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Modern Approach to the Treatment of Acute Respiratory Failure – from nasal cannula to ECMO

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ABSTRACT

Introduction

Respiratory failure is a major healthcare issue, significantly threatening patient life. Early diagnosis and appropriate oxygen therapy are critical for improving prognosis. This article aims to summarize and compare current oxygen therapy methods and their clinical indications.

Material and Methods
Oxygen therapy methods were discussed in the context of acute respiratory failure in the emergency department. The therapies reviewed included conventional oxygen therapy (COT), high-flow nasal oxygen therapy (HFNOT), noninvasive ventilation (NIV), invasive ventilation, and extracorporeal membrane oxygenation (ECMO). Indications were based on the latest guidelines from the European Respiratory Society, American Thoracic Society, and other medical organizations.
Results
High-flow nasal oxygen therapy (HFNOT) is superior to conventional oxygen therapy in treating acute hypoxemic respiratory failure, reducing the need for therapy escalation. Noninvasive ventilation (NIV) is effective for patients with respiratory acidosis and COPD exacerbations. ECMO is a life-saving option when other treatments fail, but its use is limited to patients with reversible causes of respiratory failure.
Conclusions
The choice of oxygen therapy depends on the patient's clinical condition. Modern approaches, such as HFNOT and NIV, offer advantages in reducing mortality and the need for invasive ventilation in acute respiratory failure, compared to traditional therapies. ECMO remains effective in severe cases but is reserved for specific indications. Further research is needed to optimize oxygen therapy use, focusing on reducing mortality and complications.

Keywords: Respiratory failure; Non-invasive ventilation NIV; Intubation; Extracorporeal membrane oxygenation

Introduction

Respiratory failure is a significant challenge for the Polish healthcare system. The number of hospitalizations due to respiratory failure in Poland in 2023 was 19,468, with emergency admissions accounting for 77.88% (n=11,814) [1]. Modern medical technologies offer a wide range of solutions and therapeutic possibilities that can be successfully utilized in the treatment of acute respiratory failure. These include passive oxygen therapy methods such as nasal cannulas and face masks with or without a reservoir, high-flow nasal oxygen therapy, non-invasive positive pressure ventilation, invasive ventilation and continuous extracorporeal blood oxygenation.

In the context of an Emergency Department (ED), the rapid establishment of a correct diagnosis and the planning of subsequent actions are crucial for the appropriate management of the patient. The proper selection of oxygen therapy methods and their parameters, taking into account the overall clinical picture of the patient, contributes to a reduction in mortality and complications.

The aim of this article is to present and compare the currently available methods of oxygen therapy in the treatment of acute respiratory failure, along with the associated guidelines from scientific societies. The techniques for applying individual methods, as well as recommendations regarding the setting of parameters and the selection of appropriate equipment are beyond the scope of this publication.

Respiratory failure

Respiratory failure is defined as the impairment of oxygenation (the ability to extract oxygen from the atmospheric air) and ventilation (the ability to remove carbon dioxide from the blood). The commonly accepted threshold values for the diagnosis of hypoxemia and hypercapnia, and consequently respiratory failure, are $PaO_2 < 60$ mmHg and $PaCO_2 > 45$ mmHg in arterial blood. Based on these parameters, respiratory failure is classified into hypoxemic (partial, type 1) and hypoxemic-hypercapnic (total, type 2) types. The tables present the causes of acute respiratory failure (Table 1) [2] and its clinical symptoms (Table 2) [3].

Hypoxemic respiratory failure	Hypoxemic-hypercapnic respiratory failure
• **Mismatch between alveolar ventilation and pulmonary blood flow (V/Q)** • **Impaired alveolar-capillary diffusion** • **Shunt of deoxygenated blood** • **Decreased partial pressure of oxygen in the alveoli** • **Alveolar hypoventilation**	• **Alveolar hypoventilation** • **Increased dead space** • **Increased CO_2 production** • **Decreased tidal volume**

Table 1. Causes of acute respiratory failure

Symptoms of impaired blood oxygenation	Peripheral cyanosis, headache, asterixis, sweating, skin vasodilation, hypertension, drowsiness, confusion, disorientation, altered consciousness, coma, circulatory failure (tachycardia, hypotension)
Symptoms of respiratory effort	Tachypnea > 25/min, use of accessory respiratory muscles, intercostal retractions, abdominal muscle involvement, difficulty speaking
Symptoms of exhaustion	Bradypnea < 12/min, paradoxical breathing

Table 2. Symptoms of acute respiratory failure

The guidelines of the European Society of Anaesthesiology (ESA) [4] , taking into account the circumstances of intensive care units, propose the diagnostic criteria for hypoxemia as oxygenation index (Horowitz index) $PaO_2/FiO_2 < 300$ mmHg, which may be particularly useful in patients receiving oxygen therapy with a precisely defined oxygen concentration in the inhaled gas mixture.

In monitoring the severity of acute respiratory distress syndrome (ARDS), an alternative to the oxygenation index worth considering is the SpO_2/ FiO_2 ratio, with values of 315 and 235 corresponding to PaO_2/ FiO_2 values of 300 and 200 respectively [5].

Indications for the use of explicit oxygen therapy methods, including substitute breathing or extracorporeal blood oxygenation, are outlined below in the sections of the article dedicated to each individual solution. The general indication for initiating oxygen therapy is the finding of hypoxemia.

Oxygenation target is a subject of debate, and the results of various studies comparing mortality rates across different ranges of SpO_2 and PaO_2 values do not provide conclusive outcomes. Zhao et al. [6] in their meta-analysis suggest that both PaO_2 levels ranging from 55-70 mmHg and >150 mmHg increase mortality, recommending a safe target range for PaO_2 of 70-150 mmHg and SpO_2 of 94-98%. However, the article emphasizes the need for further research in this area. In patients with chronic hypercapnia, primarily due to chronic obstructive pulmonary disease (COPD), SpO_2 values in the range of 88-92% are considered safe [7].

Conventional oxygen therapy

Conventional oxygen therapy (COT) methods allow for oxygen flow up to 15 L/min, primarily through nasal cannulas and various types of face masks. Their advantages include low cost, ease of use, and high availability. However, they are characterized by unstable oxygen concentration in therapy for patients with high inspiratory flow demand. The main indication for their use is the diagnosis of hypoxemia. The flow ranges of O2 and the achievable FiO_2 for these methods are as follows [3]:

- **Nasal cannulas: 0.5-5 L/min, FiO_2 24-40%**
- **Simple face mask: 5-8 L/min, FiO_2 40-60%**
- **Reservoir mask: 8-15 L/min, FiO_2 40-90%**

High-flow nasal oxygen therapy

High-flow nasal oxygen therapy (HFNOT) is a method that utilizes a device capable of achieving respiratory gas flow rates of 10-70 L/min and FiO_2 of 21-100% through precisely designed nasal cannulas, tailored to the anatomy and gas flow dynamics.

In addition to the increased oxygen delivery provided by this method, studies on its use have identified several physiological mechanisms that enhance its effectiveness [8–12]:

- **The effect of CO_2 washout from the airways, particularly noticeable in patients with COPD**
- **Generation of positive pressure and reduction of resistance in the upper airways, thereby decreasing airway resistance and respiratory effort [13,14]**
- **Reduction of physiological microatelectasis, which is an additional factor improving oxygenation[9–11]**
- **Conditioning of inhaled gases by controlling their temperature and humidity. This approach supports the function of the airway epithelium related to airway cleaning and ciliary transport, as well as reducing airway resistance [15–17]. There are also reports suggesting that the ability to adjust these parameters contributes to the effectiveness of this therapy and enables its long-term and safe use [15]**
- **Maintenance of a constant FiO_2. Conventional oxygen therapy methods allow for a maximum oxygen flow of 15 L/min. In patients with high inspiratory flow demand, this limitation causes an increased amount of ambient air to be drawn into the inhaled gas mixture, resulting in a decrease in effective FiO_2. High gas flow in HFNOT ensures the stabilization of O_2 concentration in the mixture**

Indications for the use of HFNOT in acute respiratory failure

In 2022, the European Respiratory Society (ERS) published guidelines for the use of high-flow nasal oxygen therapy (HFNOT) in patients with acute respiratory failure [18]. The task force responsible for developing these guidelines used the GRADE method (Grading of Recommendations, Assessment, Development, and Evaluation) to assess the available clinical data and provided the following recommendations.

Moderate quality of evidence, conditional recommendation:

- **HFNOT over COT in acute hypoxemic respiratory failure**

Low quality of evidence, conditional recommendation:

- **HFNOT over NIV in acute hypoxemic respiratory failure**
- **HFNOT over COT during breaks from NIV in acute hypoxemic respiratory failure**
- **COT or HFNOT in patients after extubation with low risk of respiratory complications, and HFNOT or NIV in patients after extubation with high risk of respiratory complications**
- **HFNOT over COT in non-surgical patients after extubation**
- **NIV over HFNOT in patients with high risk of reintubation, provided NIV is not contraindicated**

- **NIV before initiating HFNOT in patients with COPD and acute hypercapnic respiratory failure**

The authors argue that in the studies they reviewed comparing HFNOT with COT, no significant differences were observed in mortality and $PaCO_2$. However, some studies suggest small differences in length of hospitalization, with an extended ICU stay of 1.97 days and a shortening of overall hospitalization by 0.72 days. They also describe certain significant advantages of HFNOT, including a lower risk of escalation to NIV and intubation, reduction in discomfort and dyspnea in patients undergoing therapy, and a slight improvement in PaO_2 levels.

It is worth noting that Nasiłkowski J. [19] in the commentary to the above guidelines states that, due to the high cost of high-flow therapy and, in most cases, low quality of the data supporting the presented recommendations, the use of HFNOT is justified only in patients for whom COT is ineffective (SpO_2 < 92% with FiO_2 > 50%, significant respiratory effort, or respiratory rate > 30/min).

The management guidelines formulated at the SRLF-SFMU conference (Société de Réanimation de Langue Française, Société Française de Médecine d'Urgence) [8], published in September 2024, present similar recommendations:

- **It is suggested to use HFNOT over COT in patients with acute hypoxemic respiratory failure (moderate quality of evidence)**
- **It is suggested to use HFNOT over NIV in patients with acute hypoxemic respiratory failure (moderate quality of evidence)**

Noninvasive Mechanical Ventilation

Noninvasive ventilation (NIV) is a method of delivering oxygen to the lungs by generating positive pressure in the airways without the need for intubation. This is achieved through a specialized setup consisting of a NIV device, one of several available types of face masks (nasal, oronasal, full-face, or helmet ventilation), and one or two tubes connecting the central unit to the mask [20]. The device generates pressure up to 30 cm H_2O, allowing for the adjustment of inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP).

There are several physiological mechanisms underlying the effectiveness of NIV therapy[20–22] that include:

- **Increased minute ventilation and alveolar ventilation, leading to the removal of CO2 and an increase in alveolar oxygen concentration**
- **Recruitment of collapsed pulmonary alveoli and reduction of functional dead space**
- **Reduction of respiratory effort by decreasing the work of respiratory muscles required to maintain adequate ventilation**
- **Prevention of upper airway collapse by maintaining positive pressure**
- **Impact on the central respiratory control center in the brainstem, resulting in reduced dyspnea and centrally driven respiratory effort through the provision of adequate ventilation.**

Indications for the Use of NIV in Acute Respiratory Failure

The American Thoracic Society (ATS) and European Respiratory Society (ERS) published the following recommendations in 2017 [23], based on available data at the time, regarding the use of NIV in acute respiratory failure:
Strong Recommendations:

- **NIV is recommended for acute respiratory acidosis or exacerbation of chronic respiratory acidosis in COPD (pH ≤ 7.35)**
- **A trial of NIV is recommended for patients for whom intubation and mechanical ventilation are being considered, provided their clinical condition does not deteriorate**
- **NIV or CPAP is recommended for patients with cardiogenic pulmonary edema**

Conditional Recommendations:

- **Early initiation of NIV for immunocompromised patients with acute respirory failure**
- **Postoperative acute respiratory failure**
- **As palliative therapy for patients with dyspnea in a terminal condition**
- **Patients with thoracic trauma and acute respiratory failure**
- **Prevention of post-intubation hypercapnic respiratory failure in patients at high risk of developing it**

The mechanisms mentioned above, which contribute to improved ventilation in patients undergoing this therapy, also simultaneously contribute to the potential occurrence of adverse events, such as patient discomfort leading to increased catecholamine secretion, risk of aspiration, ventilation-perfusion mismatch, increased right ventricular afterload, pressure and volume-induced lung injury, or pneumothorax [21,24] . For this reason, during the therapy selection process, contraindications to NIV should be considered as outlined below [22].

Absolute Contraindications:

- **Trauma or burns to the facial or craniofacial region**
- **Upper airway obstruction**
- **Vomiting**
- **Apnea or cardiac arrest**

Relative Contraindications:

- **Recent facial, upper airway, or upper gastrointestinal surgery**
- **Inability to secure the airway**
- **Life-threatening hypoxemia**
- **Hemodynamic instability**
- **Altered mental status or agitation**

- **Bowel obstruction**
- **Significant secretions in the airways**
- **Untreated pneumothorax**
- **Severe comorbidities**

When discussing the indications for NIV, it is worth mentioning the guidelines of the European Society of Anaesthesiology (ESA) and the European Society of Intensive Care Medicine (ESICM) [4] , which primarily address the use of oxygen therapy in postoperative patients. These guidelines recommend the use of NIV perioperatively in patients with hypoxemia, as well as after extubation, to reduce mortality, reduce the risk of reintubation, hospital-acquired pneumonia and the development of postoperative respiratory failure.

Plant et al. [25] in their publication demonstrate that the use of NIV in patients with COPD exacerbation contributes to a reduction in hospitalization costs, primarily by limiting the need to transfer patients to the intensive care unit.

The authors of publications on the use of NIV in acute respiratory failure [23,26,27] primarily emphasize its effectiveness in reducing the need for intubation and invasive mechanical ventilation. At the same time, studies on this topic have not demonstrated a clear impact on mortality or length of hospitalization. However, it should be noted that some of these studies suggest that delaying the decision to perform intubation may be a contributing factor to the observed outcomes.

Invasive Ventilation

Invasive mechanical ventilation, which replaces or supports the patient's own breathing, is a potentially life-saving medical intervention that requires the involvement of qualified medical personnel, the use of an endotracheal tube, a ventilator, and patient sedation for intubation. In addition to providing adequate ventilation, invasive ventilation offers additional benefits related to intubation, such as securing the airway and preventing aspiration. It also allows for the aspiration of secretions from the airways and the performance of bronchoscopy. Invasive ventilation is used to stabilize patients with hypoxemic and hypercapnic respiratory failure, reduces respiratory effort, and, by relieving respiratory muscle load, facilitates the redistribution of blood from muscles to other tissues in the body. It also enables the use of lung-protective ventilation strategies in patients with ARDS through the setting of low tidal volumes [28].

General indications for intubation include [29–32]:

- **Apnea or cardiac arrest**
- **Ineffectiveness of other methods in the treatment of potentially reversible respiratory failure, taking into account SpO_2, PaO_2, $PaCO_2$, pH, and clinical symptoms of respiratory failure**
- **Altered mental status**
- **Loss of consciousness (Glasgow Coma Scale ≤ 8)**
- **Risk of airway obstruction.**

Physiological indications for endotracheal intubation are not unequivocal [33,34], and various authors in their publications suggest initiating invasive ventilation in patients with hypoxemia at SpO_2 levels below 92%, 90%, 88%, or 85% [35–42], based on PaO_2 levels below 65 mmHg, 60 mmHg, 50 mmHg, or 45 mmHg [36,43–45], or making the decision based on the PaO_2/ FiO_2 ratio falling below 200, 100, or 85 [35,40,46,47] . However, each of these methods has significant limitations, which affect their full translation into actual oxygen delivery to the tissues.
In the previously mentioned literature on noninvasive ventilation, the point of reference for its effectiveness is typically the need for implementation of the invasive strategy in patients with acute respiratory failure.

Extracorporeal Membrane Oxygenation

Extracorporeal Membrane Oxygenation (ECMO) is a method that provides extracorporeal oxygenation of blood and removal of carbon dioxide using extracorporeal circulation in either a venovenous (VV) or venoarterial (VA) configuration [48–50] , with the latter potentially achieving higher PaO_2 values [51]. Due to the high complexity of the procedure, it can only be used in a selected group of patients with potentially reversible causes of respiratory failure.

Indications for the use of ECMO in adult populations with respiratory failure, according to ELSO guidelines [51], are as follows:
Physiological Indications:

- **PaO_2/ FiO_2 < 80 with FiO_2 > 90%**
- **Hypercapnia with PaO_2 > 80 mmHg**
- **Inability to achieve plateau pressure ≤ 30 cm H_2O**
- **Severe air leak outside the physiologically ventilated space**
- **Lack of response to other treatment methods**

Clinical Indications:

- **ARDS;**
- **Need for lung rest;**
- **Transplanted lung failure**
- **Pulmonary hemorrhage**

Contraindications for ECMO are primarily related to the irreversibility of the clinical condition and poor prognosis.
Absolute Contraindications:

- **7 days of mechanical ventilation with FiO_2 of 90% and plateau pressure > 30 cm H_2O**
- **Irreversible heart failure with no possibility of heart transplantation or use of ventricular assist devices**
- **Absolute neutrophil count < 400/µL**
- **Bleeding into the central nervous system or irreversible CNS damage**
- **Severe organ failure**
- **Disseminated malignancy**
- **Prolonged resuscitation with insufficient perfusion**

- **Severe pulmonary hypertension**

Relative Contraindications:

- **Advanced age**
- **Obesity**
- **Inability to implement systemic anticoagulation**

Özlüer et al. [52] in their publication outlined the benefits that a patient may experience with the early implementation of ECMO in the emergency department setting, including improvement in vital signs, reduction in the need for vasopressor medications, and lowering of $PaCO_2$. They also suggested the development of treatment algorithms for this therapy in the emergency department.

Conclusions

The treatment of acute respiratory failure is a comprehensive subject, and the oxygen therapy methods presented in this article represent only a subset of the management options that should be considered for patients presenting to emergency departments with this condition. These methods are arranged in order of progressive escalation, from conventional oxygen therapy to noninvasive ventilation techniques, invasive ventilation, and finally extracorporeal oxygenation. Noninvasive ventilation techniques played a significant role during the COVID-19 pandemic as an alternative to intubation in situations of equipment and personnel shortages. Research on their use indicates a trend in the direction of respiratory failure treatment; however, it is important to note that studies addressing their impact on mortality do not provide definitive results. Furthermore, current guidelines for their inclusion in therapy are based on low-quality evidence and weak recommendations. The optimization of management in respiratory failure requires further research, and therapeutic decisions, which depend on the overall clinical picture of the individual patient, the availability of materials, and the number and skill level of the staff, remain the responsibility of the attending physician.

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