Respiratory Failure in Adults: A Multidisciplinary Approach For Emergency, Prehospital, Nursing, And Healthcare Professionals-An Updated Review

Ziyad Badi H. Alharbi[1], Rayan Mohammed Mubarak Alotaibi[1], Faisal Ahmed Hassan Khormi[1], Alsheri Saeed Rafi S[1], Saad Mosluh Alqahtani[1], Khalid Hachan Al Salea[1], Manal Abdulaziz Alaradi[2], Saud Sanhat Zaban Al-Harbi[3], Abdulaziz Mahal Rakkad Alanazi[3], Al Harbi Nauwaf Daiye D[3], Jamal Omar Salem Bahaj[3], Hezam Nasser F. Alotaibi[3]

[1] National Guard Health Affairs, Kingdom of Saudi Arabia (KSA)
[2] Prince Sultan Military Medical City, Riyadh, Kingdom of Saudi Arabia (KSA)
[3] Ministry of National Guard, Kingdom of Saudi Arabia (KSA)

Abstract:
Background: Respiratory failure is a life-threatening clinical syndrome characterized by the inability of the respiratory system to maintain adequate oxygenation, ventilation, or both. It represents the final common pathway of numerous pulmonary and extrapulmonary disorders and is a major cause of emergency department visits, intensive care unit admissions, and mechanical ventilation. Prompt recognition and appropriate management are essential to reduce morbidity and mortality.
Aim: This article aimed to provide a comprehensive, evidence-based review of adult respiratory failure, emphasizing its etiology, epidemiology, pathophysiology, clinical presentation, diagnostic evaluation, management strategies, prognosis, and complications.
Methods: A narrative literature review was conducted using current evidence from peer-reviewed publications and established clinical guidelines. The review synthesizes contemporary knowledge regarding the classification of respiratory failure into hypoxemic (Type 1) and hypercapnic (Type 2) forms, diagnostic approaches including arterial blood gas analysis and imaging modalities, and current principles of supportive and definitive management.
Results: Respiratory failure results from diverse mechanisms affecting gas exchange, including ventilation-perfusion mismatch, diffusion impairment, right-to-left shunting, alveolar hypoventilation, and respiratory pump dysfunction. Early diagnosis relies on comprehensive clinical assessment supported by arterial blood gas analysis, pulse oximetry, imaging studies, capnography, and bedside lung ultrasonography. Management focuses on airway stabilization, optimization of oxygenation and ventilation, treatment of the underlying cause, and timely implementation of noninvasive or invasive mechanical ventilation when indicated. Prognosis varies according to the underlying disease, severity of respiratory dysfunction, and speed of therapeutic intervention, while delayed recognition increases the risk of multiorgan dysfunction and mortality.
Conclusion: Respiratory failure remains a medical emergency requiring rapid assessment, accurate diagnosis, and multidisciplinary management. A thorough understanding of its pathophysiology and evidence-based therapeutic strategies is fundamental for improving patient outcomes and reducing complications across emergency, critical care, and general clinical practice.

Keywords: Respiratory failure; Acute respiratory failure; Chronic respiratory failure; Hypoxemia; Hypercapnia; Mechanical ventilation; Noninvasive ventilation; Arterial blood gas; Oxygen therapy; Critical care.

Introduction

The respiratory system is fundamental to the preservation of human life by maintaining efficient gaseous exchange between the external environment and the pulmonary alveoli, thereby supporting the metabolic demands of body tissues. Through this highly coordinated physiological process, oxygen is transported into the bloodstream for cellular aerobic metabolism, while carbon dioxide, the principal byproduct of metabolic activity, is eliminated to maintain acid-base homeostasis. The integrity of respiratory function depends on the harmonious interaction of pulmonary ventilation, alveolar gas diffusion, pulmonary perfusion, and effective regulation by the central and peripheral nervous systems. Disruption of any of these physiological mechanisms can impair gas exchange and ultimately compromise systemic oxygen delivery or carbon dioxide elimination, resulting in respiratory failure [1]. Respiratory failure represents a serious clinical syndrome characterized by the inability of the respiratory system to maintain adequate oxygenation, ventilation, or both. It is traditionally classified into two principal categories according to the predominant physiological abnormality. Type 1 respiratory failure, also known as hypoxemic respiratory failure, develops when the lungs fail to adequately oxygenate arterial blood, resulting in clinically significant hypoxemia. In contrast, Type 2 respiratory failure, or hypercapnic respiratory failure, occurs when alveolar ventilation becomes insufficient to eliminate carbon dioxide effectively, leading to elevated arterial carbon dioxide concentrations and

subsequent hypercapnia. Although these two forms differ in their underlying pathophysiological mechanisms, they may coexist in many acute and chronic pulmonary disorders, necessitating a comprehensive clinical assessment to determine the primary cause and guide appropriate therapeutic interventions [1].

Respiratory failure may also be categorized according to the duration and progression of the underlying condition as acute, chronic, or acute-on-chronic respiratory failure. Acute respiratory failure develops rapidly over a relatively short period, often leaving insufficient time for physiological compensatory mechanisms to occur, and therefore requires immediate recognition and intervention. Chronic respiratory failure evolves gradually over weeks, months, or years, allowing partial physiological adaptation despite persistent abnormalities in gas exchange. Acute-on-chronic respiratory failure describes the sudden deterioration of a patient with established chronic respiratory insufficiency, frequently precipitated by infection, cardiac dysfunction, or other acute medical conditions, and is associated with increased morbidity and mortality [1]. Because respiratory failure represents the final common pathway of numerous pulmonary, cardiovascular, neuromuscular, and systemic disorders, early identification of its clinical manifestations and prompt initiation of evidence-based management are essential to improve patient outcomes. Failure to recognize either hypoxemic or hypercapnic respiratory failure in a timely manner may result in progressive respiratory compromise, severe tissue hypoxia, worsening acid-base disturbances, respiratory muscle fatigue, and multiorgan dysfunction. If left untreated, respiratory failure can rapidly progress to respiratory arrest, coma, irreversible organ injury, and death. Consequently, healthcare professionals working in emergency, critical care, internal medicine, and prehospital settings must possess a thorough understanding of its underlying pathophysiology, clinical presentation, diagnostic evaluation, and therapeutic principles. This article discusses the comprehensive approach to adult patients with suspected hypoxemic or hypercapnic respiratory failure, with particular emphasis on the diagnosis and management of both acute and chronic forms of this life-threatening condition [1].

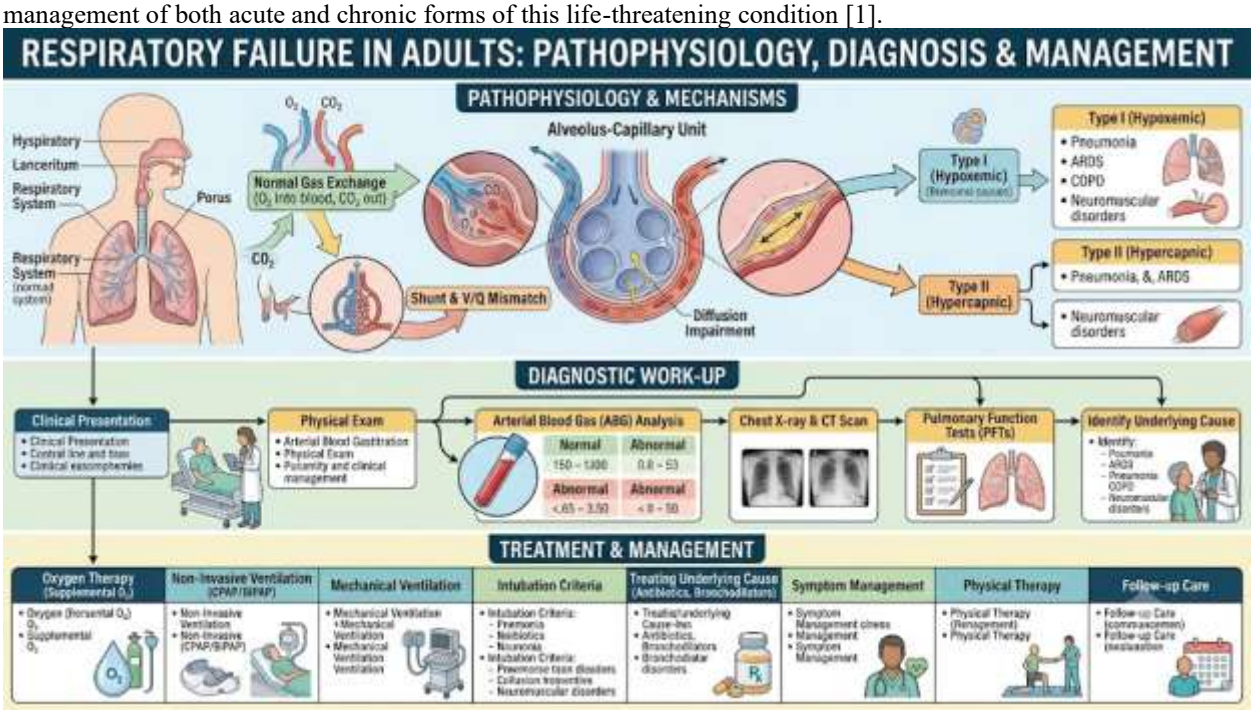

Fig. 1: Respiratory Failure in Adults.

Etiology

Respiratory failure is a complex clinical syndrome that develops when one or more components of the respiratory system fail to maintain adequate oxygenation, ventilation, or both. Rather than representing a single disease entity, respiratory failure constitutes the final common pathway of numerous pathological processes affecting different anatomical structures and physiological mechanisms. Effective respiration depends on the integrated function of the upper and lower airways, pulmonary parenchyma, pulmonary vasculature, respiratory muscles, chest wall, and the central and peripheral nervous systems. Dysfunction involving any of these components may impair gas exchange and ultimately result in respiratory insufficiency [1]. Disorders affecting the upper airway can produce respiratory failure through mechanical obstruction that limits airflow to the lower respiratory tract. Common causes include upper airway edema, foreign body aspiration, laryngeal trauma, epiglottitis, anaphylaxis, and obstructive sleep apnea. Similarly, diseases involving the lower respiratory tract, including asthma, chronic obstructive pulmonary disease (COPD), bronchiectasis, and bronchiolitis, can obstruct airflow and increase airway resistance, resulting in inadequate alveolar ventilation and progressive hypercapnia. Pulmonary parenchymal disorders such as pneumonia, pulmonary edema, pulmonary fibrosis, acute respiratory distress syndrome (ARDS), and diffuse alveolar hemorrhage impair alveolar gas exchange by reducing the effective surface area available for oxygen diffusion, frequently leading to hypoxemic respiratory failure [1].

Neurological disorders represent another important category of etiological factors. Respiratory drive originates within the brainstem and is regulated through complex neural pathways that coordinate respiratory muscle activity. Conditions affecting the central nervous system, including traumatic brain injury, stroke, intracranial hemorrhage, brain tumors, encephalitis, drug overdose, and sedative-induced respiratory depression, may suppress respiratory drive and produce alveolar hypoventilation. Likewise, diseases involving the peripheral nervous system, such as Guillain-Barré syndrome, myasthenia gravis, amyotrophic lateral sclerosis, spinal cord injury, and critical illness polyneuropathy, interfere with neuromuscular transmission or respiratory muscle function, ultimately compromising effective ventilation [1]. Mechanical abnormalities involving the chest wall and respiratory muscles also contribute significantly to respiratory failure. Severe kyphoscoliosis, obesity hypoventilation syndrome, flail chest, multiple rib fractures, diaphragmatic paralysis, and advanced neuromuscular disorders restrict thoracic expansion and reduce lung volumes, thereby impairing ventilation. In addition, respiratory muscle fatigue resulting from prolonged increased work of breathing may precipitate acute decompensation in patients with chronic respiratory diseases. Cardiovascular disorders, including acute heart failure and pulmonary embolism, further contribute by disrupting pulmonary perfusion and ventilation-perfusion matching, thereby reducing oxygen delivery despite relatively preserved ventilation. Metabolic disorders, severe sepsis, trauma, burns, and poisoning may also increase metabolic oxygen demand or impair oxygen utilization, further exacerbating respiratory dysfunction.

In clinical practice, respiratory failure frequently results from the interaction of multiple pathological processes rather than a single isolated abnormality. For example, a patient with advanced COPD may develop bacterial pneumonia, resulting in worsening airflow limitation, increased ventilation-perfusion mismatch, and respiratory muscle fatigue, all of which contribute to acute-on-chronic respiratory failure. Similarly, critically ill patients often experience simultaneous pulmonary, cardiovascular, and neurological impairments that collectively compromise respiratory function. Consequently, identifying the underlying etiology is fundamental because successful management extends beyond supportive respiratory care to include prompt treatment of the precipitating disease process. A comprehensive understanding of the diverse causes of respiratory failure is therefore essential for accurate diagnosis, risk stratification, and implementation of appropriate evidence-based therapeutic interventions [1].

Epidemiology

Respiratory failure represents a major global public health challenge and remains one of the leading causes of emergency department visits, intensive care unit admissions, mechanical ventilation, and hospital mortality. Because respiratory failure is a clinical syndrome rather than a distinct disease, its epidemiological characteristics are influenced by the incidence and prevalence of the numerous disorders capable of impairing pulmonary gas exchange or ventilatory function. Consequently, determining its true global burden remains difficult, as reported rates vary according to diagnostic definitions, patient populations, healthcare systems, and methods of data collection. Nevertheless, available epidemiological evidence consistently demonstrates that respiratory failure contributes substantially to healthcare utilization, resource consumption, and mortality worldwide [2]. In the United States, respiratory failure is associated with a considerable disease burden across both community and hospital settings. A large epidemiological analysis conducted in 2017 estimated an incidence of approximately 1,275 cases per 100,000 adults. This estimate incorporated all diagnostic codes containing respiratory failure as a component of the patient's diagnosis, highlighting the widespread occurrence of this syndrome across diverse clinical conditions [2]. The incidence increases markedly with advancing age because older adults are more likely to develop chronic respiratory diseases, cardiovascular disorders, neuromuscular conditions, and systemic illnesses that predispose them to respiratory compromise. Additionally, improvements in critical care medicine have increased the survival of patients with chronic illnesses, thereby expanding the population at risk for recurrent episodes of acute-on-chronic respiratory failure.

The epidemiology of respiratory failure varies considerably according to the underlying etiology. Acute myocardial infarction complicated by respiratory failure remains an important cause of critical illness. Between 2000 and 2014, approximately 439,436 hospital admissions were attributed to acute myocardial infarction-related respiratory failure, with nearly 57% of affected patients requiring intensive care management and approximately 43% receiving mechanical ventilation, reflecting the severity of cardiopulmonary compromise in this population [3]. Similarly, acute respiratory distress syndrome (ARDS) continues to represent one of the most serious causes of acute hypoxemic respiratory failure. Worldwide estimates suggest an annual incidence ranging from 10 to 80 cases per 100,000 population, although considerable regional variation exists because of differences in diagnostic criteria, healthcare practices, and thresholds for endotracheal intubation. Current evidence indicates that approximately 10% of all intensive care unit admissions and nearly one-quarter of mechanically ventilated patients satisfy the diagnostic criteria for ARDS [4]. The emergence of Coronavirus Disease 2019 (COVID-19) dramatically altered the epidemiology of acute respiratory failure by producing an unprecedented surge in critically ill patients requiring advanced respiratory support. During the early stages of the pandemic, reports indicated that up to 79% of hospitalized patients with severe COVID-19 developed respiratory failure necessitating invasive mechanical ventilation, emphasizing the devastating pulmonary consequences of severe viral pneumonia and diffuse alveolar injury [5]. Although advances in vaccination, antiviral therapy, and supportive care have substantially reduced mortality in many regions, COVID-19 highlighted

the vulnerability of healthcare systems to large-scale outbreaks of respiratory disease and reinforced the importance of preparedness for future pandemics.

Chronic respiratory diseases also account for a substantial proportion of respiratory failure cases. Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) remain among the most frequent causes of hospitalization for acute respiratory failure and represent the third most common etiology in hospitalized patients with this syndrome [6]. The growing prevalence of smoking-related lung disease, environmental pollution, occupational exposures, and population aging continues to increase the global burden of COPD-related respiratory failure. Collectively, these epidemiological trends underscore the substantial clinical and economic impact of respiratory failure and emphasize the need for preventive strategies, early recognition, evidence-based management, and continued public health efforts aimed at reducing the incidence and severity of the underlying diseases responsible for this life-threatening syndrome.

Pathophysiology

Respiratory failure develops when the respiratory system is unable to maintain adequate oxygenation, ventilation, or both, resulting in impaired gas exchange and disruption of normal physiological homeostasis. The underlying pathophysiological mechanisms differ according to whether hypoxemia, hypercapnia, or a combination of both predominates. Accordingly, respiratory failure is classified into Type 1 (hypoxemic) and Type 2 (hypercapnic) respiratory failure. Understanding these mechanisms is fundamental for accurate diagnosis, interpretation of arterial blood gas analysis, and selection of appropriate therapeutic interventions.

Type 1 Respiratory Failure

Type 1 respiratory failure is characterized by impaired oxygenation, defined by an arterial partial pressure of oxygen (PaO_2) below 60 mmHg, while the arterial partial pressure of carbon dioxide ($PaCO_2$) remains normal or decreased. The degree of hypoxemia depends on the underlying pathological process, and evaluation of the alveolar-arterial (A-a) oxygen gradient provides important diagnostic information regarding the mechanism responsible for oxygen transfer impairment. Depending on the etiology, the A-a gradient may remain normal or become significantly increased.

The A-a gradient is calculated using the following equation:

$$\textbf{A-a gradient} = PAO_2 - PaO_2$$

where PAO_2 represents the alveolar partial pressure of oxygen and PaO_2 represents the arterial partial pressure of oxygen.

Calculation of PAO_2 is based on the alveolar gas equation:

$$PAO_2 = FiO_2 (PB - Pwater) - PaCO_2/0.8$$

or

$$PIO_2 = (PB - 47) \times FiO_2$$

where FiO_2 is the fraction of inspired oxygen, PB is the atmospheric (barometric) pressure, Pwater is the water vapor pressure at body temperature (47 mmHg), and $PaCO_2$ is the arterial carbon dioxide tension [7]. These equations provide the physiological framework for understanding the causes of hypoxemia and differentiating disorders affecting oxygen delivery from those impairing pulmonary gas exchange. A normal A-a gradient generally indicates that oxygen transfer across the alveolar-capillary membrane remains intact and that hypoxemia results from reduced oxygen availability or inadequate alveolar ventilation. One of the principal mechanisms is alveolar hypoventilation, in which inadequate ventilation causes progressive retention of carbon dioxide. According to the alveolar gas equation, elevation of $PaCO_2$ proportionally decreases alveolar oxygen tension (PAO_2), resulting in reduced arterial oxygen tension without widening the A-a gradient because both PAO_2 and PaO_2 decline proportionally. Initially, hypoxemia may occur without significant hypercapnia, but persistent or severe hypoventilation eventually leads to Type 2 respiratory failure as carbon dioxide accumulates beyond the compensatory capacity of the respiratory system [8]. A second cause of hypoxemia with a normal A-a gradient is exposure to environments with reduced atmospheric pressure or reduced inspired oxygen concentration. At high altitude, declining barometric pressure lowers inspired oxygen tension, thereby reducing alveolar oxygen pressure despite structurally normal lungs. In response to hypoxemia, peripheral chemoreceptors stimulate hyperventilation, producing a reduction in $PaCO_2$ while maintaining a normal A-a gradient. This physiological adaptation enables partial compensation but cannot completely overcome the reduced oxygen availability encountered at high elevations [9].

In contrast, an increased A-a gradient indicates impaired transfer of oxygen from the alveoli into the pulmonary circulation despite adequate alveolar oxygen tension. One important mechanism is diffusion limitation. Oxygen and carbon dioxide diffuse across the alveolar-capillary membrane according to concentration gradients, membrane thickness, surface area, and pulmonary capillary transit time. Structural abnormalities that increase membrane thickness or reduce available alveolar surface area impede oxygen diffusion much more than carbon dioxide because carbon dioxide possesses substantially greater diffusibility. Consequently, hypoxemia develops without significant hypercapnia during the early stages of diffusion impairment [10]. Classic disorders associated with diffusion limitation include emphysema, in which destruction of alveolar walls markedly reduces gas exchange surface area, and interstitial lung diseases, where fibrosis thickens the alveolar-capillary membrane and prolongs diffusion distance. Ventilation-perfusion (V/Q) mismatch represents the most common mechanism responsible for Type 1 respiratory

failure [11]. Efficient gas exchange requires appropriate matching between alveolar ventilation and pulmonary perfusion. Ideally, the V/Q ratio approaches 1.0; however, under normal physiological conditions the average V/Q ratio is approximately 0.8 because ventilation and blood flow vary from the lung apex to the base. When ventilation exceeds perfusion, dead-space ventilation develops, whereas excessive perfusion relative to ventilation produces physiological shunting. Disorders producing heterogeneous ventilation or perfusion create regions with abnormal V/Q ratios, resulting in arterial hypoxemia. Unlike true shunts, hypoxemia caused by V/Q mismatch usually responds to supplemental oxygen because at least partial ventilation persists in affected lung regions. Common causes include acute respiratory distress syndrome, chronic obstructive pulmonary disease, congestive heart failure, and pulmonary embolism [11]. True right-to-left shunting represents the most severe form of V/Q mismatch, occurring when the V/Q ratio reaches zero because pulmonary perfusion continues despite complete absence of alveolar ventilation. Under these circumstances, venous blood bypasses functional gas exchange units and enters the systemic circulation without oxygenation. Because oxygen cannot reach completely unventilated alveoli, hypoxemia caused by true shunting responds poorly to supplemental oxygen therapy [12]. Pulmonary arteriovenous malformations, complete atelectasis, severe pneumonia, and extensive pulmonary edema are among the principal causes of intrapulmonary right-to-left shunts. Intracardiac abnormalities, including atrial septal defects and patent foramen ovale, may also produce similar physiological consequences by allowing deoxygenated blood to bypass pulmonary circulation altogether [12].

Type 2 Respiratory Failure

Type 2 respiratory failure, also known as hypercapnic respiratory failure, is characterized by impaired alveolar ventilation leading to arterial carbon dioxide retention. It is defined by a $PaCO_2$ greater than 45 mmHg accompanied by respiratory acidosis with an arterial pH below 7.35. Although hypoxemia frequently accompanies hypercapnia, the defining abnormality is failure of carbon dioxide elimination rather than oxygen uptake. The principal pathophysiological mechanism is respiratory pump failure, although excessive carbon dioxide production may contribute in selected clinical situations. The relationship between carbon dioxide production and alveolar ventilation is described by the modified alveolar ventilation equation:

$$\mathbf{PaCO_2 = VCO_2 / VA}$$

where VCO_2 represents carbon dioxide production and VA represents alveolar ventilation. Alveolar ventilation itself is determined by the equation:

$$\mathbf{VA = VE \times (1 - VD/VT)}$$

where VE represents minute ventilation, VD is dead-space volume, and VT is tidal volume [13]. These relationships demonstrate that arterial carbon dioxide concentration increases either when carbon dioxide production rises excessively or, more commonly, when alveolar ventilation decreases. Clinically, hypercapnic respiratory failure develops through two fundamental mechanisms often summarized as patients who "will not breathe" and those who "cannot breathe." The former results from impaired central respiratory drive, whereas the latter reflects failure of the respiratory pump despite preserved neural stimulation. Disorders reducing central respiratory drive include sedative medications, alcohol intoxication, opioid overdose, benzodiazepines, traumatic brain injury, stroke, encephalitis, brain tumors, and spinal cord injury. These conditions suppress medullary respiratory centers, resulting in inadequate ventilatory effort and progressive alveolar hypoventilation [14]. Failure of neural transmission or respiratory muscle activation constitutes another major mechanism. Diseases such as amyotrophic lateral sclerosis, Guillain-Barré syndrome, myasthenia gravis, botulism, poliomyelitis, organophosphate poisoning, tetanus, transverse myelitis, and spinal cord injury impair neuromuscular transmission or muscle contraction, thereby reducing effective ventilation despite preserved respiratory drive [14]. Similarly, disorders affecting the chest wall or pleural cavity, including severe kyphoscoliosis, obesity hypoventilation syndrome, flail chest, massive pleural effusions, thoracoplasty, and chronic pulmonary hyperinflation, restrict thoracic expansion and increase the work of breathing until respiratory muscles fatigue and alveolar ventilation declines.

Respiratory muscle dysfunction itself may further compromise ventilation. Diaphragmatic paralysis, muscular dystrophies, diffuse skeletal muscle atrophy, critical illness myopathy, and traumatic diaphragmatic rupture diminish inspiratory force generation, reducing tidal volume and promoting carbon dioxide retention. In patients with chronic respiratory diseases, prolonged increases in respiratory workload frequently result in respiratory muscle fatigue, precipitating acute hypercapnic decompensation. Dead-space ventilation also contributes substantially to hypercapnic respiratory failure. Dead space refers to portions of the respiratory tract where ventilation occurs without effective perfusion and therefore does not participate in gas exchange. Diseases such as emphysema, bronchiectasis, bronchitis, ARDS, and pulmonary embolism increase physiological dead space by disrupting ventilation-perfusion relationships. Hypercapnia generally develops once dead-space ventilation exceeds approximately one-half of total ventilation, substantially reducing effective alveolar ventilation despite apparently adequate minute ventilation [15]. Tachypnea may paradoxically worsen hypercapnia by increasing the dead-space-to-tidal-volume ratio, particularly in patients with COPD, where increased physiological dead space and severe ventilation-perfusion mismatch constitute major mechanisms of carbon dioxide retention [15]. Although relatively uncommon, excessive carbon dioxide production may overwhelm normal ventilatory capacity. Carbon dioxide generation increases during fever, strenuous exercise, sepsis, hyperalimentation, malignant hyperthermia, and thyrotoxicosis. Under normal circumstances, healthy

individuals compensate through increased minute ventilation. Hypercapnia develops only when this compensatory response is impaired or when underlying respiratory disease prevents adequate ventilatory reserve [16].
Finally, persistent alveolar hypoventilation remains the central pathophysiological process linking both forms of respiratory failure. Progressive reduction in alveolar ventilation initially produces hypoxemia and, if left untreated, eventually results in carbon dioxide retention and transition from isolated hypoxemic respiratory failure to combined hypoxemic-hypercapnic respiratory failure [8]. Understanding these interconnected mechanisms provides the physiological basis for interpreting arterial blood gas abnormalities and selecting targeted therapeutic strategies in patients with respiratory failure.

History and Physical

The evaluation of respiratory failure begins with a comprehensive clinical history and meticulous physical examination, both of which are essential for identifying the underlying etiology and guiding subsequent diagnostic and therapeutic decisions. Because respiratory failure is a clinical syndrome arising from numerous pulmonary, cardiovascular, neurological, metabolic, and systemic disorders, clinicians should obtain detailed information regarding symptom onset, progression, severity, precipitating factors, associated medical conditions, medication use, and potential environmental or occupational exposures. Patients commonly present with respiratory symptoms including dyspnea, cough, sputum production, wheezing, and hemoptysis. However, associated systemic manifestations such as chest pain, fever, fatigue, reduced appetite, heartburn, and unintended weight loss may provide important diagnostic clues. During outbreaks of viral respiratory infections, particularly Coronavirus Disease 2019 (COVID-19), recent exposure to infected individuals, loss of smell, or unprotected contact with confirmed cases should be carefully assessed, especially in high-risk populations such as older adults, men, and individuals with severe obesity [17]. In patients with chronic respiratory diseases, evaluation should include adherence to inhaled medications, inhaler technique, recent corticosteroid use, and exposure to known environmental triggers. Medication history should also identify drugs associated with respiratory symptoms, including angiotensin-converting enzyme inhibitors. Social, occupational, and family histories are equally important, with attention to tobacco smoking, vaping, alcohol use, recreational drug exposure, occupational inhalants, animal exposure, recent travel, and hereditary conditions such as alpha-1 antitrypsin deficiency or cystic fibrosis [18,19]. Physical examination should focus on identifying signs of respiratory distress and underlying systemic disease. General inspection may reveal tachypnea, use of accessory respiratory muscles, diaphoresis, conversational dyspnea, obesity, cachexia, altered mental status, or pursed-lip breathing. Head and neck examination should assess central cyanosis, conjunctival pallor, jugular venous distention, lymphadenopathy, tracheal deviation, and other abnormalities. Chest examination includes evaluation of respiratory rate and pattern, chest expansion, percussion note, tactile fremitus, and auscultation for crackles, wheezes, rhonchi, stridor, bronchial breath sounds, pleural rubs, or diminished breath sounds. Examination of the abdomen and extremities may demonstrate hepatomegaly, digital clubbing, asterixis, peripheral cyanosis, edema, tremor, unilateral leg swelling suggestive of deep venous thrombosis, or tobacco staining, all of which may provide valuable clues to the underlying cause of respiratory failure [20].

Evaluation

The evaluation of respiratory failure requires a systematic and comprehensive approach aimed at confirming the diagnosis, determining its severity, identifying the underlying etiology, and guiding appropriate management. Because respiratory failure is a clinical syndrome resulting from numerous pulmonary and extrapulmonary disorders, no single diagnostic algorithm is applicable to every patient. Instead, investigations should be individualized according to the clinical presentation and suspected cause. Initial laboratory evaluation commonly includes a complete blood count with differential, comprehensive metabolic panel, serum magnesium and phosphate, inflammatory biomarkers such as procalcitonin, cardiac biomarkers including troponin, and thyroid-stimulating hormone when endocrine disorders are suspected. Additional investigations may include blood and sputum cultures, respiratory pathogen testing, urinary antigen assays, and a 12-lead electrocardiogram to identify infectious, cardiac, or metabolic contributors to respiratory compromise. Arterial blood gas (ABG) analysis remains the gold standard for diagnosing respiratory failure and provides critical information regarding oxygenation, ventilation, and acid-base status. Essential parameters include arterial pH, partial pressure of oxygen (PaO_2), partial pressure of carbon dioxide ($PaCO_2$), and serum bicarbonate (HCO_3^-). Although bicarbonate values reported on arterial blood gas analysis are calculated rather than directly measured, interpretation should ideally incorporate the measured serum bicarbonate obtained from a basic metabolic panel for greater accuracy. A PaO_2 below 60 mmHg confirms hypoxemia, whereas a $PaCO_2$ exceeding 45 mmHg indicates hypercapnia. Furthermore, arterial blood gas analysis assists in distinguishing acute from chronic respiratory failure by evaluating renal compensation. In chronic respiratory acidosis, the kidneys gradually increase bicarbonate reabsorption over several days, producing higher serum bicarbonate concentrations than those observed in acute respiratory acidosis, where renal compensation remains incomplete [21].
Capnometry provides continuous assessment of exhaled carbon dioxide and may be performed qualitatively using colorimetric devices or quantitatively through infrared technology. Quantitative capnometry measures end-tidal carbon dioxide ($PETCO_2$), which normally approximates arterial carbon dioxide tension, with $PaCO_2$ typically exceeding $PETCO_2$ by only 2–3 mmHg. In conditions associated with impaired ventilation-perfusion matching or

increased physiological dead space, this gradient widens, reflecting inefficient gas exchange [22,23]. Continuous waveform capnography further enhances clinical assessment by displaying characteristic respiratory patterns that facilitate the recognition of apnea, bronchospasm, hypoventilation, hyperventilation, and airway obstruction, making it particularly valuable during emergency care, procedural sedation, and mechanical ventilation [24]. Imaging studies play an indispensable role in identifying structural and pathological abnormalities responsible for respiratory failure. Chest radiography is usually the initial imaging modality and may reveal pneumonia, pulmonary edema, pleural effusion, pneumothorax, or chronic lung disease. Depending on the clinical scenario, further evaluation with computed tomography, magnetic resonance imaging, nuclear medicine studies, pulmonary angiography, or thoracic ultrasonography may be indicated to establish a definitive diagnosis [25].

Pulse oximetry is a rapid, noninvasive method for continuous monitoring of arterial oxygen saturation (SpO_2). This technique utilizes spectrophotometry to distinguish oxygenated from deoxygenated hemoglobin by measuring light absorption at wavelengths of approximately 660 nm and 940 nm. Analysis of pulsatile arterial blood allows estimation of oxygen saturation, providing immediate bedside assessment of oxygenation and facilitating continuous monitoring of disease progression and therapeutic response [26]. Point-of-care lung ultrasonography has emerged as an essential diagnostic tool in patients with acute respiratory failure. The Bedside Lung Ultrasound in Emergency (BLUE) protocol enables rapid and standardized evaluation using six predefined thoracic examination points. Characteristic ultrasonographic findings include A-lines and lung sliding in normal lungs, B-lines indicating interstitial syndrome, tissue-like and fractal signs suggesting pulmonary consolidation, quad and sinusoid signs associated with pleural effusions, and the stratosphere sign or lung point characteristic of pneumothorax [27]. Additional investigations, including bronchoscopy, echocardiography, pulmonary function testing, and nocturnal polysomnography, may be required in selected patients to establish the underlying diagnosis, with pulmonary specialist consultation recommended when advanced diagnostic evaluation is indicated.

Treatment / Management

The management of respiratory failure focuses on correcting life-threatening abnormalities in oxygenation and ventilation while simultaneously identifying and treating the underlying cause. Since respiratory failure represents a clinical syndrome rather than a specific disease, successful treatment requires an individualized approach based on the patient's clinical presentation, severity of illness, and underlying pathophysiological mechanism. Initial management should follow the principles of airway, breathing, and circulation (ABC), with immediate assessment of airway patency, respiratory effort, oxygenation, and hemodynamic stability. Prompt stabilization is essential to prevent progressive hypoxemia, hypercapnia, respiratory muscle fatigue, and multiorgan dysfunction. Supportive care should be initiated without delaying definitive treatment of the precipitating condition, such as pneumonia, pulmonary edema, asthma exacerbation, pulmonary embolism, or neuromuscular disease. Correction of hypoxemia is the primary therapeutic objective in patients with Type 1 respiratory failure. The goal is to ensure adequate tissue oxygen delivery by maintaining an arterial oxygen tension (PaO_2) of at least 60 mmHg or an arterial oxygen saturation (SaO_2) of approximately 90%. Oxygen therapy should be carefully titrated because excessive oxygen administration may contribute to oxygen toxicity and worsen hypercapnia in susceptible patients, particularly those with chronic hypercapnic respiratory failure. Therefore, the inspired oxygen concentration should be adjusted to achieve target oxygen saturation levels, generally between 90% and 94%, while avoiding unnecessary hyperoxia. Oxygen delivery devices are selected according to the severity of respiratory compromise and include nasal cannulae, simple face masks, non-rebreather masks, and high-flow nasal cannula systems. In patients with refractory hypoxemia despite optimal conventional therapy, extracorporeal membrane oxygenation (ECMO) may be considered as a rescue intervention in specialized centers [28].

Management of hypercapnic respiratory failure aims to improve alveolar ventilation, correct respiratory acidosis, and reduce carbon dioxide retention through treatment of the underlying disorder and provision of ventilatory support when indicated [29]. Mechanical ventilatory assistance becomes necessary when spontaneous ventilation is inadequate to maintain acceptable gas exchange. The principal objectives of ventilatory support include correction of hypoxemia, reversal of acute respiratory acidosis, reduction of the work of breathing, and prevention of respiratory muscle fatigue. Common indications for mechanical ventilation include apnea or respiratory arrest, persistent tachypnea exceeding 30 breaths per minute, altered consciousness or coma, respiratory muscle exhaustion, hemodynamic instability, failure of supplemental oxygen to achieve a PaO_2 of 55–60 mmHg, and severe hypercapnia associated with an arterial pH below 7.25 [30]. The choice between invasive mechanical ventilation and noninvasive ventilation (NIV) depends on the patient's clinical status, the severity of respiratory failure, and the underlying disease process [31]. Whenever appropriate, NIV is preferred because it improves gas exchange while avoiding complications associated with endotracheal intubation, including ventilator-associated pneumonia and airway trauma. Strong evidence supports the use of NIV in acute exacerbations of chronic obstructive pulmonary disease, acute cardiogenic pulmonary edema, and obesity hypoventilation syndrome, where it reduces intubation rates, shortens hospital stay, and improves survival [32][33][34][33][35][36]. Continuous clinical monitoring and frequent reassessment remain essential to ensure treatment effectiveness and permit timely escalation of respiratory support when necessary.

Prognosis

The prognosis of respiratory failure varies considerably according to its underlying etiology, severity, duration, patient age, pre-existing comorbidities, and the timeliness of diagnosis and treatment. Because respiratory failure is a clinical syndrome rather than a single disease, outcomes differ substantially among affected populations. Patients with reversible conditions such as acute asthma or drug-induced respiratory depression generally have favorable outcomes when prompt intervention is provided, whereas those with severe pneumonia, acute respiratory distress syndrome (ARDS), or advanced chronic cardiopulmonary disease often experience significantly higher morbidity and mortality. A large epidemiological study conducted in the United States reported an overall in-hospital mortality rate of approximately 12% for patients diagnosed with respiratory failure [2]. Mortality varies by etiology, reaching 9.8% in mechanically ventilated patients with asthma exacerbation, 38.3% in acute exacerbations of chronic obstructive pulmonary disease, 48.4% in pneumonia requiring mechanical ventilation [37][38][39], and approximately 44.3% among patients with ARDS [40]. Early recognition, appropriate ventilatory support, and effective treatment of the underlying disease remain the most important determinants of improved survival and long-term functional recovery.

Complications

Respiratory failure is associated with numerous pulmonary and systemic complications that may substantially increase morbidity, prolong hospitalization, and worsen clinical outcomes. Pulmonary complications commonly include ventilator-associated or nosocomial pneumonia, pneumothorax, pulmonary embolism, bronchopleural fistula, and progressive pulmonary fibrosis, particularly in patients with prolonged mechanical ventilation or severe acute respiratory distress syndrome. Persistent hypoxemia and hypercapnia may further exacerbate pulmonary vascular dysfunction and impair respiratory mechanics. Extrapulmonary complications result primarily from inadequate tissue oxygenation, systemic inflammation, and multiorgan dysfunction. These include acid-base disturbances, reduced cardiac output, gastrointestinal hemorrhage, hepatic dysfunction, paralytic ileus, secondary infections, increased intracranial pressure, malnutrition, renal failure, thrombocytopenia, and, in rare cases, pneumoperitoneum [41][42]. Critically ill patients are particularly vulnerable because prolonged immobilization, invasive procedures, and mechanical ventilation increase the risk of thromboembolic events, pressure injuries, and healthcare-associated infections. Continuous clinical monitoring, early preventive measures, multidisciplinary management, and timely recognition of emerging complications are essential to reduce adverse outcomes and improve both short- and long-term patient prognosis [41][42].

Conclusion

Respiratory failure remains one of the most challenging emergencies encountered across emergency medicine, critical care, and general clinical practice because it encompasses a broad spectrum of pulmonary and extrapulmonary disorders that impair oxygenation, ventilation, or both. Effective management depends on early recognition of clinical deterioration, prompt assessment of airway, breathing, and circulation, and rapid identification of the underlying pathophysiological mechanism responsible for gas exchange abnormalities. Comprehensive evaluation using arterial blood gas analysis, pulse oximetry, imaging studies, capnography, and bedside ultrasonography enables timely diagnosis and appropriate therapeutic decision-making. Treatment should combine supportive respiratory care with targeted management of the precipitating disease while minimizing complications associated with prolonged hypoxemia, hypercapnia, and mechanical ventilation. Advances in noninvasive ventilation, high-flow oxygen therapy, lung ultrasonography, and extracorporeal life support have significantly improved outcomes in selected patient populations. Nevertheless, respiratory failure continues to be associated with substantial morbidity, mortality, and healthcare utilization. A multidisciplinary, evidence-based approach remains essential to optimize survival, preserve organ function, reduce complications, and improve both short-term and long-term clinical outcomes in adult patients with respiratory failure.

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