Chapter

Respiratory Support for Obstructive Syndromes

Alexey Gritsan

Abstract

This chapter will present data on the biomechanics of respiration and gas exchange in acute respiratory failure of obstructive etiology. This chapter delineates main general principles of respiratory support, including non-invasive ventilation, and "traditional" mechanical ventilation. The principles of choosing positive end-expiratory pressure (PEEP) depending on the auto-PEEP are substantiated. The most commonly used respiratory support parameters for obstructive acute respiratory failure are presented. It is argued that the volume control (VC) ventilation modality is preferable in patients with asthma, since in this regimen positive inspiratory pressure (PIP) and inspiratory plateau pressure (Pplat) can be directly controlled, in contrast to the pressure control (PC) ventilation modality. The main options for selecting the ventilation mode will be presented.

Keywords: COPD, bronchial asthma, respiratory support, ventilation graphics, obstructive pulmonary disease

1. Introduction

Chronic obstructive pulmonary disease and bronchial asthma exacerbation are manifested by severe respiratory failure, which requires various methods of respiratory therapy. To date, enough information has already been accumulated to develop clinical recommendations for respiratory support in these diseases. We believe that special attention should be paid to the biomechanics of respiration in obstructive pulmonary diseases, the algorithm (step by step) of respiratory support, and indications and contraindications for non-invasive ventilation of the lungs. The choice of parameters for conventional lung ventilation is presented within the framework of the concept of protective ventilation; all the main complexities of mechanical ventilation management are identified; as well as the principles of weaning the patient from the ventilator.

2. Biomechanics of respiration and gas exchange in acute respiratory failure of obstructive genesis

It is well known that, like other skeletal muscles, the respiratory muscles can work with a load of about 60% of their maximum power indefinitely and without fatigue.

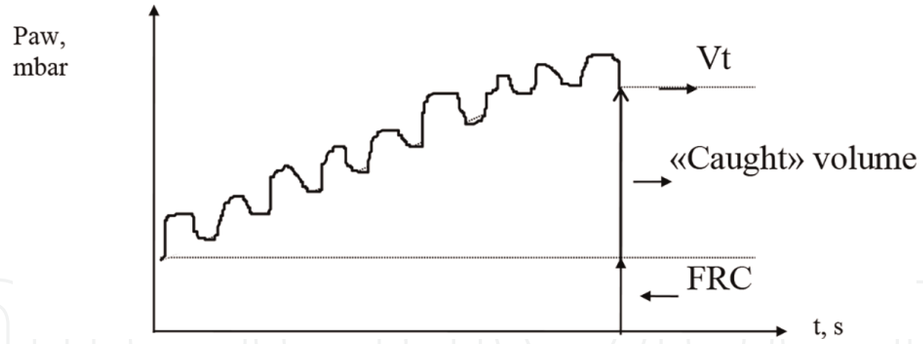

Figure 1.
Mechanism of formation of PEEPi, due to early expiratory closure of the airways (adapted from: Tuxen and Lane [1]).

Conceptually, if the load on the respiratory muscle's increases, or their maximum contractility decreases, then the respiratory muscles become fatigued, and eventually respiratory failure occurs. In bronchial asthma and chronic obstructive pulmonary disease (COPD), respiratory failure can occur against the background of the above factors (breathing demand and power (contractility) of the respiratory muscles).

Respiratory failure in bronchial asthma (BA) or obstructive pulmonary disease is associated with a sufficiently large increase in airway resistance (Raw) and increased work of breathing. As a rule, this is due to the presence of bronchospasm, the presence of a large amount of mucus in the tracheobronchial tree, inflammatory or fibrotic changes in the airways, or decreased lung compliance in emphysema.

The phenomenon of early expiratory airway closure that develops against this background leads to air entrapment (tidal volume (Vt) > exhaled tidal volume (Vte)), an increase in functional residual lung capacity (FRC), and, consequently, to overdistension of the alveoli with the formation of internal positive end-expiratory pressure (PEEPi) (**Figure 1**). The captured volume increases FRC and results in PEEPi (auto-PEEP). After each respiratory cycle, the "residual" volume increases. The consequence of these disorders is increased work of breathing, hypoxemia, and hypercapnia.

It is important to note that in bronchial asthma, these changes are usually acute (occuring during an exacerbation), while in COPD, the patient may be on the verge of respiratory muscle fatigue almost constantly, because of which even small changes in his somatic status can lead to respiratory failure.

Acute respiratory failure (ARF) of obstructive genesis is usually accompanied by overdistension of the lungs, which in most cases moves spontaneous breathing to a higher (less elastic) part of the volume/pressure curve (Vt/Paw), which inevitably leads to an increase in the elastic and resistive components of the work of breathing [2].

An increase in the work of breathing inevitably causes an increase in oxygen consumption and carbon dioxide production. Attempts to maintain the patient's $PaCO_2$ and pH at normal levels due to the more active work of the respiratory muscles lead to even greater production of CO_2.

Patients with COPD also have higher levels of dead space ventilation (up to 60–70% of Vt), which inevitably requires even higher minute ventilation and more work of the respiratory muscles to maintain pH at a safe level.

In patients with COPD, the activity of the respiratory center is also increased, but they are not capable of it in response to an additional load on the respiratory muscles.

The high stimulus manifests itself in high inspiratory flow rates with a corresponding increase in the work of breathing during the inspiratory phase. This failure of the respiratory center may add a central component to the development of respiratory failure.

As the demand for work of breathing increases, the ability of the respiratory muscles to do work is hampered by the obstructive process. Hyperdistention of the lungs is the single most significant mechanism in COPD, acting in such a way that the diaphragm enters a biomechanically unfavorable position in which it becomes unable to perform adequate work of breathing. Therefore, prevention and correction of lung hyperdistention are the two main goals of respiratory support in the management of patients with obstructive acute respiratory failure.

It is generally known that the tension developed by a contracting muscle is directly proportional to the length of the muscle at rest. In an emphysematous (inflated) chest, the diaphragm flattens and therefore geometrically shortens. The resulting shortening of the muscle fiber in the relaxation (rest) phase reduces the maximum level of contraction that can develop with diaphragmatic contraction.

The tension (T) that occurs in this case is inversely proportional to the speed of muscle contraction. When a patient with COPD or asthma and respiratory failure breathes rapidly and shallowly, the rate of diaphragmatic contraction increases, and maximum tension decreases. The amount of pressure that can be generated by a contracting diaphragm is determined by La Place's law:

$$P = 2T/R, \tag{1}$$

which means that the transdiaphragmatic pressure (P) for a given contraction is inversely proportional to the radius (R) of the curvature of the diaphragm. The increased radius of the flattened diaphragm significantly hinders its force of contraction.

As the overstretched diaphragm descends, its position in relation to the ribs becomes more horizontal, which prevents the ribs in the lower chest from participating in the inspiratory phase (Hoover's syndrome).

It is important to remember that diaphragmatic contractility is also affected by hypoxemia, hypercapnia, and acidosis.

The level of gas exchange disorders in obstructive ARF is characterized by hypercapnia with mild to moderate hypoxemia. Hypoxemia is caused by the following combination of factors:

1. violation of the ventilation–perfusion ratio (VA/Q)

2. intrapulmonary shunting of blood (Qs/Qt)

3. decrease in alveolar oxygen tension (PAO_2) due to hypoventilation of the alveoli.

As a rule, hypoxemia is easily corrected by a moderate increase in the oxygen fraction in the inhaled gas mixture.

The increase in $PaCO_2$ is due to decreased ventilation, increased carbon dioxide production, and increased dead space (Vd). Hypercapnia may further increase with the correction of hypoxemia through (Haldane), the essence of which is to raise the level of $PaCO_2$ with an increase in PaO_2 [3].

Thus, changes in the biomechanics of respiration and gas exchange during exacerbation of chronic obstructive pulmonary diseases and bronchial asthma, on which the

tactics and strategy of respiratory support depend, are characterized by the following key criteria [4]:

1. increase in airway resistance (Raw)

2. increased work of breathing and flattening of the diaphragm

3. hyperextension of the lungs due to emphysema, the phenomenon of early expiratory airway closure, and a decrease in pulmonary-thoracic compliance (Clt) as a result

4. high Vd/Vt ratio

5. an increase in oxygen consumption and carbon dioxide production

6. hypercapnia and hypoxemia due to impaired VA/Q, Qs/Qt, and decreased PAO_2.

3. Basic principles of intensive care

The principles of intensive care in patients with obstructive acute respiratory failure depend on the severity of the ARF itself and are aimed at the following main goals:

1. elimination of bronchial obstruction (bronchodilators; corticosteroids; methods that facilitate the drainage of sputum from the tracheobronchial tree)

2. correction and maintenance of adequate gas exchange

3. maintaining adequate cardiac output against the background of PEEPi (infusion therapy, drugs for inotropic support of hemodynamics)

4. normalization of metabolism and acid–base state (ACS)

5. prevention of secondary bacterial infection (according to indications, the appointment of antibiotic therapy)

6. prevention of gastrointestinal bleeding against the background of the use of glucocorticosteroids (stress ulcer prophylaxis)

In this chapter, we will focus more on methods of correcting and maintaining adequate gas exchange using various respiratory support options.

4. Respiratory support

In the 80s, on an average, about 15–16% of patients with acute severe bronchial asthma required intubation and mechanical ventilation [5–7], while currently it is 2–4% on average [8, 9]. Bronchial asthma is a rather labile pathological process which may rapidly develop manifestations of acute respiratory failure requiring an

immediate initiation of mechanical ventilation. However, in some cases, "aggressive" therapy aimed at eliminating bronchospasm, removing sputum from the tracheobronchial tree and/or mask (non-invasive) positive pressure ventilation can avoid intubation and mechanical ventilation.

Emergency intubation of a patient with bronchial asthma may become necessary in the following cases [9]:

1. the presence of cyanosis, PaO_2 < 60 mm Hg (despite oxygen therapy)

2. progressively increasing hypercapnia ($PaCO_2$ > 55 mm Hg) with altered sensorium with a GCS score of 9 or less

3. the presence of pathological pattern of breathing, silent chest, or respiratory arrest

4. the appearance of life-threatening cardiac arrhythmias or cardiac arrest.

4.1 Evidence of progressive exhaustion

At the same time, it should be remembered that the lack of response to drug therapy, severe metabolic acidosis, persistent hypoxemia, and patient anxiety can also be indications for patient intubation and respiratory support.

In patients with chronic obstructive pulmonary diseases, indications of mechanical ventilation include alveolar hypoventilation, a decrease in pulmonary-thoracic compliance, inadequate work of breathing, and unstable neuro-respiratory drive [10]. It should be remembered that patients with COPD, depending on the neuro-respiratory drive, are divided into two types: "Pink Puffer"—an almost normal respiratory drive and "normal" $PaCO_2$ and "Blue Bloaters"—a reduced respiratory drive and increased $PaCO_2$.

Tracheal intubation should be performed using a low-pressure cuffed endotracheal tube, and the largest possible endotracheal tube diameter should be used to reduce airway pressure levels. Orotracheal intubation is less comfortable for the patient, and there is a greater risk (compared to nasotracheal intubation) of unintentional extubation.

The main tasks of respiratory support in obstructive ARF are as follows:

1. maintaining alveolar ventilation

2. maintaining oxygenation at a sufficient level

3. ensuring the rest of the respiratory muscles, sufficient to recover from the state of fatigue that accompanies ARF.

However, it should be remembered that mechanical ventilation is a form of "physiological" support and should be carried out in combination with "aggressive" drug therapy for the underlying disease. Respiratory support should not exacerbate existing pathophysiological processes; it should be carried out in such a way as to minimize the occurrence of various complications. Withdrawal of respiratory support should not be attempted until the patient's underlying condition and comorbidities (if any) have improved.

4.2 Respiratory support algorithm

Correction and maintenance of gas exchange at various stages of intensive care in obstructive ARF is carried out using various types of mechanical ventilation modes: continuous mechanical ventilation (CMV), assist control mechanical ventilation (A/C MV), continuous positive pressure ventilation (CPPV), pressure support ventilation (PSV), intermittent mandatory ventilation/synchronized intermittent mandatory ventilation (IMV/SIMV), or continuous positive airway pressure (CPAP) or their analogues.

Because airway resistance (Raw) can change very quickly in this type of acute respiratory failure, pressure-controlled (PC) ventilation cannot guarantee adequate minute ventilation. Therefore, volume-controlled ventilation (VC, CMV) is preferred for most patients. A high level of Raw can lead to quite high values of peak inspiratory pressure (PIP), and therefore, a modern respirator is needed that can provide a given Vt at a PIP of at least 80 mbar. However, in some cases, when ventilation in VC (CMV) mode is unable to overcome high airway resistance, it may be necessary to switch to PC mode. In such a situation, dynamic control of the gas composition of the blood, SaO_2 and $PetCO_2$, is mandatory.

Typically, the starting mode of ventilation for patients with obstructive ARF is A/C MV. CMV is preferred for restless patients who have difficulty in comfortable synchronization with the ventilator and for patients with extremely high PIPs. Complete control of the patient's ventilation can be achieved through continuous sedation as well as the administration of muscle relaxants. Typically, CMV is continued until airway resistance and wheezing decrease. In patients with BA, improvement in the condition can be observed within a few hours, while in COPD this process may extend for several days.

Modes A/CMV or SIMV (or their equivalents) are more suitable for patients with comorbidities who are not prone to hyperventilation. However, when using these modes of respiratory support, the respiratory muscles perform part of the work of breathing, most of which can be spent to initiate mechanical (hardware) inspiration. At the same time, the fatigue of the respiratory muscles will persist, and the dependence on the respirator will be prolonged. Patients with extremely high respiratory drive may ventilate with A/CMV or SIMV at a high respiratory rate, which will inevitably lead to an increase in PEEPi and hemodynamic disturbances.

The respiratory support algorithm for obstructive ARF is presented as follows (**Figure 2**).

Based on this algorithm, the tactics and strategy of respiratory support are carried out in the following order.

Firstly, attention is given to oxygen inhalation or the so-called oxygen therapy. This technique is not a separate option for respiratory support; however, oxygen inhalations quite often accompany medical treatment of patients with COPD and BA in a hospital setting. One of the main goals of oxygen therapy is to achieve a satisfactory level of oxygenation ($PaO_2 \geq 60$ mmHg or $SaO_2 \geq 90\%$), which is quickly achieved in non-severe forms of obstructive ARF.

Since asthma has a low level of carbon dioxide retention, oxygen therapy is prescribed with medications (if there are no obvious contraindications). The starting level of oxygen concentration varies within 40–50% through a face mask or at a rate of 5 l/min through nasal cannulas. Subsequently, based on the data of the gas analysis of blood, the oxygen fraction in the inhaled gas mixture is corrected.

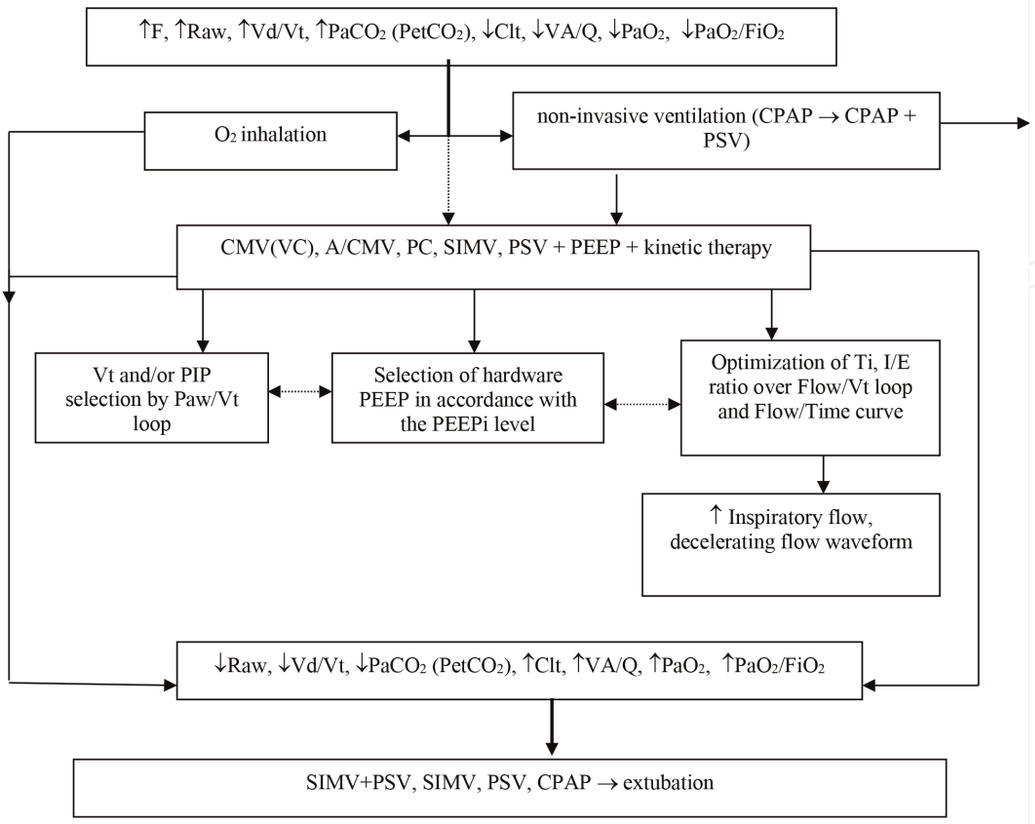

Figure 2.
Respiratory support algorithm for obstructive ARF.

At the same time, in most patients with COPD, the level of $PaCO_2$ in response to oxygen therapy will first increase by an average of 10–15, and then, it will stabilize. Therefore, a starting FiO_2 is set between 24 and 30% using a face mask or 3–4 L/min via nasal cannulas. At the same time, the $PaCO_2$ level should be carefully monitored (risk of carbon dioxide retention).

If, after 20–30 minutes of oxygen inhalation in a patient with obstructive ARF, the effectiveness of oxygen therapy is minimal or absent, and a decision should be made on the use of assisted ventilation.

When signs of ARF appear (increase in F, Raw, Vd/Vt, $PaCO_2$ ($PetCO_2$), decrease in Clt, V_A/Q, PaO_2, PaO_2/FiO_2), respiratory support begins with oxygen therapy or non-invasive ventilation (CPAP) followed by transition to CPAP + PSV. If NIV is ineffective, they switch to traditional mechanical ventilation in the following modes: CMV (VC), A/CMV, PC, SIMV, PSV + PEEP + kinetic therapy. Individual selection of Vt and/or PIP is carried out by the Paw/Vt loop, and the value of the hardware PEEP is selected in accordance with the level of PEEPi. Correction of Ti, I/E ratio is done on the Flow/Vt loop and flow/time curve by increasing the inspiratory flow rate and/or applying a decelerating flow waveform. With regression of signs of ARF (decrease in F, Raw, Vd/Vt, $PaCO_2$ ($PetCO_2$), increase in Clt, V_A/Q, PaO_2, PaO_2/FiO_2), respiratory support is withdrawn, followed by extubation. Detailed description is shown in the text below. Abbreviations: F—number of breaths, Raw —airway resistance, Vd/Vt—ratio of dead space ventilation to tidal volume, снижение Clt—pulmonary-thoracic compliance, V_A/Q—ventilation/perfusion ratio, CPAP—continuous positive airway pressure, PSV—pressure support ventilation,

CMV—continuous mechanical ventilation, VC—volume control, A/CMV—assisted CMV, PC—pressure control, SIMV—synchronized intermittent mandatory ventilation, PSV—pressure support ventilation, Vt—tidal volume, PIP—peak inspiratory pressure, Paw/Vt loop—tidal volume/airway pressure loop, PEEPi—internal positive end-expiratory pressure, Ti—inspiratory time, and I/E ratio—ratio of the phases of inhalation and exhalations.

4.3 Non-invasive respiratory support

Non-invasive respiratory support includes the actual non-invasive artificial ventilation of the lungs (through masks or helmets), as well as high-flow oxygenation through special nasal cannulas.

Non-invasive ventilation of the lungs (compared to "invasive" ventilation through an endotracheal tube and standard oxygen therapy) has several advantages and disadvantages.

The advantages of NIV over invasive ventilation are as follows:

1. absence of complications from tracheal intubation and prolonged need for the endotracheal tube

2. reduction in the frequency of nosocomial infections

3. reducing the need for medical sedation

4. the non-invasive nature of the procedure and its simplicity

5. the possibility of early mobilization of the patient

6. economic benefits.

The advantages of NIV over standard oxygen therapy through a face mask or nasal prongs are as follows:

1. providing positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP)

2. providing inspiratory pressure (Pinsp or inspiratory positive airway pressure (IPAP)) with inspiratory and expiratory trigger adjustment

3. adequate humidification and heating of the respiratory mixture.

The disadvantages of NIV are as follows:

1. the need for active cooperation of the patient with medical personnel

2. inability to apply high inspiratory and expiratory pressures

3. lack of direct access to the respiratory tract for oral hygiene

4. high risk of aerophagia

5. high risk of aspiration of the contents of the mouth and stomach

6. maceration and necrosis of the skin in places where the mask fits

7. hypoxemia when the mask is displaced

8. conjunctivitis

9. drying of the oropharynx and nasopharynx

10. nosebleed.

The use of non-invasive mechanical ventilation leads to an improvement in gas exchange, a decrease in the work of breathing, and an improvement in the prognosis compared with oxygen therapy alone (through a face mask or cannulas) in exacerbation of COPD (with the development of moderate respiratory acidosis ($7.35 > pH > 7.25$) and compensated ARF) [11–14].

The criterion for choosing non-invasive ventilation during exacerbation of COPD is the presence of respiratory acidosis, and not the level of hypercapnia: in the absence of respiratory acidosis, NIV has no advantages over standard oxygen therapy, at pH = 7.25–7.35 NIV should be used to prevent tracheal intubation, and when pH less than 7.20—as an alternative to mechanical ventilation [15–17].

In general, the main indications for the initiation of non-invasive respiratory support are the following clinical and laboratory criteria:

1. increase in the work of breathing (severe dyspnea at rest, respiratory rate > 25–30 resp./min, participation of accessory muscles, and abdominal paradox)

2. hypercapnia ($PaCO_2 > 45$ mm Hg and/or its progressive increase)

3. pH level < 7.35 and its progressive decrease

4. hypoxemia ($PaO_2 \leq 60$ mm Hg, $SaO_2 \leq 90\%$ with FiO2 = 0.4–0.5) and gas exchange disorders ($PaO_2/FiO_2 < 300$ mm Hg with FiO2 = 0.21, $Qs/Qt \geq 10\%$)

5. increase in airway resistance (Raw) from the norm by 1.5–2 times.

Non-invasive respiratory support should not be used in the following cases:

1. lack of spontaneous breathing (apnea)

2. unstable hemodynamics (hypotension, ischemia or myocardial infarction, life-threatening arrhythmias, and uncontrolled arterial hypertension)

3. inability to protect the respiratory tract (impaired coughing and swallowing) and a high risk of aspiration

4. excessive bronchial secretion

5. signs of impaired consciousness (excitation or depression of consciousness), inability of the patient to cooperate with medical personnel

6. facial trauma, burns, and anatomical disorders that prevent the installation of the mask

7. severe obesity

8. inability of the patient to remove the mask from the face in case of vomiting

9. active bleeding from the gastrointestinal tract

10. obstruction of the upper respiratory tract

11. discomfort from the mask

12. operations on the upper respiratory tract.

Tt is recommended to initiate non-invasive ventilation with a standard technique.

For non-invasive respiratory support, the PEEP (CPAP) mode with a pressure level of 5 to 10–12 mbar, or its combination with PSV (IPAP). Currently, NIV modes are practically no different from "invasive" ventilation modes (CPAP, CPAP + PS, pressure-controlled ventilation volume guaranteed (PCV-VG)), proportional auxiliary ventilation (proportional assist ventilation (PAV) and proportional pressure ventilation (PPV)), adaptive support ventilation (adaptive support ventilation (ASV)), in the settings of the device there is a setting for the backup mode of ventilation, and it is also possible to set both inspiratory and expiratory triggers. Randomized trials have not shown the benefits of any regimen for NIV [18–20].

The standard technique for conducting NIV is as follows:

- Set the value of PEEP 5 mbar
- Select the level of inspiratory pressure support (PS, IPAP) individually by stepwise increase from 5 to 8 mbar until reaching a tidal volume equal to 6–8 ml/kg of proper body weight (DMT) [calculation of DMT (kg) is carried out according to the following formulas: men = 50 + 0.91 × (height, cm—152.4), women = 45.5 + 0.91 × (height, cm −152.4)]. As a rule, this is achieved with a PS value of 10–16 cm of mbar.
- Set the minimum trigger sensitivity at which there is no auto-triggering (−1.5–2.0 mbar for pressure trigger, 2–3 L/min for flow trigger).
- Set the inspiratory fraction of oxygen in the inhaled gas mixture (FiO_2) to the minimum level that provides SpO_2 88–95%,
- Adjust the expiratory trigger sensitivity to improve synchronization with the ventilator (the standard setting of 25% is usually not suitable for patients with active inspiratory attempts and COPD, and such patients should set the sensitivity to 40–50%),

- Increase PEEP to 8–10 mbar in patients with SpO_2 less than 88% against the background of FiO_2 0.3 with an increase in PEEP tolerance.

High levels of PEEP/CPAP (>12 mbar) and/or PS (>20 mbar), despite a temporary improvement in oxygenation, lead to patient discomfort and reduced efficacy of NIV.

Reduction of dyspnea is usually achieved soon after an adequate ventilation regimen is established, while correction of hypercapnia and/or hypoxemia may take several hours.

In the first hours, assisted non-invasive ventilation of the lungs should be carried out continuously. Further, after a gradual decrease in respiratory support, it is possible to switch to NIV sessions for 3–6 hours a day until it is completely liberated.

It should be noted that NIV can also be carried out in volume, also equal to 6–8 ml/kg of proper body weight [21].

In the process of conducting NIV, it is necessary to monitor and evaluate the effectiveness of non-invasive ventilation of the lungs. If mask ventilation is ineffective, the patient should be intubated immediately, and "invasive" mechanical ventilation should be started.

Criteria for the ineffectiveness of NIV:

1. Inability of the patient to wear the mask due to discomfort or pain
2. Failure of mask ventilation to improve gas exchange or reduce dyspnea
3. The need for endotracheal intubation for secretion management and airway protection.
4. Hemodynamic instability
5. Myocardial ischemia or life-threatening arrhythmias
6. Impaired sensorium or delirium
7. Increase in F
8. Increasing the F/Vt ratio above 100
9. PaO_2/FiO_2 below 175 mm Hg one hour after the start of NIV
10. Increase in the $PaCO_2$.

4.4 Invasive (traditional) mechanical ventilation

In those cases when the patient's non-invasive ventilation is ineffective (or unavailable), invasive (traditional) ventilation is performed. This type of respiratory support is selected initially if there are indications for its implementation upon admission of the patient.

The main indications for the start of invasive mechanical ventilation are the following clinical and laboratory criteria:

1. ineffectiveness of non-invasive respiratory support

2. cyanosis, increased work of breathing (severe dyspnea at rest, respiratory rate > 35 resp./min, accessory muscle use, pathological rhythms of breathing, etc.)

3. severe hypercapnia ($PaCO_2$ > 55–60 mm Hg and/or its progressive increase)

4. severe acidosis (pH < 7.25 and its progressive decrease)

5. the presence of persistent and/or increasing hypoxemia ($PaO_2 \leq 50$ mm Hg, $SaO_2 \leq 85\%$ with $FiO_2 \geq 0.5$ or $PaO_2 < 35$ mm Hg when breathing atmospheric air) and gas exchange disorders ($PaO_2/FiO_2 \leq 200$ mm Hg, $Qs/Qt \geq 15\%$)

6. an increase in Raw from the norm by two times or more, and a decrease in Clt from the norm by 20–35%.

Initial modes (depending on the clinical situation) can be CMV (VC), PC, A/CMV, PSV, or SIMV (and their analogues). When using CMV, A/CMV, PC, and SIMV, it is most appropriate to use the following starting ventilation parameters: Vt = 6–8 ml/kg (with PC PIP level = 25–30 mbar), FiO_2 = 0.6, F = 80% of the age norm), I/E = 1:2, PEEP = 5 mbar, and flow = 35–40 l/min. If the PSV mode is selected, the selection of parameters is carried out similarly to the technique used for non-invasive PSV (see above).

A/CMV and PSV modes (or their analogues) require the installation of a trigger pressure on the respirator ((−1.5)–(−2.0) mbar) or flow (3–4 l/min).

Upon reaching, against the background of the above parameters of respiratory support, sufficient chest excursion, improvement in the conduction of respiratory sounds, $PaO_2 \geq 65$ mm Hg, SaO_2 = 93–95%, the oxygen concentration in the inhaled gas mixture is reduced to 0.45–0.3 under the control of SaO_2.

If the movements of the chest are limited, then it is necessary to increase Vt in steps by 30–50 ml (or PIP by 2–3 mbar) until a "normal" level of chest excursion is reached and evaluate the result.

While maintaining PaO_2 at a level of less than 60 mmHg at FiO_2 = 0.6, it is necessary to increase the level of PEEP in steps of 1–2 mbar until $PaO_2 \geq 65$ mm Hg, $SaO_2 \geq 92\%$.

Hypoxemia in obstructive ARF is usually a consequence of alteration of the ventilation–perfusion ratio and easily responds to a moderate increase in FiO_2. Setting FiO_2 = 30–45% is usually sufficient for SaO_2 > 90% or PaO_2 = 60–70 mmHg [2, 22]. High levels of oxygen concentration in the inhaled gas mixture may be necessary for patients with concomitant shunt-diffusive respiratory failure associated with acute respiratory distress syndrome, pulmonary edema, etc.

Further, after the improvement of oxygenation, hypercapnia, acidosis, the phenomenon of early expiratory closure of the airways and hyper distension of the lungs are corrected by optimizing the main parameters of respiratory support (Vt, MV, PEEP, Ti, I/E, and flow) in accordance with the concept of "safe" mechanical ventilation.

During selection of tidal volume, it is advisable to carry out based on the analysis of the Vt/Paw loop as follows: a stepwise increase or decrease in Vt by 20–30 ml until the "beak" appears or disappears on the volume/pressure loop (when ventilation is in PC mode, change the PIP value step by step by 1–2 mbar). That is, with the "optimal" Vt, there should not be a "beak" on the Vt/Paw loop.

Minute ventilation (MV) should be managed to correct the patient's respiratory acidosis over several hours by changing the number of machine breaths and/or Vt. It is important to note that pH is a much more important parameter than the $PaCO_2$ at which this pH is reached. Rapid correction of hypercapnia and acidosis can lead to post-hypercapnic metabolic alkalosis, hypokalemia, and hypophosphatemia.

In patients with COPD, one should not achieve a $PaCO_2$ value of 40 mm Hg and a pH of 7.40, since it is more physiological for them to maintain these indicators at the level that they have in remission. Slight hypercapnia and a moderate decrease in pH to 7.35–7.38 will help to avoid the occurrence of alkalosis and will not cause a decrease in neuro-respiratory drive or an increase in the severity of ARF during the transition to spontaneous breathing [2, 22].

4.4.1 Internal positive end-expiratory pressure and selection of hardware positive end-expiratory pressure

In everyday clinical practice, the most difficult is the selection of positive airway pressure, considering the level of internal positive end-expiratory pressure (PEEPi) [23].

PEEPi is the result of overstretching and high residual volume. PEEPi is detected in most patients with obstructive respiratory failure at levels often exceeding 10 mbar [24, 25]. If the expiratory time is insufficient, the high alveolar pressure will encourage exhalation to continue at the start of the next ventilatory breath. PEEPi has the same hemodynamic consequences as externally applied PEEP and can cause significant hypotension with tachycardia after just a few machine breaths in hyperventilated patients. Quickly disconnecting the patient from the ventilator helps identify the cause of hypotension, as blood pressure returns to normal immediately.

PEEPi also places additional stress on the respiratory muscles and contributes to the difficulty in withdrawing respiratory support. The value of auto-PEEP can be minimized by limiting the value of Vt and the frequency of machine breathing, as well as by lengthening the exhalation time and machine PEEP.

Clinical experience has shown that two techniques can be used to select the "optimal" level of PEEP and eliminate the phenomenon of early expiratory airway closure.

The essence of the first (the simplest) is to titrate the hardware PEEP (from the starting level) in steps of 1–2 mbar until the moment when, during auscultation of the lungs, the patient's exhalation becomes audible until the start of the next hardware breath.

The second technique is carried out under the control of $PaCO_2$ and $PetCO_2$ as follows:

1. The arithmetic difference between the partial tension of carbon dioxide in arterial blood and PetCO2 is determined, which in obstructive ARF varies within 8–15 mm Hg, with the norm of this difference being 4.5–6.0 mm Hg. That is, the utilization of carbon dioxide with exhaled air is insufficient.

2. The titration of the hardware PEEP begins by increasing it by 1 mbar every 5–7 min. When the level of PEEP becomes approximately equal to PEEPi, the utilization of CO_2 from the alveoli increases, which is accompanied by an

increase in $PetCO_2$ by an average of 15–25% of the initial level. An increase in $PetCO_2$ is observed within 20–40 min, followed by a decrease to 37–40 mm Hg.

In both cases, after selection, the value of the hardware PEEP varies within 9–14 mbar.

The criteria for obtaining an effect when using the methods are as follows: (1) a decrease in $PaCO_2$ by 25–35% of the initial level (according to the control gas analysis of blood taken 2–3 hours after the selection of PEEP); (2) spontaneous synchronization of the patient with the respirator, including after the abolition of sedation and/or muscle relaxation (if they were used).

4.4.2 Further steps of the respiratory support algorithm

The next step in "optimizing" the respiratory support parameters is the selection of the inspiratory time and the I/E ratio.

As previously stated, since lung hyper distension is always present in obstructive ARF, normalization of lung volume becomes the main goal. Functional residual capacity (FRC) depends on the ratio between the time needed to empty the lungs and the time to exhale. If the duration of the expiratory phase is insufficient, then the functional residual capacity of the lungs will exceed the normal FRC value. Each successive breath progressively increases lung volume until a new steady state is reached, typically 2–4 L above normal FRC [26, 27].

The time required to empty the lungs is a function of Raw and Clt and can be represented as a time constant (TC) that is the product of Raw and Clt. Since the time constant is the time required for exhalation from the lungs of 63% of the tidal volume that originally entered the lungs, the normal time constant for humans is about 0.42 s, while in COPD or bronchial asthma, these values are twice as high. Therefore, to avoid air entrapment, the expiratory time (Te) should be 3.5–4.0 TC, or 2.5–3 s [27, 28]. Large tidal volumes can also increase gas retention in the lungs.

Thus, to ensure sufficient expiratory time, Ti should be set as short as possible, and the I/E ratio should be set equal to 1: 2–1:4. At frequencies of 8–12 breaths/min, 4–6 s in each respiratory cycle will be available for exhalation, which in most cases is sufficient to ensure a full exhalation.

In addition to the empirical selection of inspiratory time and I/E ratio, it is advisable to use a graphical analysis of the flow/Vt loop and the flow/time curve (**Figure 3**). Increasing the length of expiration time by decreasing Ti and/or the number of machine respiratory cycles is carried out until a completely closed flow/Vt loop is obtained and the expiratory flow reaches the isoline on the flow/Vt curve at the end of inspiration.

Reducing the inspiratory time, of course, requires a change in the inspiratory flow rate (flow) to deliver a given tidal volume to the airways. That is, "large" Vt and short Ti require high flow rates.

However, one should not forget that the inspiratory flow delivered at a high level of airway resistance (which is present in patients with obstructive ARF) during ventilation in the CMV (VC) mode leads to an increase in peak inspiratory pressure (PIP). Because high PIP has long been suspected of causing pneumothorax and pneumomediastinum, it has been recommended that initial inspiratory flow rates are limited to 35–40 L/min. However, in practice, most of the peak inspiratory pressure is dissipated in the airways and is a less important factor in barotrauma than lung overdistension. Therefore, peak inspiratory flow rates reaching (if necessary for a particular patient) 80–100 l/min can be used [1, 5, 8, 27].

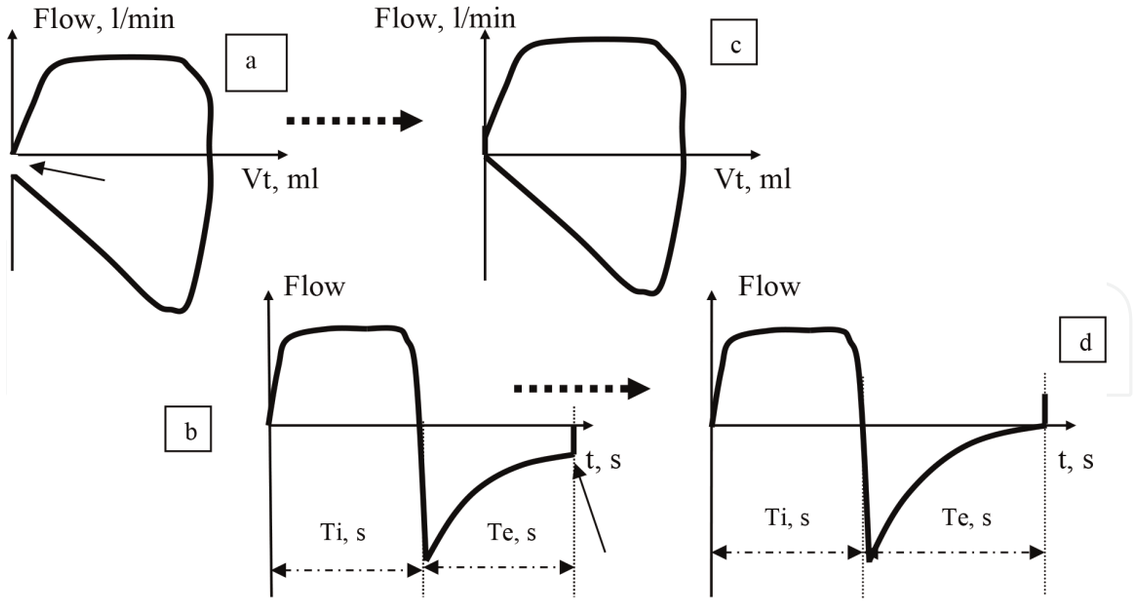

Figure 3.
Selection of inspiratory time (Ti) and exhalation time (Te)—According to the flow/Vt loop and the flow/t curve. The left side of the figure (a) shows an open flow/Vt loop (a) (shown by a solid arrow) and a flow/Vt curve (b) in which the expiratory flow to the beginning of the next breath (shown by a solid arrow), indicating insufficient time to ensure adequate exhalation (lung emptying). The right side of the figure shows the same graphs after adjusting Ti and expiratory time Te: The flow/Vt loop is closed (s), and the expiratory part of the flow/time curve reaches the isoline by the time the next breath begins (d).

If the technical capabilities of the respirator allow you to change the waveform of the inspiratory flow, then it is better to use a decelerating waveform, which leads to better gas exchange in the lungs compared to a constant or sinusoidal waveform of the inspiratory flow.

In general, based on this algorithm for the individual choice of mechanical ventilation options, it offers for everyday clinical practice the most used parameters of respiratory support for obstructive ARF, presented in **Table 1**.

Parameter	**Values**
Ventilation mode	VC
F, breath/min	8–14
Pplat, mbar	No more than 30
PEEP, mbar	5–15
I/E, ratio	1:3.0–1: 4.0
Ti, s	0.7–1.5
Te, s	4–5
Flow, l/min	Up to 80–100
Vt, ml/kgPBW	6–8
FiO_2 (0.21–1.0)	0.3–0.5 (until SaO_2 is 94%)

Table 1.
Most commonly used respiratory support parameters for obstructive acute respiratory failure (based on data from Laher and Buchanan [9]).

5. Difficulties in managing mechanical ventilation

Key issues related to the provision of mechanical ventilation in patients with acute and severe asthma and exacerbation of COPD include (1) methods for assessing pulmonary hyperinflation (described at the beginning of this chapter), (2) the effect of mechanical ventilation parameters on the severity of hyperinflation, and (3) the consequences and correction of hypercapnia [8].

It is known that the most common method for assessing hyperinflation is to measure the inspiratory plateau pressure (Pplat) and PEEPi during mechanical ventilation (**Figure 4**).

It should be remembered that PEEPi in severe asthma is often in the range of 10 to 15 mbar (cm H_2O) but may be higher.

Hypercapnia is common with mechanical ventilation in patients with severe asthma. At the same time, the $PaCO_2$ level can reach 68 mm Hg, at a pH less than 7.2, and a minute ventilation of 9 l/min [8]. However, the term "permissive" hypercapnia may not be entirely accurate when applied to severe asthma. Since hypercapnia is a consequence of increased dead space ventilation, attempts to lower $PaCO_2$ by increasing minute ventilation will lead to increased hyperinflation and a further increase in physiological dead space.

Serious adverse effects of hypercapnia are rare. Of greatest concern is the effect on the central nervous and cardiovascular systems. Cerebral edema and subarachnoid

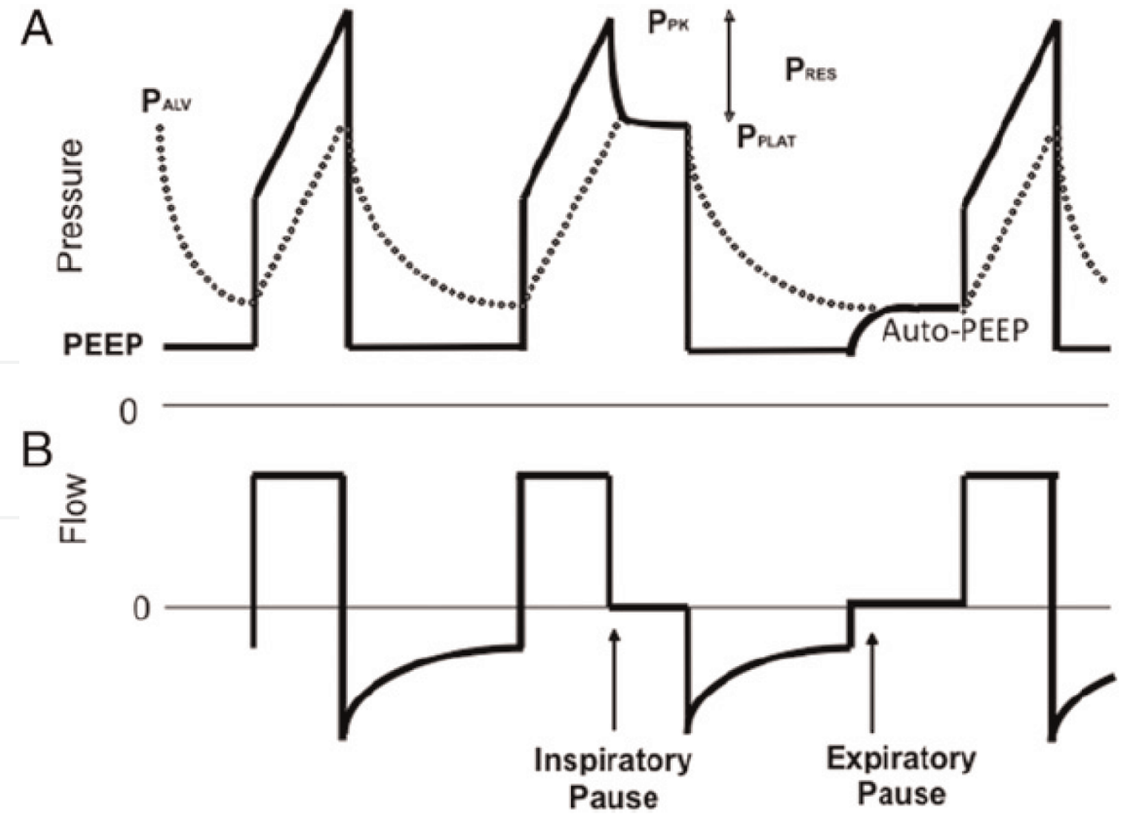

Figure 4.
Schematic representation of airway pressure (A) and flow (B) during mechanical ventilation. Note that the flow is maintained at the end of exhalation, indicating that the final exhalation of alveolar pressure exceeds circuit pressure (i.e., PEEPi is present). The dotted line represents Palv. Palv—Alveolar pressure; PEEP—Positive end-expiratory pressure; Ppk—Peak inspiratory pressure; Pplat—Inspiratory plateau pressure; Pres—Inspiratory airway resistance.

hemorrhage have been associated with hypercapnia but are rare. Acute hypercapnia increases cerebral blood flow and intracranial pressure, an effect of greatest concern in the setting of cerebral anoxia due to circulatory arrest prior to intubation. The cardiac effects of acute hypercapnia include a decrease in intracellular pH, which decreases contractility, but sympathetic activation more than compensates for this direct effect on cardiac contraction and cardiac output, which tend to increase. Arrhythmias associated with hypercapnia are not uncommon in the absence of underlying heart disease.

Alkaline agents may be considered when arterial pH is consistently less than 7.1. Unfortunately, sodium bicarbonate has a limitation in correcting respiratory acidosis. The CO_2 produced readily permeates cell membranes and can potentially lead to a significant decrease in intracellular pH during rapid infusions. In addition, even partial correction of severe respiratory acidosis may require several hundred milliequivalents of sodium bicarbonate. Therefore, in the absence of an urgent reason to correct the acidosis (e.g., severe arrhythmias, hyperkalemia, and unexplained hemodynamic instability), it may be prudent to withhold "alkaline therapy" and wait for the hypercapnia to decrease. Many patients experience a decrease in hypercapnia during the first 12 hours of intubation.

Another important point, especially for patients with asthma exacerbation, is the choice of ventilation mode.

The choice of ventilation mode must consider the degree of lower airway resistance and the presence of alveolar hyperinflation and "permissive" hypercapnia (as above). A high PIP, together with an increase in the pressure gradient of PIP to Pplat in the analysis of the graphical ventilation curves, indicates the presence of high resistance. PIP > 80–100 mbar is not an uncommon finding during mechanical ventilation in patients with severe asthma. Because the pathophysiology of asthma is not directly related to the alveoli, Pplat (which reflects lung compliance or alveolar pressure) is expected to be within normal limits (<20 mbar). Therefore, an increase in Pplat suggests the presence or increase in bronchospasm with an increase in hyperinflation or pneumothorax (**Figure 5**).

The VC mode is preferred in patients with asthma because PIP and Pplat can be directly controlled in this mode, in contrast to the PC mode. This should be kept in mind as long as Pplat is maintained below 30 mbar, even a very high PIP level (which is a sign of asthma) will not damage the alveoli (barotrauma).

When ventilating asthma patients, it is important to lower the upper pressure limit to a value that is higher than the patient's internal PIP. Failure to do so may result in fatal alveolar hypoventilation secondary to premature cessation of delivery of a given volume. This is better understood with the following example. If the upper pressure limit is set to 40 mbar in an asthmatic patient with severe bronchospasm, then tidal volume delivery will be terminated as soon as 40 mbar is reached. Because the anatomical dead space volume is one third (approximately 150 ml in an adult) of the normal volume (6 ml/kg), alveolar hypoventilation will occur. Therefore, the upper pressure limit should be set above the PIP (> 80 mbar in this hypothetical scenario) to prevent fatal alveolar hypoventilation. With a sudden improvement in bronchospasm (and a decrease in PIP), the patient will continue to receive the target tidal volume without an increase in alveolar pressure (**Figure 6**).

In contrast, PIP and Pplat cannot be controlled in a given pressure ventilation mode. Therefore, the patient will only receive adequate tidal volumes in this mode if the pressure limit as well as the set pressure is maintained above the internal airway pressure. With fluctuations in the degree of bronchospasm and associated changes in airway pressure, which can be sudden, there is a risk of either creating extremely high

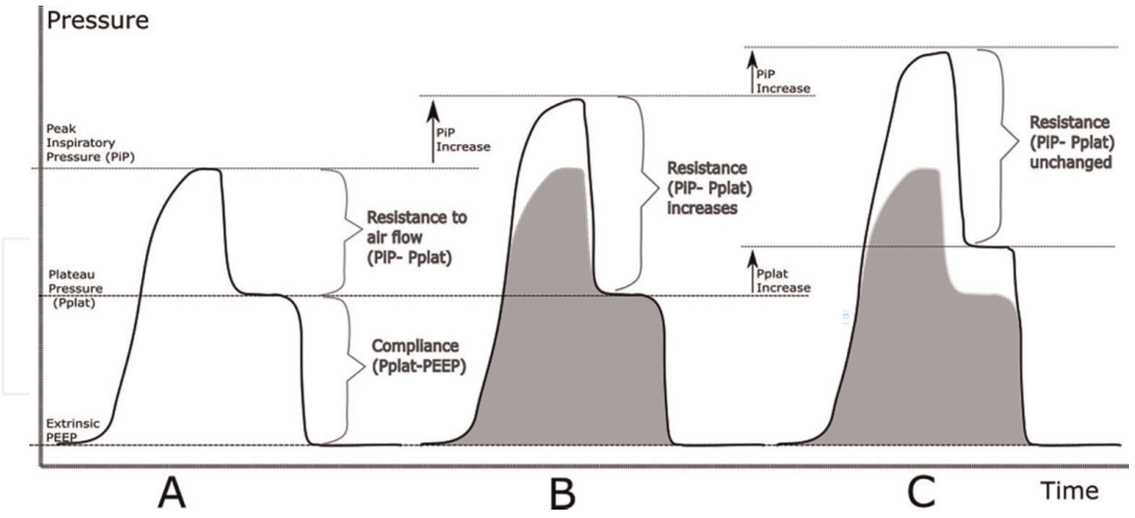

Figure 5.
Interpretation of the paw/time VC pressure–time curve in patients with asthma. A, Normal shape curve. B. Paw/time shape changes secondary to bronchospasm without hyperinflation. Note the increase in both PIP and PIP-Pplat gradient. Since Pplat remains the same as in A, this means an increase in airway resistance only in the absence of gas retention, since there is no change consistent with that in A. C. Changes in paw-time shape, indicating either (1) bronchospasm with gas retention or (2) pneumothorax. Note the same degree of increase in both PIP and Pplat. Since the PIP-Pplat gradient remains the same as in B, no further increase in the degree of bronchospasm occurs (shaded area, normal paw/time form). (Modified from Laher and Buchanan [9]).

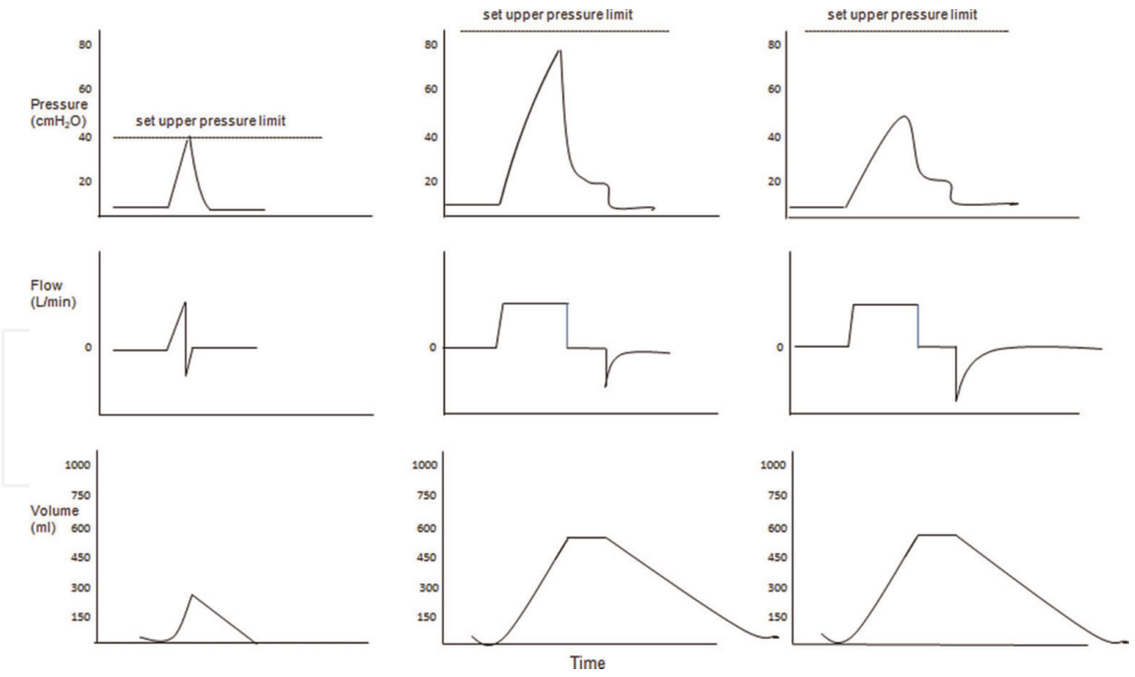

Figure 6.
Ventilate asthma patients using VC (recommended). Left: Patient with severe bronchospasm and PIP = 80 mbar. The upper pressure limit was set too low at 40 mbar; consequently, inhalation stops prematurely. Note the low tidal volume of 270 ml resulting in alveolar hypoventilation. Middle: Same patient with severe bronchospasm and PIP—80 cm mbar. The upper pressure limit is now correctly set to over 80 cm H_2O, with the patient now receiving an adequate tidal volume > 450 ml. Note that despite the high PIP (80 mbar), the plateau pressure is 20 mbar, which is within the recommended safe pressure limits. Right: Same patient with sudden improvement in bronchospasm (PIP—50 mbar). Although the upper pressure limit remains unchanged at >80 mbar, delivered tidal volume and plateau pressure remain unchanged at >450 ml and 20 mbar, respectively. (Modified from Laher and Buchanan [9]).

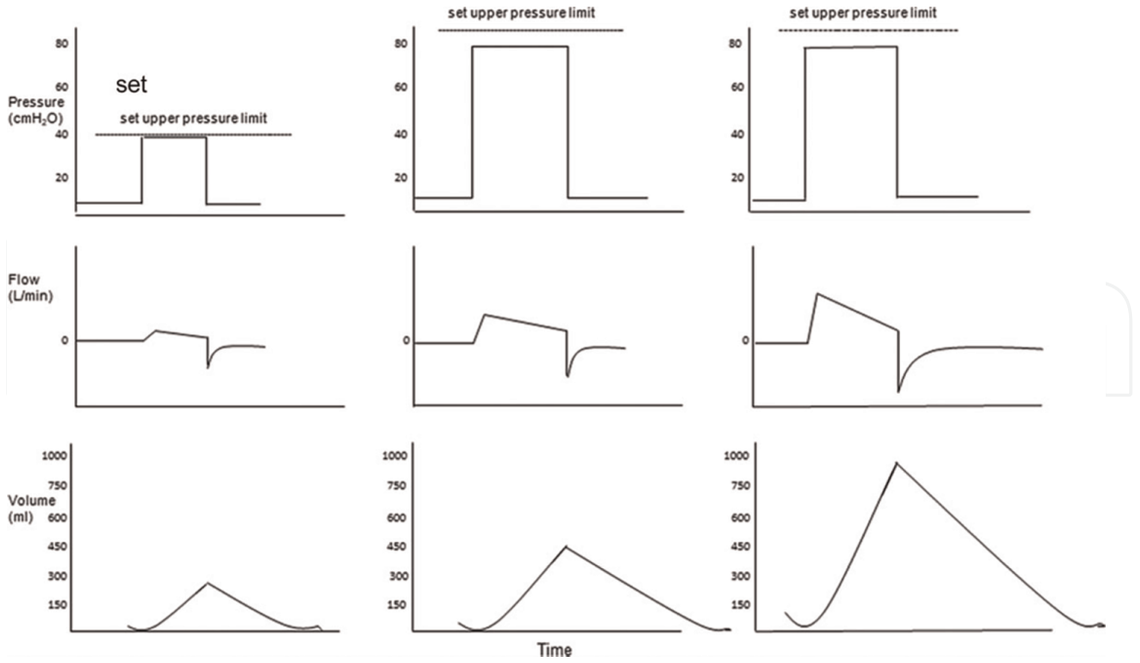

Figure 7.
Ventilate asthma patients using PC mode (not recommended). Left: Patient with severe bronchospasm and PIP—80 mbar. The upper pressure limit was set too low at 40 mbar, allowing only a tidal volume of 270 ml, resulting in alveolar hypoventilation. Middle: Same patient with severe bronchospasm and PIP—80 mbar. To achieve an adequate tidal volume > 450 ml, pressure control was set to 80 mbar, and the upper pressure limit was set to >80 mbar. Note that in this mode the plateau pressure cannot be determined; therefore, potential causes of high plateau pressure in an asthmatic patient (pneumothorax or gas retention) cannot be easily suspected in this mode. Right: Same patient with sudden improvement in bronchospasm (PIP—50 mbar) and established pressure control >80 mbar. Due to the sudden drop in airway pressure, the tidal volume (controlled by the 80 mbar pressure regulator) is now dangerously high (1000 ml), increasing the risk of barotrauma and pneumothorax. (Modified from Laher and Buchanan [9]).

and harmful or unacceptably low tidal volumes that may go unnoticed if alarm limits are not meticulously set and the patient is not under close supervision.

For example, if the above patient has severe bronchospasm and an underlying PIP (airway pressure) of 80 mbar, the patient will only receive adequate tidal volumes if an upper pressure limit as well as a pressure control/pressure maintenance level has been set >80 mbar. In case of worsening of bronchospasm, when PIP is increased (e.g., 90 mbar), the patient receives suboptimal tidal volumes, while if bronchospasm is suddenly eliminated (and PIP decreases), the patient is at risk of receiving extremely high and dangerous tidal volumes (**Figure** 7).

6. Weaning of respiratory support

If the underlying obstructive process is amenable to drug therapy, withdrawal of respiratory support and restoration of spontaneous breathing may be considered.

The patient's respiratory mechanics should be significantly improved by reducing expiratory time, dyspnea, reducing airway resistance and PEEPi, and increasing pulmonary-thoracic compliance. Sufficient oxygenation must be maintained at FiO_2 less than 40%.

Patients with asthma may be ready to withdraw within hours, while patients with COPD may not be ready for several weeks. Once the decision to initiate withdrawal has been made, all sedation and muscle relaxation should be discontinued.

With obstructive ARF, it is advisable to use the following additional criteria to make a decision on weaning a patient: (1) a decrease in peak inspiratory pressure to 17–20 mbar up to 8–11 mbar, PEEP up to 4–7 mbar; (2) improvement in the biomechanics of respiration (reduction of Raw to 6–9 mbar/l/s) and gas exchange (SaO_2 > 93–94%, $PaO_2 \geq 80$ mm Hg, $PaCO_2 \leq 40$–44 mm Hg at $FiO_2 < 0.35$) [4].

One should draw attention to the fact that when canceling respiratory support, it is necessary to strive to optimize the response of the respirator to the patient's inspiratory effort, following the following rules:

1. Gradual (reasonable) decrease in the sensitivity of the trigger (from the maximum sensitivity of the triggering threshold equal to (−1)–(−1.5) mbar to −3 mbar)

2. The inspiratory and expiratory times set on the respirator should be as close as possible to the patient's respiratory pattern.

3. The flow rate of the gas mixture created by the respirator (both basic and inspiratory) must correspond to the needs of the patient.

To stop respiratory support in patients with regression of ARF, SIMV and BIPAP modes have been used since the advent of microprocessor ventilators, gradually reducing the number of machine breaths, PSV mode, and breathing through a T-shaped tube.

Several subsequent multicenter randomized controlled trials demonstrated the benefit of the spontaneous breathing test using the PSV regimen with pressure support of 7–8 mbar. Over the spontaneous T-tube test and the superiority of both methods over SIMV weaning in duration of ventilator weaning and failure rate [29–31].

The largest and methodologically well-designed study demonstrated a higher rate of successful weaning from mechanical ventilation using a 30-minute spontaneous breathing test with a support pressure of 8 mbar compared with a simple 2-hour T-tube spontaneous breathing test (without pressure support) [29].

Currently, to assess weaning from respiratory support, a spontaneous breathing test (SBT) is recommended for 30 minutes with a small level of pressure support to compensate for the work of breathing to overcome the resistance of the tube [29]:

1. Set CPAP/PEEP mode ≤ mbar. With PS ≤ 8 mbar.

2. Within 30 minutes, assess for intolerance to SBT:

   a. excitation or depression of consciousness—A score on the Glasgow coma scale of 13 points or less,

   b. $SpO_2 < 90\%$,

   c. RR >35 per minute,

   d. Tobin index <70,

   e. HR > 140 per minute or more than 20% of baseline or the appearance of arrhythmia,

f. decrease in blood pressure below 90 mm Hg. or more than 20% higher than the original,

g. participation in breathing of auxiliary muscles,

h. paradoxical movements of the anterior abdominal wall during breathing,

i. profuse sweating.

3. If the 30-minute spontaneous breathing test is tolerated, consideration should be given to disconnection from the ventilator and/or extubation.

4. In case of test intolerance, it is necessary to return to the previous ventilation parameters.

We pay attention to the following factors:

1. with all options for canceling mechanical ventilation during its implementation, it is necessary to maintain $PaO_2 > 60$ mm Hg, pH ≥ 7.35 at $FiO_2 \leq 0.4$

2. after extubation in some patients (especially with a long period of mechanical ventilation), it is advisable to consider using non-invasive respiratory support as a bridge.

In cases where it is difficult to wean from respiratory support in this category of patients, it is possible to use a semi-sitting position at an angle of 45° to reduce the level of PEEPi and reduce the load on the respiratory muscles [32].

7. Conclusion

In general, provision of respiratory support in patients with obstructive ARF against the background of COPD and BA requires the physician to both understand the main pathophysiological processes of the occurrence of ARF and a certain patience in the selection of respirator settings due to dynamic changes in the mechanical properties of lungs during therapy.

Conflict of interest

The authors declare no conflict of interest.

Author details

Alexey Gritsan
Department of Anesthesiology and Intensive Care, V.F. Voino-Yasenetsky
Krasnoyarsk State Medical University, Krasnoyarsk, Russia

Address all correspondence to: gritsan67@mail.ru

IntechOpen

References

[1] Tuxen DV, Lane S. The effects of ventilatory pattern on hyperinflation, airway pressures, and circulation in mechanical ventilation of patients with severe air-flow obstruction. The American Review of Respiratory Disease. 1987;**136**(4):872-879. DOI: 10.1164/ajrccm/136.4.872

[2] Honig EG. Chronic obstructive pulmonary disease and asthma. In: Perel A, Stock MC, editors. Mechanical Ventilatory Support. Baltimore: Williams & Wilkins; 1992. pp. 227-246

[3] Aubier M, Murciano D, Milic-Emili J, Touaty E, Daghfous J, Pariente R, et al. Effects of the administration of O2 on ventilation and blood gases in patients with chronic obstructive pulmonary disease during acute respiratory failure. The American Review of Respiratory Disease. 1980;**122**(5):747-754. DOI: 10.1164/arrd.1980.122.5.747

[4] Gritsan AI, Kolesnichenko AP, Lebedinsky KM, Kirov MY, Nikolaenko EM. Recommendations for respiratory support during exacerbation of chronic obstructive pulmonary disease and bronchial asthma. In: Collection of Recommendations for Respiratory Support. Krasnoyarsk: KrasSMU; 2009. pp. 117-132

[5] Higgins B, Greening AP, Crompton GK. Assisted ventilation in severe acute asthma. Thorax. 1986; **41**(6):464-467. DOI: 10.1136/thx.41.6.464

[6] Luksza AR, Smith P, Coakley J, Gordan IJ, Atherton ST. Acute severe asthma treated by mechanical ventilation: 10 years' experience from a district general hospital. Thorax. 1986; **41**(6):459-463. DOI: 10.1136/thx.41.6.459

[7] Dales RE, Munt PW. Use of mechanical ventilation in adults with severe asthma. Canadian Medical Association Journal. 1984;**130**(4): 391-395. PMID: 6362813; PMCID: PMC1876100

[8] Leatherman J. Mechanical ventilation for severe asthma. Chest. 2015;**147**(6): 1671-1680. DOI: 10.1378/chest.14-1733

[9] Laher AE, Buchanan SK. Mechanically ventilating the severe asthmatic. Journal of Intensive Care Medicine. 2018;**33**(9):491-501. DOI: 10.1177/0885066617740079

[10] Muir JF, Levi-Valensi P. When should patients with COPD be ventilated? European Journal of Respiratory Diseases. 1987;**70**(3): 135-139. PMID: 3569443

[11] Zabolotskikh IB, Gritsan AI, Kirov M.Yu., Lebedinsky KM, Mazurok VF, Trembach NV perioperative management of patients with concomitant respiratory failure. Russian FAR recommendations. Annals of Intensive Care. 2012(4):67-78

[12] Plant PK, Owen JL, Elliott MW. Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: A multicentre randomised controlled trial. Lancet. 2000;**355**(9219):1931-1935. DOI: 10.1016/s0140-6736(00)02323-0

[13] Girou E, Schortgen F, Delclaux C, Brun-Buisson C, Blot F, Lefort Y, et al. Association of noninvasive ventilation with nosocomial infections and survival in critically ill patients. Journal of the American Medical Association. 2000; **284**(18):2361-2367. DOI: 10.1001/jama.284.18.2361

[14] Girou E, Brun-Buisson C, Taillé S, Lemaire F, Brochard L. Secular trends in nosocomial infections and mortality associated with noninvasive ventilation in patients with exacerbation of COPD and pulmonary edema. Journal of the American Medical Association. 2003; **290**(22):2985-2991. DOI: 10.1001/jama.290.22.2985

[15] Keenan SP, Powers CE, McCormack DG. Noninvasive positive-pressure ventilation in patients with milder chronic obstructive pulmonary disease exacerbations: A randomized controlled trial. Respiratory Care. 2005; **50**(5):610-616. PMID: 15871754

[16] Barbé F, Togores B, Rubí M, Pons S, Maimó A, Agustí AG. Noninvasive ventilatory support does not facilitate recovery from acute respiratory failure in chronic obstructive pulmonary disease. The European Respiratory Journal. 1996;**9**(6):1240-1245. DOI: 10.1183/09031936.96.09061240

[17] Jurjević M, Matić I, Sakić-Zdravcević K, Sakić S, Danić D, Buković D. Mechanical ventilation in chronic obstructive pulmonary disease patients, noninvasive vs. invasive method (randomized prospective study). Collegium Antropologicum. 2009;**33**(3):791-797. PMID: 19860105

[18] Briones Claudett KH, Briones Claudett M, Chung Sang Wong M, Nuques Martinez A, Soto Espinoza R, Montalvo M, et al. Noninvasive mechanical ventilation with average volume assured pressure support (AVAPS) in patients with chronic obstructive pulmonary disease and hypercapnic encephalopathy. BMC Pulmonary Medicine. 2013;**13**:12. DOI: 10.1186/1471-2466-13-12

[19] Ankjærgaard KL, Tønnesen P, Laursen LC, Hansen EF, Andreassen HF, Wilcke JT. Home non invasive ventilation (NIV) treatment for COPD patients with a history of NIV-treated exacerbation; a randomized, controlled, multi-center study. BMC Pulmonary Medicine. 2016;**16**:32. DOI: 10.1186/s12890-016-0184-6

[20] Gantzhorn EK, Prior TS, Hilberg O. Long-term non-invasive ventilation for stable chronic hypercapnic COPD. European Clinical Respiratory Journal. 2019;**6**(1):1644893. DOI: 10.1080/20018525.2019.1644893

[21] Oscroft NS, Chadwick R, Davies MG, Quinnell TG, Smith IE. Volume assured versus pressure preset non-invasive ventilation for compensated ventilatory failure in COPD. Respiratory Medicine. 2014; **108**(10):1508-1515. DOI: 10.1016/j.rmed.2014.07.010

[22] Lindenauer PK, Stefan MS, Shieh MS, Pekow PS, Rothberg MB, Hill NS. Hospital patterns of mechanical ventilation for patients with exacerbations of COPD. Annals of the American Thoracic Society. 2015;**12**(3): 402-409. DOI: 10.1513/AnnalsATS.201407-293OC

[23] Wright PE, Marini JJ, Bernard GR. In vitro versus in vivo comparison of endotracheal tube airflow resistance. The American Review of Respiratory Disease. 1989;**140**(1):10-16. DOI: 10.1164/ajrccm/140.1.10

[24] Broseghini C, Brandolese R, Poggi R, Polese G, Manzin E, Milic-Emili J, et al. Respiratory mechanics during the first day of mechanical ventilation in patients with pulmonary edema and chronic airway obstruction. The American Review of Respiratory Disease. 1988; **138**(2):355-361. DOI: 10.1164/ajrccm/138.2.355

[25] Rossi A, Gottfried SB, Higgs BD, Zocchi L, Grassino A, Milic-Emili J. Respiratory mechanics in mechanically ventilated patients with respiratory failure. Journal of Applied Physiology. 1985;**58**(6):1849-1858. DOI: 10.1152/jappl.1985.58.6.1849

[26] Kimball WR, Leith DE, Robins AG. Dynamic hyperinflation and ventilator dependence in chronic obstructive pulmonary disease. The American Review of Respiratory Disease. 1982; **126**(6):991-995. DOI: 10.1164/arrd.1982.126.6.991

[27] García Vicente E, Sandoval Almengor JC, Díaz Caballero LA, Salgado Campo JC. Ventilación mecánica invasiva en EPOC y asma [Invasive mechanical ventilation in COPD and asthma]. Medicina Intensiva. 2011;**35**(5): 288-298. Spanish. DOI: 10.1016/j.medin.2010.11.004

[28] Bergman NA. Intrapulmonary gas trapping during mechanical ventilation at rapid frequencies. Anesthesiology. 1972;**37**(6):626-633. DOI: 10.1097/00000542-197212000-00011

[29] Subirà C, Hernández G, Vázquez A, Rodríguez-García R, González-Castro A, García C, et al. Effect of pressure support vs T-piece ventilation strategies during spontaneous breathing trials on successful Extubation among patients receiving mechanical ventilation: A randomized clinical trial. Journal of the American Medical Association. 2019; **321**(22):2175-2182. DOI: 10.1001/jama.2019.7234

[30] Esteban A, Alía I, Gordo F, Fernández R, Solsona JF, Vallverdú I, et al. Extubation outcome after spontaneous breathing trials with T-tube or pressure support ventilation. The Spanish lung failure collaborative group. American Journal of Respiratory and Critical Care Medicine. 1997;**156**(2 Pt 1): 459-465. DOI: 10.1164/ajrccm.156.2.9610109

[31] Brochard L, Rauss A, Benito S, Conti G, Mancebo J, Rekik N, et al. Comparison of three methods of gradual withdrawal from ventilatory support during weaning from mechanical ventilation. American Journal of Respiratory and Critical Care Medicine. 1994;**150**(4):896-903. DOI: 10.1164/ajrccm.150.4.7921460

[32] Deye N, Lellouche F, Maggiore SM, Taillé S, Demoule A, L'Her E, et al. The semi-seated position slightly reduces the effort to breathe during difficult weaning. Intensive Care Medicine. 2013; **39**(1):85-92. DOI: 10.1007/s00134-012-2727-5