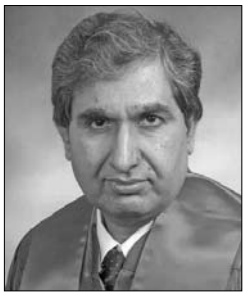


Acute Respiratory Failure - Algorithmic Approach -Diagnosis and Management

GC Khilnani[*], C Bammigatti[**]

[*]Additional Professor , [**]Senior Resident,
Departments of Medicine, All India Institute of Medical Sciences, New Delhi-110029

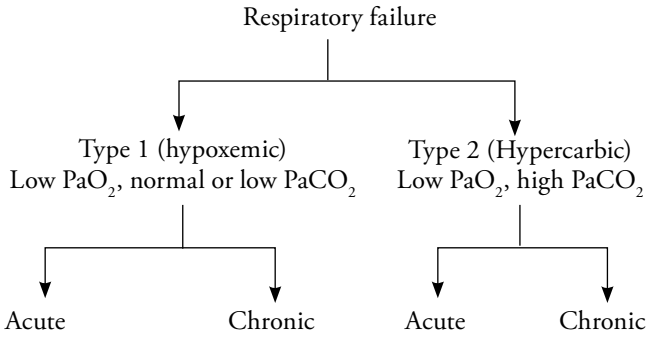
ABSTRACT

Acute respiratory failure is a common clinical condition encountered in emergency department and intensive care units (ICU). This clinical entity has varied etiology and high morbidity and morality despite aggressive monitoring and treatment. The aim of this chapter is to understand the classification, etiology, clinical features, diagnosis and management of acute respiratory failure. Type 1 (hypoxaemic) respiratory failure is most often associated with those conditions that affect the interstitium and alveolar walls of the lungs. It is often associated with marked VA/Q mismatching and oxygen is the critical therapy in the management of these patients. Alveolar hypoventilation leads to type 2 (hypercapnic) respiratory failure, the most common cause of which is acute exacerbation of COPD. Various clinical features helps in assessment of patients with acute respiratory failure, however, arterial blood gas analysis is the mainstay of diagnosis. The management of patients with acute respiratory failure varies according to the etiology with the primary aim to maintain a patent airway and ensure adequate alveolar ventilation. Lung protective ventilation is found to improve outcome of ARDS patients markedly. In carefully selected patients, non-invasive positive pressure ventilation (NIPPV) is found to decrease the rate of intubation, mortality and nosocomial pneumonia. Quite often patients with acute respiratory failure need mechanical ventilation, which require intricate management depending upon the cause of respiratory failure. With the currently available advanced ventilators for mechanical ventilation, a large proportion of patients can be liberated from mechanical ventilation.

Respiratory failure is a syndrome in which the respiratory system fails to maintain an adequate gas exchange at rest or during exercise resulting in hypoxemia with or without concomitant hypercarbia. Despite many technical advances in diagnosis, monitoring and therapeutic intervention, acute respiratory failure continues to be a major cause of morbidity and mortality in intensive care unit (ICU) setting. This chapter describes the classification, etiology, clinical features, diagnosis and management of this common condition of varied etiology.

Respiratory failure (RF) is diagnosed when the patient loses the ability to ventilate adequately or to provide sufficient oxygen to the blood and systemic organs. Clinically respiratory failure is diagnosed when PaO_2 is less than 60mm of Hg with or without elevated CO_2 level, while breathing room air. High mortality rates are common for patients with acute respiratory failure, even in ICUs specializing in modern critical care techniques. In an International multicenter study, only 55.6% patients with acute respiratory failure survived their hospitalization whereas 44.4% died in the hospital.[1] Urgent resuscitation of the patient requires airway control, ventilator management, and stabilization of the circulation. At the same time patient should be evaluated for the cause of respiratory failure and therapeutic plan should be derived from an informed clinical and laboratory examination supplemented by the results of special intensive care unit (ICU) interventions. Recent advances in the ICU management and monitoring technology facilitates early detection of the pathophysiology of vital functions, with the potential for prevention and early titration of therapy for the patients with acute respiratory failure which improves the outcome.

Respiratory failure is classified as type 1 respiratory failure or type 2 respiratory failure (Fig.1).[2] *Type 1 respiratory failure* is defined by a PaO_2 of <60mmHg with a normal or low $PaCO_2$. *Type 2 respiratory failure* is defined by a PaO_2 of <60mHg and a $PaCO_2$ of >45mHg.[3] Respiratory failure is also classified as acute, acute on chronic or chronic.[3] This distinction is important in deciding on whether the patient needs to be treated in intensive care unit (ICU) or can be managed in general medical ward and most appropriate treatment strategy, particularly in type 2 respiratory failure.



* *Hypoxemia and hypercarbic respiratory failure frequently coexist. Either may be acute or chronic.*

Fig.1 : Classification of respiratory failure

Table 1 : Common causes of type 1 (hypoxaemic) respiratory failure

Chronic bronchitis and emphysema
Pneumonia
Pulmonary edema
Pulmonary fibrosis
Asthma
Pneumothorax
Pulmonary embolism
Thromboembolic pulmonary hypertension
Lymphatic carcinomatosis
Pneumoconiosis
Granulomatous lung disease
Cyanotic congenital heart disease
Acute respiratory distress syndrome
Fat embolism
Pulmonary arteriovenous fistulae

- ***Acute*** hypercarbic respiratory failure is characterized by a patient with no, or minor, evidence of pre-existing respiratory disease and arterial blood gas tensions will show high $PaCO_2$, low pH, and normal bicarbonate.
- ***Acute on chronic*** hypercarbic respiratory failure is characterized by an acute deterioration in an individual with significant pre-existing hypercarbic respiratory failure, high $PaCO_2$, low pH, and high bicarbonate.
- ***Chronic*** hypercarbic respiratory failure is characterized by the evidence of chronic respiratory disease, high $PaCO_2$, normal pH and high bicarbonate.

The causes of respiratory failure are diverse. In general most pulmonary and cardiac causes of respiratory failure lead to hypoxemia without hypercarbia (Type 1 respiratory failure). This type of respiratory insufficiency is most often associated with those conditions that affect the interstitium and alveolar walls of the lungs, e.g. fibrosing alveolitis and pulmonary edema, but is also seen in other conditions such as pulmonary embolism and pneumonia. It may also be seen in obstructive lung disease, such as COPD and asthma (Table 1).

In all these conditions V_A/Q mismatching is marked, resulting in either increased dead space or wasted ventilation (increased lung units with high V_A/Q ratios) or venous admixture (increased lung units with low V_A/Q ratios). V_A/Q mismatching accounts for the hypoxemia in the great majority of cases. As control of ventilation in these patient is usually intact, ventilation increase in response to a raised $PaCO_2$, so that the excess CO_2 is excreted by the normal areas of the lungs. This hyperventilation cannot result in further improvement in the normal areas of the lungs, since the blood there is already fully oxygenated.

Table 2 : Common causes of type 2 respiratory failure

Chronic bronchitis and emphysema
Asthma
Drug overdose
Poisoning
Myasthenia gravis
Polyneuropathy
Poliomyelitis
Primary muscle disorders
Porphyria
Cervical cord disorders
Primary alveolar hypoventilation
Sleep apnea syndrome
Pulmonary oedema
Acute respiratory distress syndrome
Laryngeal oedema
Foreign body

Alveolar hypoventilation leads to type 2 respiratory failure. When the $PaCO_2$ rises due to alveolar hypoventilation, the PaO_2 must fall; knowing one of these values, the other may be predicted using the alveolar air equation. The most common cause of type 2 respiratory failure is COPD. Other causes leading to type 2 respiratory failure are listed in Table 2.

If respiratory failure is of sudden onset, the acute rise in $PaCO_2$ results in a rise in hydrogen ion concentration leading to fall in pH. If respiratory failure develops slowly, renal compensation with retention of bicarbonate results in near-normal pH.[4]

CLINICAL FEATURES

Clinical features of hypoxemia

Hypoxemia results in central cyanosis that is best assessed by examining the oral mucous membranes, since blood flow at these sites is well maintained when the periphery may be vasoconstricted. The relationship between cyanosis and hypoxemia, however, is variable and there is wide inter-observer variation.[5,6] Cyanosis is more easily observed in polycythaemic patients, whereas in anemic patients there may be insufficient reduced hemoglobin to produce a blue color to the mucus membranes.

Hypoxemia affects the central nervous system (CNS), causing irritability, impaired intellectual function and clouding of consciousness, which may progress to convulsions, coma and death. A level of acute hypoxemia that might be dangerous to a previously healthy individual may be well tolerated by patients with chronic hypoxia. Hypoxemia stimulates ventilation via the carotid chemoreceptor, increases heart rate and cardiac output and dilates peripheral vessels. Cardiac dysrhythmias may occur, which may be exaggerated by concomitant digitalis or hypokalemia.[7] The pulmonary arteries respond to hypoxia by

vasoconstricting, producing increased vascular resistance and pulmonary hypertension, with the later development of right ventricular enlargement or cor pulmonale. Persistent hypoxia results in secondary polycythaemia due to increased production of erythropoietin.

Clinical features of hypercarbia

The effects of hypercarbia are variable from patient to patient. There is a poor correlation between $PaCO_2$ and the development of these effects, as changes in $PaCO_2$ may be more important than the actual level. The central nervous system (CNS) manifestation of hypercarbia is irritability, confusion, somnolence and coma.[8,9] Coma is uncommon in patients with COPD and respiratory failure when breathing room air because the level of $PaCO_2$ necessary to cause coma is usually associated with a PaO_2 incompatible with life.[10] The rapidity of the increase in $PaCO_2$ and the severity of the associated hypoxaemia also contribute to the level of consciousness. Hypercarbia also produces tremor, myoclonic jerks, asterixis, and even seizures.[8] The vasodilator properties of CO_2 may results in increased cerebral blood flow and an increase in intracranial pressure, producing headache and papilloedema.[9,11] Hypercarbia tends to dilate the vessels of the peripheral circulation by a direct effect on vascular smooth muscle, but also produces vasoconstriction by sympathetic stimulation. These properties result in a warm flushed skin with a bounding pulse.[12] Sympathetic stimulation is also responsible for tachycardia and sweating. Marked hypercarbia, producing generalized vasodilation, may be associated with hypotension. Other features occasionally encountered in severe and well-established respiratory failure are gastric dilation and paralytic ileus. Headache on waking is common in chronic hypercarbia, presumably due to a progressive increase in CO_2 retention during sleep.

Diagnosis

The mainstay of diagnosis of respiratory failure is arterial blood gas analysis. The conventional definition of respiratory failure is a PaO_2 of < 60mmHg when breathing air at sea level.[13] Since mixed metabolic and respiratory acid-base disturbances can occur, and because a rise in $PaCO_2$ is a normal compensatory response to metabolic alkalosis, it is important to measure the arterial pH or to determine the primary acid-base disturbance. In addition the chronicity of respiratory failure should be assessed by evaluating the pH and the degree to which this is compensated by an increase in the serum bicarbonate. An acute increase in $PaCO_2$ of 10mmHg is roughly associated with a decrease in pH of 0.08 units and an increase in serum bicarbonate of 1 mEq/L, whereas a chronic increase in $PaCO_2$ of 10mmHg is associated with a decrease in pH of 0.03 units and an increase in bicarbonate of 3.5 mEq/L.[14,15] Plotting blood gas and acid-base parameters on an acid-base diagram is a useful way of determining the acid-base status and also following the response to treatment in patients with acute exacerbation of COPD and respiratory failure.

MANAGEMENT

The management of acute respiratory failure varies according to the etiology. The primary aims of treatment are (i) to maintain a patent airway and ensure adequate alveolar ventilation and oxygenation; and (ii) to treat, the primary condition.

- **Type 1 respiratory failure**

  This condition usually presents little difficulty and apart from the use of oxygen, treatment of the primary cause (e.g. antibiotics for lobar pneumonia), may be all that it required.

  Arterial hypoxemia when extremely severe can be life threatening and therefore should have the highest priority when managing acute respiratory failure. The goal should be to increase hemoglobin O_2 saturation to at least 85-90% without risking significant oxygen toxicity. Very high FiO_2 levels can be safely used for brief periods of time. The use of positive end-expiratory pressure (PEEP), changes in position, sedation and paralysis may be helpful in lowering FiO_2. Fever, agitation, overfeeding, vigorous respiratory activity and sepsis can all markedly increase VO_2. Measures to eliminate these factors should be undertaken.

  Prolonged exposure to high concentration of oxygen (FiO_2>50%) should be avoided because pulmonary toxicity depends on both the duration of treatment and FiO_2.[16] Failure of high FiO_2, to improve PaO_2 implies a significant intrapulmonary shunt, as occurs in ARDS. ARDS is the most severe form of acute lung injury and is characterized by bilateral, widespread radiographic pulmonary infiltrate, normal pulmonary capillary wedge pressure (≤18 mm Hg) and a PaO_2/FIO_2 ratio ≤ 200 regardless of level of positive end-expiratory pressure (PEEP). Acute lung injury (ALI) is a mild form of ARDS, and differs from ARDS based on less severe hypoxemia (PaO_2/FIO_2 ratio ≤ 300).[17] The mainstay of supportive care of ALI/ARDS is mechanical ventilation.[18]

The general indication for mechanical ventilation are

1. Inadequate oxygenation despite an increasing FiO_2;
2. Increased $PaCO_2$ associated with decreased mental status or increasing fatigue;
3. Failure to control secretions.

Ventilation with small tidal volumes (≤ 6 ml/kg) and limited airway pressures (Lung protective ventilation) can reduce ventilator-associated lung injury from over distension in patients with ALI/ARDS, because one of the clinical hallmarks of ALI/ARDS is decreases respiratory system compliance.[19] Clinical evidence supporting this strategy came initially from two observational studies[20,21] in which mortality rates of ARDS patients treated with small tidal volumes and permissive hypercapnia were compared to mortality rates predicted from historical control subjects. A large trial by the National Institute of Health (NIH) ARDS Network[22] of traditional vs. lower tidal volume ventilation in patients with or at risk for ALI/ARDS, revealed that, mortality was reduced substantially from 40% [traditional strategy (tidal volume of 10-15 ml/kg)] to 31% (lower tidal volume strategy). These were also more ventilator-free and organ-failure-free days in patients who received the lower volume strategy.

Most ALI/ARDS patients require support for arterial oxygenation with a combination of increased FiO_2 and PEEP. Both of these treatments have potential adverse effects that must be carefully considered in individual patients. In humans, no detectable oxygen toxicity occurred in normal subjects when the FiO_2 was <50%,[23] but impaired gas exchange was apparent after

breathing 100% oxygen at sea level for approximately 40 hours.[24] Diseased lungs may be more susceptible to injury from moderate hyperoxia.[25] Although the relationship of FiO_2 to oxygen induced lung injury has not been clearly defined in ALI/ARDS patients, a $FiO_2 \leq 0.6$ is usually considered to be safe.[26] PEEP reduces intrapulmonary shunt and improves arterial oxygenation,[18] thus allowing adequate arterial oxygenation at a lower FiO_2, which may reduce pulmonary oxygen toxicity. However adverse effects of PEEP include decreased cardiac output,[27] increased pulmonary edema formation, increased dead space, increased resistance of the bronchial circulation, and increased lung volume and stretch during inspiration which may cause further lung injury or barotrauma. Thus, beneficial effects of PEEP on arterial oxygenation must be weighed carefully in relation to potential adverse effects.[28] The best strategy for using PEEP and FiO_2 in individual patients has not yet been defined. Several other promising new approaches for improving pulmonary gas exchange are currently being assessed in clinical trials and could contribute further to improve outcomes in patients with ALI/ARDS. They are, high frequency ventilation; lung protective ventilation with higher PEEP; non-invasive positive pressure ventilation; tracheal gas insufflation; proportional assist ventilation; inverse ratio ventilation and airway pressure release ventilation; surfactant replacement therapy; extracorporeal gas exchange; prone positioning; and fluorocarbon liquid-assisted gas exchange.[28] None of these modalities are found to be unequivocally beneficial, although prone position ventilation is found to be beneficial in uncontrolled studies. Detailed description of these modalities is beyond the scope of this chapter.

Type 2 respiratory failure

By far the commonest cause of type 2 or hypercapnic respiratory failure is an exacerbation of COPD.

The development of arterial hypoxaemia occurs insidiously in most patients with COPD, although in some the fall in PaO_2 can be rapid. Hypoxaemia that develops slowly may produce little effects and chronic hypercapnia can be tolerated for many years with few symptoms, although early morning headache is relatively common. Many patients tolerate arterial hypoxaemia well for many years before decompensation occurs.

Once acute respiratory failure is suspected the diagnosis must be confirmed by arterial blood gas analysis. The pH (hydrogen ion concentration) is helpful in assessing the degree of acute vs. chronic respiratory failure.

The general principles of management are : (i) to correct life threatening hypoxaemia; (ii) to correct life threatening acidosis; (iii) to treat the underlying cause; and (iv) to prevent complications.

- ***Relief of hypoxaemia***

  The first priority in treatment of acute-on-chronic respiratory failure that occurs during exacerbations of COPD is the relief of hypoxia by the cautious administration of oxygen.

  Supplemental oxygen should be administered by nasal prongs with flow of 1-3L/min or by a Venturi mask with flow set to deliver 24-28% oxygen.[29] The Venturi mask produces the most predictable inspired oxygen concentration. Concentrations from nasal prongs are less predictable, but the device is better tolerated by patients. The goal of supplemental oxygen therapy should be to achieve a PaO_2 of greater than 60mmHg.

- ***Non-invasive ventilation in exacerbation of respiratory failure***

  Non-invasive positive pressure ventilation (NIPPV) is increasingly being used in the care of patients suffering from acute respiratory failure. NIPPV is a novel method of giving positive pressure ventilation without endotracheal intubation. A tightly fitting nasal or oronasal mask is used for transmitting positive pressure ventilation. The distinct advantage of NIPPV is avoiding endotracheal intubation and its associated complications. However, this modality has its limitations. The patient should be conscious enough to cooperate in using the mask and should have intact respiratory drive. These must be understood for the optimum use of non-invasive positive pressure ventilation (NIPPV).

  High-level evidence supports the use of NIPPV to treat exacerbation of COPD. NIPPV has also been successfully used with selected patients suffering acute hypoxemic respiratory failure and to allow earlier extubation of mechanically ventilated COPD patients. The evidence for NPPV for acute cardiogenic pulmonary edema is inconclusive. With selected patients NIPPV decreases the rate of intubation, mortality, and nosocomial pneumonia. Predictors of NIPPV failure include greater severity of illness, lower level of consciousness, lower pH, more air leak around the patient-mask interface, greater quantity of secretions, poor initial response to NIPPV, and the presence of pneumonia. NIPPV obviates intubation in >50% of appropriately selected patients.[30]

- ***Mechanical ventilation***

  Approximately half of patients suffering from hypercapnic respiratory failure (COPD exacerbations) respond favourably to medical therapy, half of those within first 24 hrs and 92% within 72 hrs.[31] Therefore, half of patients require some form of ventilatory support.

  In most non-surgical patients being considered for mechanical ventilation the indications are clear-cut in that adequate respiratory effort cannot be maintained using other supportive means and alveolar hypoventilation occurs, as shown by a high or rising $PaCO_2$ and a falling pH. Patients with non-hypercapnic respiratory failure can be maintained initially by increasing the concentration of inspired oxygen via a conventional or full face mask with CPAP. Modest gains in oxygenation must be balanced against the risks of intubation and positive pressure ventilation.

  In patients with hypercapnic respiratory failure, if conventional treatment and non-invasive ventilation have failed then without mechanical ventilation the patient will die. In clinical practice, a PaO_2 of less than 60mmHg, despite a FiO_2 of greater than 0.6, and hypercapnia are the common indications for ventilation. Patients with COPD can obviously have high stable levels of $PaCO_2$ without evidence of respiratory distress. Other factors that favor the institution of mechanical ventilation are a rapid increase in hypercapnia, producing uncompensated respiratory

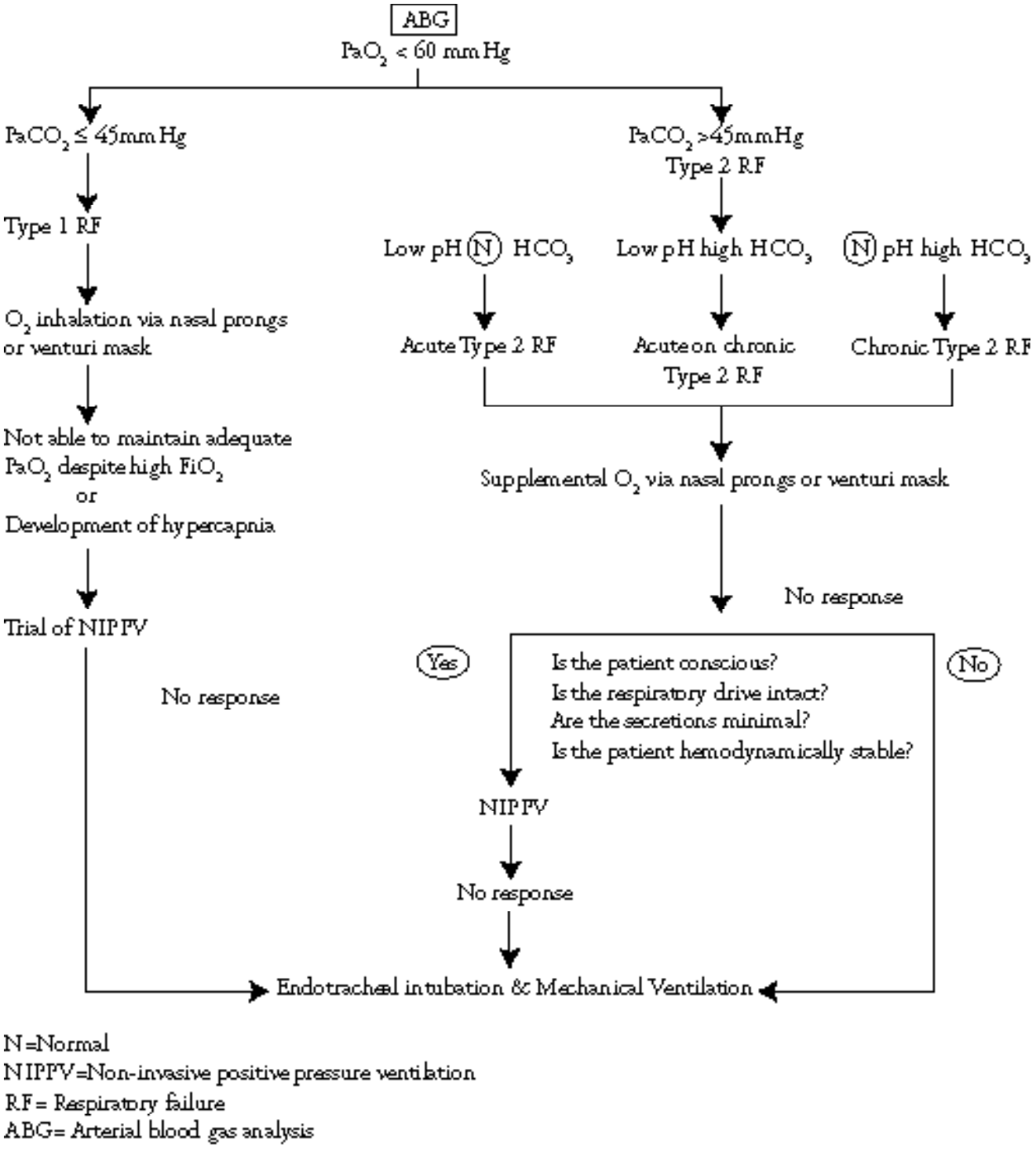


Fig. 2 : Algorithmic approach to a patient with acute respiratory failure

acidosis, mental confusion due to either severe hypercapnia or hypoxemia, tachypnoea (>35 breaths/min) and a clinical judgment of impending exhaustion in the patient.

Although patients who require intubation have the worst prognosis, the vast majority of them can be successfully liberated from mechanical ventilation. For invasively ventilated patients the clinical emphasis should be on improving patient ventilator interaction and avoiding dynamic hyperinflation (intrinsic positive end-expiratory pressure).[32] Management of acute respiratory failure in patients with COPD by mechanical ventilation cannot be in isolation. Others supportive measures such as bronchodilator therapy, systemic corticosteroids, and antibiotics to treat infection, which are found to be beneficial in the treatment of COPD exacerbation in several randomized controlled trial and meta analyses should be provided to the patients.

- ***Weaning and extubation***

  Weaning is the gradual withdrawal of mechanical ventilatory support. Each day of mechanical ventilation increases morbidity and the risk of mortality. So every patient needs to be assessed for possible weaning and extubation as soon as possible once the condition of the patient improves. In patients who have had brief periods of mechanical ventilation, the manner in which ventilatory support is discontinued often is not crucial. In patients with marginal respiratory functions, chronic underlying lung disease or in completely improved respiratory conditions, the weaning method may be critical to obtaining a favorable outcome. Successful weaning depends on the condition of the patient and on the status of the cardiovascular and respiratory systems, which should be evaluated in detail before deciding on weaning the patient from ventilator. Various modes of weaning include, synchronized intermittent mandatory ventilation (SIMV), pressure support ventilation (PSV) and spontaneous T piece breathing trial. Pressure support ventilation and spontaneous T piece breathing trial are found to be superior than synchronized intermittent mandatory ventilation in successful weaning of patients from mechanical ventilation. Algorithmic approach for the diagnosis and management of a patient with acute respiratory failure is shown in Fig. 2.

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