ventricular afterload and improves hemodynamic status.21

A study conducted by Kang et al. In acute heart failure patients receiving HFNO or intubation as initial therapy after clinical deterioration showed similar results in increased oxygen saturation and clinical outcome. So maybe HFNO can be given as initial oxygen therapy in acute heart failure.22

Patients with severe cardiogenic pulmonary edema are frequently associated with hypercapnia. Hypercapnia causes decreased consciousness and central apnea and increase the patient's intubation rate.23 NIV is known to have advantages in treating hypercapnia in patients.17 A study conducted by Marjanovic et al. compared hypercapnia in cardiogenic pulmonary edema patients receiving HFNO and NIV. Baseline reduction in PaCO$_2$ was measured in the first 1 hour, wherein HFNO patients decreased 7 mmHg while in NIV 3 mm Hg. There were no differences in respiratory rate, pH, and breathwork between the two groups.23 Of all the clinical benefits, HFNO may be provided as an alternative to heart failure patients who cannot tolerate NIV.24

The management of heart failure involves reducing preload and afterload to decrease pulmonary congestion. The physiological effect of NIV to help to reduce preload and afterload in decompensated heart failure is also mentioned in HFNO usage. In the presence of heart failure, increased work of breathing is poorly tolerated. Negative intrathoracic pressure increases systemic ventricular afterload, while increased diaphragmatic oxygen consumption reduces oxygen delivery. HFNO helps to decrease afterload by providing positive pressure and abating sympathetic nervous system activity by improving respiratory work. HFNO also decreases pulmonary vascular resistance (PVR) by restoring functional residual capacity (FRC) and improving alveolar oxygen tension in patients with pulmonary edema.25 In the study of Roca et al.,2 HFNO could reduce respiratory rate and decrease inspiratory collapse of the inferior vena cava. The right atrium is a surrogate for right ventricular preload. It can be estimated from inferior vena cava collapsibility. The decrease in inspiratory collapse indicated a reduction in right ventricular preload.13

Table 4. Study on HFNO in cardiogenic pulmonary edema

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Experiment</th>
<th>Control</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Ko et al., 2020)$^7$</td>
<td>Patients suspended for pulmonary edema due to heart failure</td>
<td>HFNO (n=36)</td>
<td>Conventional oxygen therapy (n=33)</td>
<td>Significant differences in breath rate, SpO$_2$ at 30 and 60 minutes. The differences were significant in PaO$_2$ and SpO$_2$ at 30 and 60 minutes</td>
</tr>
<tr>
<td>(Makdee et al., 2017)$^{26}$</td>
<td>ER patients with cardiogenic pulmonary edema</td>
<td>HFNO (n=63)</td>
<td>Conventional oxygen therapy (n=65)</td>
<td>Respiration rates decreased in the HFNO group at 15, 30, and 60 minutes</td>
</tr>
<tr>
<td>(Sener et al., 2020)$^{27}$</td>
<td>Patients with hypertensive pulmonary edema</td>
<td>HFNO (n=62)</td>
<td>Conventional oxygen therapy (n=50)</td>
<td>HFNO shortens the length of stay in the ER and ICU. Increased heart rate, respiratory rate, and BGA</td>
</tr>
<tr>
<td>(Chang et al., 2020)$^{28}$</td>
<td>Post-extubation heart failure patients with ejection fraction &lt;50%</td>
<td>HFNO (n=58)</td>
<td>NIPPV (n=46)</td>
<td>There was no difference in treatment failure in the two groups</td>
</tr>
<tr>
<td>(Roca et al., 2016)$^4$</td>
<td>NYHA III heart failure patients and ejection fraction &lt;45%</td>
<td>HFNO (n=10)</td>
<td>None</td>
<td>HFNO is associated with the decreased inspiratory collapse of the inferior vena cava and decreased respiratory rate</td>
</tr>
<tr>
<td>(Carratala et al., 2011)$^{20}$</td>
<td>Patients with acute heart failure were treated early on NIV and had refractory hypoxemia</td>
<td>HFNO (n=5)</td>
<td>None</td>
<td>The use of HFNO for 24 hours showed an increase in PaO$_2$, a degree of severity, and a decrease in respiratory rate</td>
</tr>
</tbody>
</table>

CONCLUSION

HFNO is oxygen therapy superior to conventional oxygen therapy and has many benefits in respiratory failure. HFNO can deliver high doses of oxygen up to a maximum of 60 liters per minute with a constant oxygen fraction between 21-100%. Compared with NIV, the use of HFNO is more comfortable for the patient and well-tolerated. HFNO is beneficial in patients with acute heart failure with hypoxemia because of its ease of use, physiological benefits, and good tolerance levels. Therefore, HFNO may benefit and be used as an alternative to acute heart failure patients who cannot tolerate NIV.
AUTHORS’ CONTRIBUTION
NPN, RJ, and SPH: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work.

Conflict of interest: Authors declared no conflict of interest.

REFERENCES

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