Personalized Mechanical Ventilation

Improving Quality of Care

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Preface

Much has been written in recent years about the emergence of "personalized medicine." Of course, medicine has always been tailored to individual circumstances, and in a sense, personalized medicine is not terribly new. However, advances in medical knowledge in terms of genetics, biomarkers, and other features, with subsequent acknowledgment of the heterogeneity of treatment effect (HTE) in clinical trials, have required clinicians to be evermore cognizant of the need to approach therapeutic endeavors by patient subgroups.

The last few decades have seen advances in patient outcomes and quality of care resulting from the initiation and use of various checklists and protocols. Yet, a one-size-fits-all approach to patients requiring mechanical ventilation is woefully insufficient to meet individual patient needs. While the use of lung-protective ventilation in ARDS has been implemented in a somewhat standardized fashion, there are multiple other circumstances intensivists confront, where the application of mechanical ventilation is far from standardized. Hence, the application of mechanical ventilation to patients also requires a personalized approach.

We are pleased then to offer this new book by Springer Incorporated entitled "Personalized Mechanical Ventilation." Over the course of 26 chapters, mechanical ventilation use in circumstances such as obesity, trauma, pregnancy, and shock, as well as many others, is addressed. Each chapter affords the intensivist a fresh perspective on how to utilize mechanical ventilation in each condition. We have secured contributions from an array of international experts to offer their perspective on a large array of clinical scenarios where mechanical ventilation is employed. We believe that busy intensivists will find this work useful as they attempt to treat their critically ill patients.

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Prologue

It is a real honor for me to be the bearer of some considerations in the prologue of this exquisite new scientific work, where authors from all over the world, mainly the Middle East, the United States, and Latin America, join together to offer their experiences about the management of mechanical ventilation focusing its use on a personalized, directed, and unique way according to the needs and problems that each group of patients deserves.

This new work makes a necessary and invaluable account of respiratory physiology and the findings found at the patient's bedside, covering in an orderly manner the elements that make up the anatomy of a ventilator, its circuits, and ventilatory modes, and which throughout history have been used for the benefit of the critically ill patient.

When talking about mechanical ventilation, it seems that everything has been said. However, it surprises us when trying to customize new methods. We find questions regarding how should patients with a unilateral lung injury be managed, postoperative ventilation, rapid extubation, when and how, and ventilation in patients with COVID 19, among others.

The authors also analyze the pros and cons of multiple ventilation with a single ventilator, almost in the style of an in-depth editorial, thus arriving at the state of the art of weaning from mechanical ventilation.

I can only congratulate the distinguished authors of this magnificent work in a very special way since it will surely give answers to many situations that arise in daily life with the use of this formidable tool considered by some as the right hand of critical medicine: "Personalized Mechanical Ventilation."

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Special Thanks

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School of Medicine University of Panama.

We would like to express our deep gratitude to Professor Jorge Sinclair, for his academic contribution, enthusiastic encouragement, and useful and constructive recommendations on this project.

Contents

Respiratory Physiology and Mechanics at the Bedside

Ahmed Mohamed Reda Taha and Prashant Nasa

1 Introduction

Mechanical ventilators are sophisticated machines working on complex algorithms to deliver positive-pressure ventilation to patients. Mechanical ventilators are often handled by healthcare professionals with limited training in their different settings and functions. The mechanical ventilation strategy for a particular disease depends on the pathophysiology of the disease and the experience or familiarity of the intensive care unit (ICU) staff to a specific ventilator mode. Understanding of basic physiology of the respiratory system and physics of airflow dynamics is paramount to optimize mechanical ventilation settings. Lung-protective ventilation (LPV) for patients on invasive mechanical ventilation has consistently shown mortality benefit. The core principle of the LPV strategy is to reduce the harm of positive-pressure ventilation, also called ventilator-induced lung injury (VILI). ICU management is progressing towards precision-based medicine, defined as treatment tailored to the pathophysiology of the disease instead of based on averages. Respiratory mechanics are a surrogate representation of lung function using pressure, volume, or flows. Understanding respiratory physiology and mechanics represents the first step towards a personalized approach to ventilator management in the ICU. This chapter reviews the applied physiology of the respiratory system, equation of motion, dynamic and static respiratory mechanics, and their implication in the management of invasive or noninvasive mechanical ventilation.

The original version of the chapter has been revised. A correction to this chapter can be found at https://doi.org/10.1007/978-3-031-14138-6_27

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2 Lung Volumes and Capacity

Understanding lung volume and capacity helps to diagnose an obstructive versus restrictive condition, response to therapeutics, prognosis, and assessment of weaning or tracheal extubation (Fig. 1). Functional residual capacity (FRC) is the volume of gas remaining in the lung after normal passive expiration. FRC can be represented mathematically as the sum of expiratory reserve volume and residual volume (Fig. 1). End-expiratory lung volume (EELV) is defined as the addition of positive end-expiratory pressure (PEEP) to the FRC of patients on mechanical ventilation. EELV is simply the volume present in the lungs before the start of the next tidal volume breath. EELV represents the balance of opposing forces and elastic recoil of lungs and chest wall, along with PEEP. The gas exchange in the lung is primarily dependent on the EELV, and mechanical ventilation settings should target optimizing the EELV, thereby reducing the risk of VILI [1]. The decrease in EELV is observed with alveolar collapse, alveolar flooding seen in pulmonary edema or severe pneumonia, and decreased thoracic compliance in obesity or abdominal surgery.

The distribution of tidal volume in a reduced EELV characterized by smaller aerated lung volume may cause VILI in the form of barotrauma or volutrauma. The PEEP titration may avoid end-expiratory alveolar collapse and hence reduction of EELV. The recruitment maneuvers are also targeted to increase the aerated portion of the lung and EELV. The personalized approach to invasive mechanical ventilation, thus, requires measurement of EELV. Unfortunately, the EELV measurement

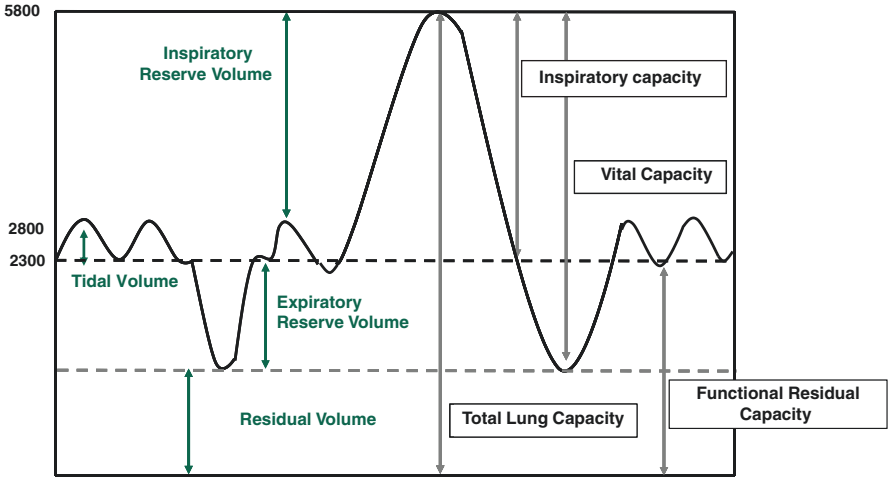

Fig. 1 Lung volumes and capacity. In approximate values: tidal volume (500 mL), expiratory reserve volume (1100 mL), residual volume (1100 mL), inspiratory reserve volume (3000 mL), total lung capacity (5800 mL), vital capacity (4600 mL), functional residual capacity (2300 mL), inspiratory capacity (3500 mL)

is laborious and impractical at the bedside because residual volume calculation needs techniques based on the dilution of trace gases. However, the newer commercial ventilators, using the alteration of a fraction of inspired oxygen, started calculating EELV during controlled ventilation modes.

3 Equation of Motion

The equation of motion is a fundamental concept that describes the overall forces required to drive gases across the respiratory system. The mathematical representation of the equation of motion helps in understanding respiratory mechanics during invasive mechanical ventilation. The equation states that the pressure required to (both inspiratory muscles and the ventilator) drive the gases into the lungs is equal and opposite to the force offered by the patient's respiratory system. The force of the respiratory system has three components: an elastic component (distension of the lung parenchyma), a resistive component (airway resistance till respiratory bronchiole), and an inertial component (changes in the lung parenchyma caused by volume acceleration). At usual respiratory frequencies of under 1 Hz (60 rpm), the inertial component is negligible and can be excluded for calculation.

Equation of motion:

$$\mathbf{P_{MUS} + P_{VENT} = Resistive\ component + Distention\ component + Inertial\ component}$$

$\mathbf{P_{MUS}}$: Pressure generated by the inspiratory muscles. In case of complete paralysis without any inspiratory muscle effort, $\mathbf{P_{MUS}}$ will become zero. $\mathbf{P_{VENT}}$**:** Pressure generated at the ventilator end and reflects airway pressure (Paw) or Pao (pressure at airway opening). Resistance component: Resistance of the respiratory system, which equals to flow ($\dot{V}$) X resistance (**R**). Distension component: Respiratory system elastance (inverse of respiratory system compliance) X change in volume (**ΔV**).

$$\mathbf{P_{MUS} + P_{VENT} = \left(\dot{V} \times R\right) + \left(\Delta V / compliance\right) + PEEP + inertance}$$

PEEP is the total PEEP, which includes set PEEP on the ventilator and intrinsic PEEP.

Inertance is the component contributed by system inertia, which is generally insignificant for calculation purpose and can be ignored.

4 Alveolar Pressure (P_{alv})

Alveolar pressure, defined as the pressure in the alveoli at the end of inflation, is a surrogate of alveolar distension during inspiration. Due to the resistance component, pressure at airway opening (Pao) is always greater than Palv. The end-inspiratory breath hold of 0.5–2 s equilibrates the system pressure, stopping the flow and reducing the resistance component to zero (Fig. 2). The measured Pao at static flow is called plateau pressure (Pplat), and once the equilibrium is achieved in the airway, it is the surrogate of alveolar pressure. Pplat is dependent on two variables, tidal volume and compliance:

$$\mathbf{P_{plat} = Vt / C_{rs}}$$

Vt: Tidal volume. C_{rs}: Compliance

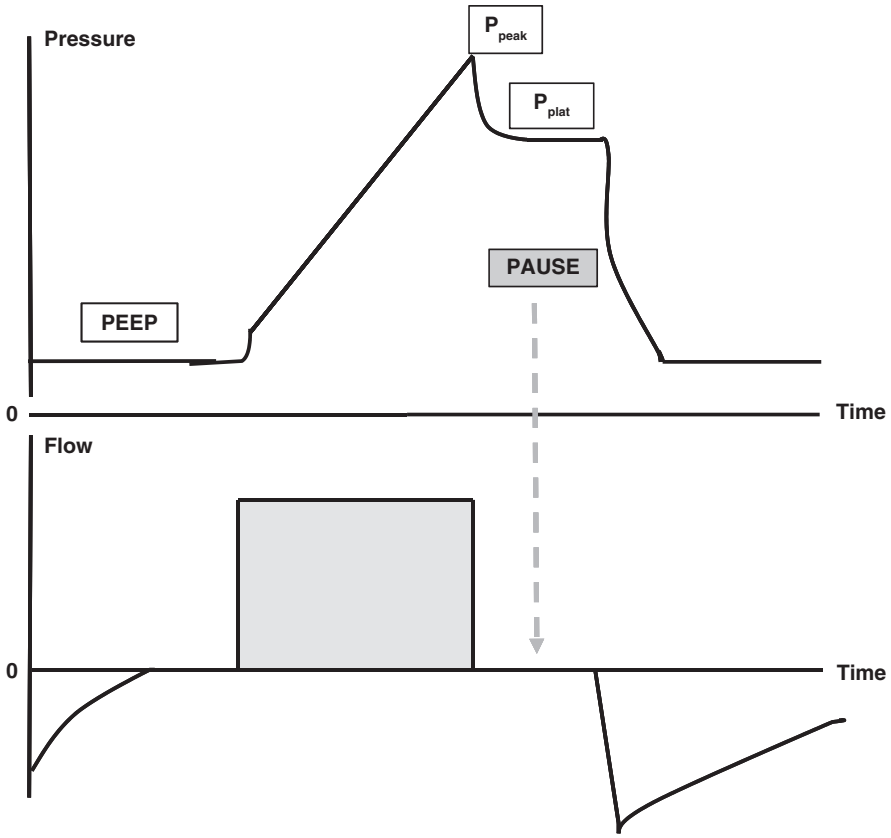

Fig. 2 Pressure-time and flow-time waveforms during volume control ventilation, illustrating the effect of an end-inspiratory pause (breath hold). In the period of no flow, the pressure equilibrates to the alveolar pressure or plateau pressure (P_{plat}). *Pplat* plateau pressure, *PEEP* positive end-expiratory pressure, *PIP* peak inspiratory pressure

The end-inspiratory pause of ≥3 s provides the most accurate P_{plat} in both diseased and healthy lung. Shorter pauses of 0.5 s may overestimate P_{plat} acute respiratory distress syndrome (ARDS) and chronic obstructive pulmonary disease (COPD) [2].

The high P_{plat} indicates alveolar overdistension and risk of VILI. The P_{plat} should be less than 30 cmH_2O to reduce VILI, and some evidence supports even lower P_{plat} targets (<25 cmH2O) in patients with ARDS [3, 4].

The newer generation ventilators can provide Pplat without the need for inspiratory breath hold. The real-time determination method of P_{plat} uses the expiratory time constant (τ_E), estimated from the expiratory flow curve:

$$\mathbf{P_{plat}} = \left(\mathbf{Vt} \times \mathbf{P_{insp}}\right) - \left(\mathbf{Vt} \times \mathbf{PEEP}\right) / \mathbf{Vt} + \tau_{\mathbf{E}} \times \dot{\mathbf{V}}\mathbf{insp}$$

Pinsp: inspiratory peak pressure, $\dot{V}$ insp: inspiratory flow.

5 Driving Pressure

Driving pressure is the pressure generated in the alveoli above PEEP while delivering the tidal volume. The driving pressure can be calculated by the difference between P_{plat} and PEEP and correlates to global lung strain:

$$\textbf{Driving pressure} = \mathbf{P_{plat}} - \mathbf{PEEP}$$

PEEP includes total PEEP, including set PEEP and intrinsic PEEP.

There is growing evidence supporting the monitoring of driving pressure during LPV strategy on invasive mechanical ventilation. The studies in intensive care and perioperative settings found driving pressure compared to tidal volume to be a better predictor of clinical outcomes [5–7]. The driving pressure greater than 15 cm of H_2O was associated with increased mortality [relative risk (RR) 1.41]; even with conventional targets of LPV, Pplat [<30 cmH_2O] and Vt [<7 mL/kg/ideal body weight (IBW)] are in target ranges for protective ventilation [6]. In a meta-analysis, during general anesthesia in the operation theatre, the driving pressure [odds ratio (OR) 1.16] was the only ventilatory parameter associated with increased risk of postoperative pulmonary complications [7].

6 Transpulmonary Pressure

The transpulmonary pressure (P_L) is the pressure required to drive the air into the lungs; it includes pressure to move the air through the airways (airway opening—alveolar pressure) and to overcome the elastic recoil of the lungs (calculated as alveolar pressure—pleural pressure):

Transpulmonary pressure (P_L) = airway opening pressure – pleural pressure.

In static flow conditions (at either end inspiration or end expiration), transpulmonary pressure approximates elastic recoil pressure and surrogates to lung stress during ventilation [8].

The pleural pressure can be calculated through an esophageal manometry with a special balloon and is not always feasible. Hence, P_{plat} pressure or driving pressure is taken as a surrogate of lung stress or VILI and approximates P_L in most situations except where chest or abdominal wall compliance is altered. The divergence of driving pressure and P_L is seen during conditions of raised intra-abdominal pressure (e.g., laparoscopic insufflation, obesity, ascites, supine position) [9–13].

7 Intrinsic PEEP

The positive pressure produced by the trapped gas in the alveoli at the end of expiration is called intrinsic PEEP, auto-PEEP, or occult PEEP. Intrinsic PEEP can be calculated by end-expiratory breath hold when the flow stops and pressure equilibrates (Fig. 3). The total PEEP includes the set PEEP on the ventilator and any intrinsic PEEP:

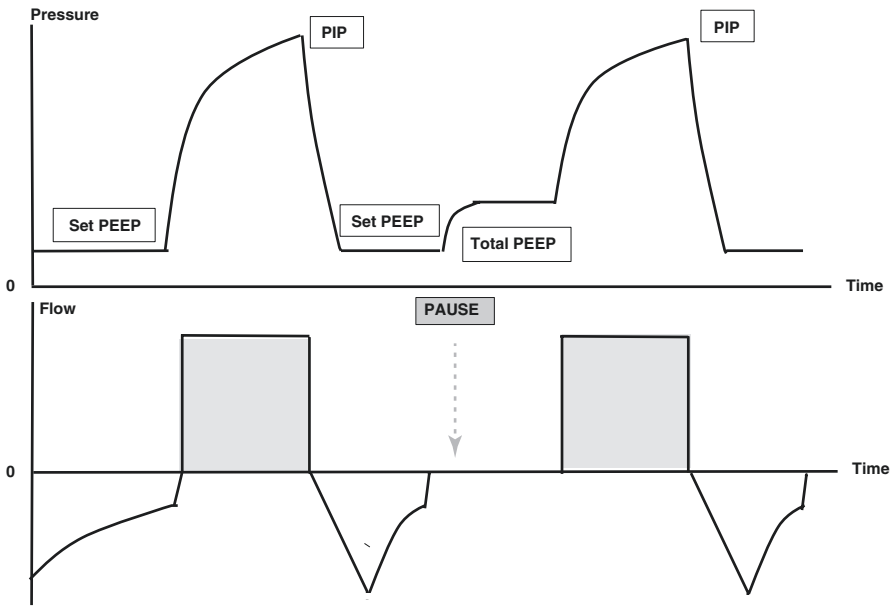

Fig. 3 Pressure-time and flow-time waveforms during volume control ventilation, illustrating the effect of an end-expiratory pause (breath hold). In the period of no flow, the pressure equilibrates to the alveolar pressure and reflects total PEEP. The difference between the total PEEP and set PEEP provides intrinsic PEEP. *PEEP* positive end-expiratory pressure, *PIP* peak inspiratory pressure

$$\textbf{Intrinsic PEEP} = \textbf{Total PEEP}\left(\textbf{end-expiratory pause}\right) - \textbf{set PEEP}$$

The pressure calculation should be done in the absence of any active expiratory effort, which may generate a positive pressure due to chest retraction at the end of expiration that can be misinterpreted as intrinsic PEEP. Intrinsic PEEP may cause dynamic hyperinflation by progressive increasing in end-expiratory lung volumes.

8 Respiratory System Compliance

Compliance (C_{rs}) is the distensibility of the lungs and is defined as the change in lung volumes per unit pressure change. C_{rs} is the inverse of the elastance and can be static or dynamic. The normal value of C_{rs} is 60–100 mL/cmH_2O. The static compliance (with no flow) reflects the elastic recoil pressures of the lungs and can be measured using the following formula:

$$\textbf{Static } \mathbf{C_{rs}} = \mathbf{Vt}/\left(\mathbf{P_{plat}} - \mathbf{PEEP}\right)$$

As the name suggests, dynamic compliance is a continuous measurement, dependent on the elastic and airway resistance. The dynamic compliance can be calculated using a pressure-volume curve. The pressure-volume curves are different for inspiration and expiration due to hysteresis, as the pressure required for lung inflation is higher than deflation (Fig. 4). However, the curves meet at two points, end

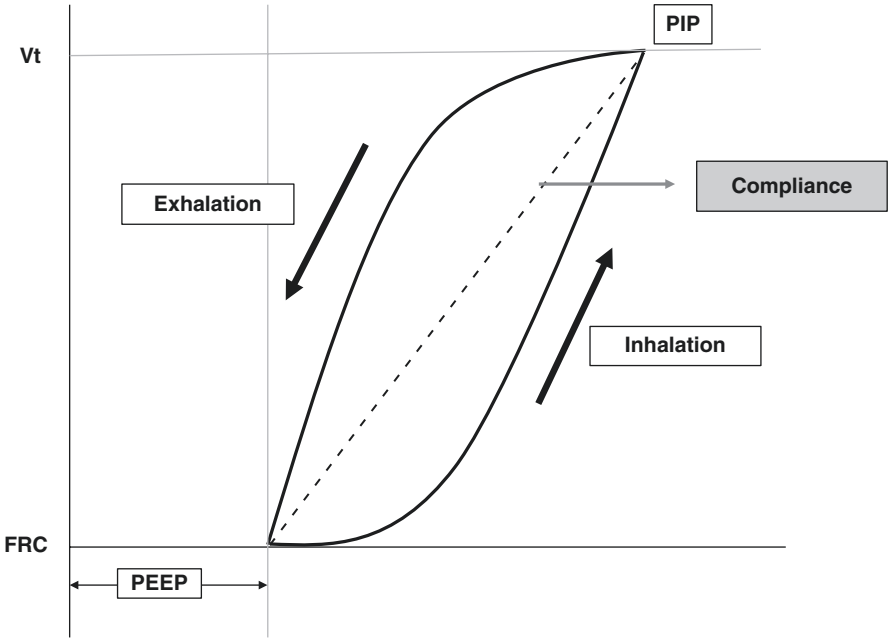

Fig. 4 Pressure-volume curve. *PIP* pressure inspiratory pressure, *PEEP* pressure end-expiratory pressure, *Vt* tidal volume, *FRC* functional residual capacity

inspiration and end expiration. The line connecting the two points provides the dynamic compliance of the lungs [14].

The ventilators may display dynamic C_{rs} (during pressure-controlled ventilation) based on the calculation:

$$\textbf{Dynamic } C_{rs} = Vt / (PIP - PEEP)$$

PIP is the peak inspiratory pressure.

A shorter inspiration time, increased airway resistance (R_{aw}), intrinsic PEEP, or active inspiratory effort can create a divergence between the static and dynamic C_{rs} [15].

9 Resistance

Resistance is the opposing friction to airflow during respiration. Resistance of the respiratory system is contributed by airway resistance (R_{aw}), viscoelastic properties of lung or chest wall, and lung parenchyma (due to unequal time constant of different regions). The normal value of resistance is 0.5–2.5 cmH_2O/L/s. R_{aw} depends on the air viscosity and density, and length and radius of airways, and increases with either changes in the flow (higher flow rates on the ventilator) or narrowing of the airways (bronchospasm). In large airways, the flow is described as turbulent when it is at a low velocity, while through narrow tubes, it tends to be more orderly and streamlined and flows in a straight line. This type of flow is called laminar flow. in the case of turbulent flow to double the airflow one needs to quadruple the driving pressure, while the laminar flow is directly proportional to the driving pressure, such that to double the flow rate, one needs only double the driving pressure (Poiseuille's Law). In case of laminar flow, the radius of the airway is a primary dependent variable. Resistance is inversely proportional to the fourth power of the radius; for example, if the radius is halved, there is a 16-fold increase in resistance. Resistance of the lung is a property of volume and decreases during lung insufflation on inspiration, while expiration has an oppositive effect [16]. On mechanical ventilation with assist volume-controlled mode and square waveform, R_{aw} can be measured with end-inspiratory occlusion:

$$\textbf{Airway resistance } (R_{aw}) = (PIP - P_{plat}) / Vt$$

However, during the pressure-controlled mode, inspiratory resistance is difficult to measure, as peak and plateau pressure are usually the same. The ventilators can calculate and display airway resistance and compliance using the equation of

motion through the linear least-squares fitting. The software digitizes the variables pressure, volume, and $\dot{V}$ at high speed (100 Hz) and provides real-time compliance and resistance. Though the least-squares fitting method can be applied during the whole breathing cycle, it is recommended to apply it during the inspiratory phase to overcome expiratory flow limitation seen in chronic obstructive pulmonary disease (COPD) [17]. There is an important assumption made (P_{MUS} is zero), and thus, the calculation is valid only in patients without any spontaneous effort [18].

The elastic component of the lung parenchyma also contributes to resistance. Resistance due to elastic component would be high in cases of increased lung and/or chest wall elastance (e.g., ARDS, idiopathic pulmonary fibrosis (IPF)).

10 Expiratory Time Constant

The time constant (TC) is defined as the time (in seconds) required to inflate (inspiratory time constant) and deflate (expiratory time constant) the lungs to a certain percentage of tidal volume. The expiratory TC (TC_{exp}) is a product of resistance and compliance, providing a real-time dynamic assessment of the respiratory mechanics.

One TC_{exp} is the time required by the alveoli to deflate 63% of its volume, while in three TC_{exp}, alveoli will be empty by 95%.

The TC_{exp} can diagnose various lung pathologies, assess the severity of the disease, monitor the effect of prone positioning, optimize settings on the ventilator, and troubleshoot respiratory events on mechanical ventilation. TC_{exp} is reliable even in patients who are spontaneously breathing and on NIV (assuming that expiration is passive and there are no unintentional leaks):

$$\mathbf{TC}_{\mathbf{exp}} = \mathbf{R}_{\mathbf{aw}} \times \mathbf{C}_{\mathbf{rs}}$$

11 Diagnosis of the Lung Conditions

The normal value of TC_{exp} in patients on invasive mechanical ventilation is between 0.5 and 0.7 s. However, pseudo-normal expiratory TC_{exp} can be seen with decreased compliance and increased resistance.

TC_{exp} less than 0.5 s implies decreased compliance in patients of lung fibrosis, kyphoscoliosis (decreased chest wall compliance), or severe ARDS [19]. TC_{exp} of longer than 0.7 s indicates increased resistance, e.g., COPD, right mainstem bronchus intubation, or kinking of the endotracheal tube (Fig. 5).

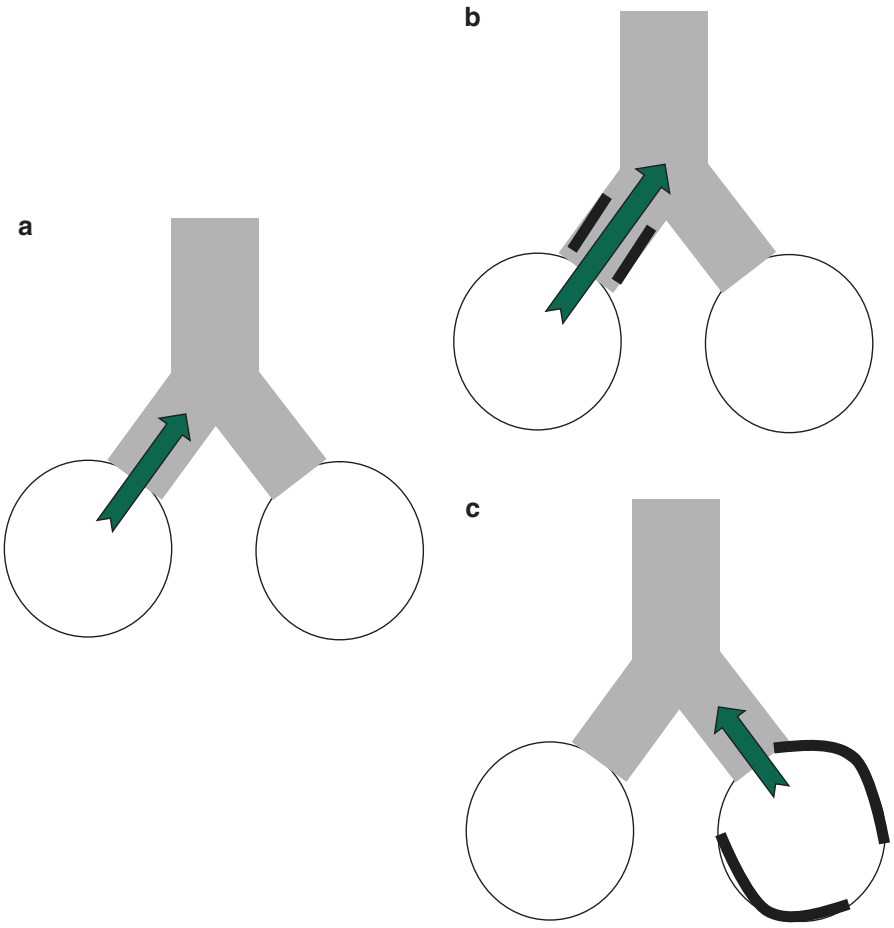

Fig. 5 Expiratory time constant. (**a**) Normal lungs with expiratory time constant (arrow). (**b**) Obstructive airway disease with longer time constant (arrow). (**c**) Restrictive airway disease with shorter time constant (arrow)

12 Optimization of Ventilatory Settings

Patients with a shorter TC_{exp} are at risk of VILI and should be closely monitored for targets of LPV (i.e., tidal volume, driving pressure, and plateau pressure). In contrast, patients with a longer expiratory TC are at risk of dynamic hyperinflammation and should be monitored periodically for the auto-PEEP.

13 Monitoring of Prone Position

During prone positioning of the intubated patient, the TC_{exp} can be used to assess the respiratory mechanics. The increase in TC_{exp} and compliance with prone positioning are markers of lung recruitment, while no increase in lung compliance but increased TC_{exp} is caused by kinking or mispositioned endotracheal tube.

14 Troubleshooting of Respiratory Events

The sudden drop in oxygen saturation or increase in airway pressure needs a rapid and correct diagnosis. The trends of TC_{exp} can help to understand respiratory mechanics in these events. An increase in TC_{exp} usually indicates an obstruction caused by one of the following: an endotracheal tube kinking, blockade or mispositioning, a patient biting the endotracheal tube, an excess of tracheal secretions, or bronchospasm. Conversely, a decrease in expiratory TC indicates a drop in compliance, e.g., pneumothorax, pleural effusion, or atelectasis. Without a change in expiratory TC, sudden desaturation indicates a drop in cardiac output or a massive pulmonary embolism.

15 Dead Space/Dead Space Fraction

The inspired gas that does not take part in gas exchange is termed dead space (Vd). It determines the fraction of wasted ventilation.

Total (or physiological) dead space includes anatomical and alveolar dead space. In a healthy adult, the alveolar dead space is negligible. Anatomical dead space represents the air that fills the conducting passages starting from the upper airway to the lower respiratory tract (up to respiratory bronchioles). This volume constitutes up to one-third of the normal tidal volume. The respiratory zone that takes part in actual gas exchanges comprises respiratory bronchioles, alveolar duct, alveolar sac, and alveoli. The abnormality of the alveolocapillary membrane or ventilation/perfusion mismatch causes the physiologic dead space to exceed above anatomical dead space.

The normal dead space-to-tidal volume (Vd/Vt) ratio is approximately 0.3. In a patient on invasive mechanical ventilation, the Vd/Vt ratio can be up to 0.7 or 0.8 due to an increase in anatomical dead space from the addition of instrumental dead space (Fig. 6).

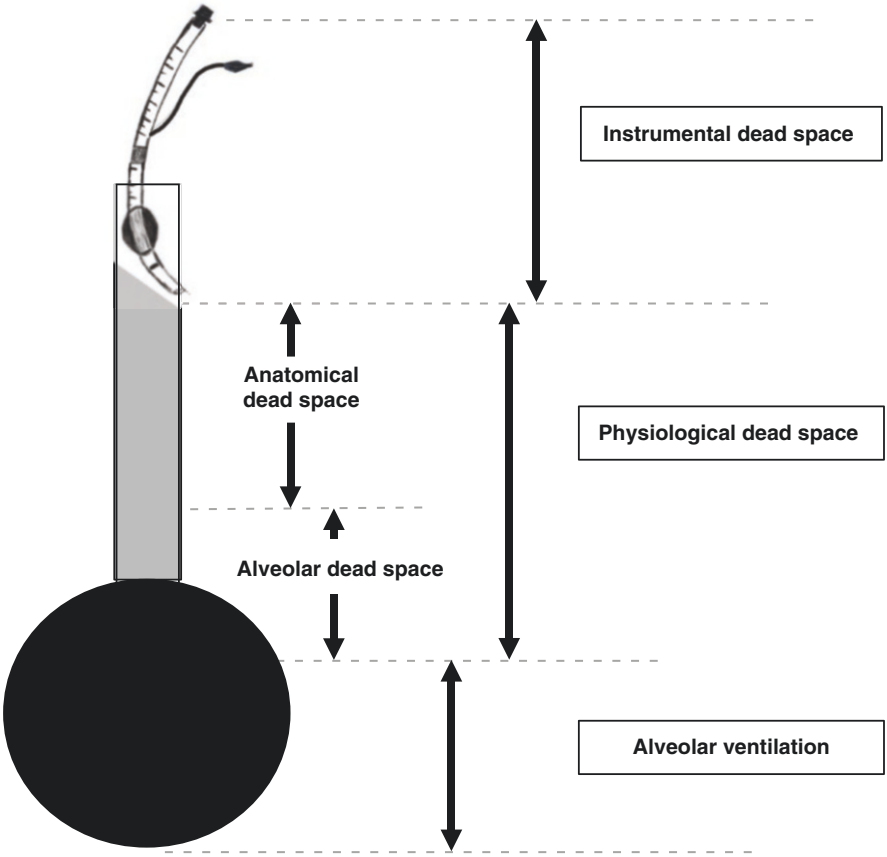

Fig. 6 Pictorial representation of total dead space

The partial pressure of arterial carbon dioxide ($PaCO_2$) is dependent on minute ventilation. Minute ventilation, defined by the total volume that enters lung in one minute, is the product of tidal volume and respiratory rate. However, the total volume of gas reaching the alveoli is not equivalent to tidal volume and must factor the gas in the anatomical dead space. Hence, the fraction of minute ventilation reaching the alveoli per unit time called alveolar ventilation is more important to consider in hypercarbia (Fig. 5):

$$\textbf{Alveolar ventilation} = \left(\textbf{Vt} - \textbf{Vd}\right) \times \textbf{respiratory rate}$$

The Bohr equation can be used to calculate the physiological dead space:

$$\textbf{Vd} = \textbf{Vt} \times \left(\textbf{PaCO}_2 - \textbf{PeCO}_2\right) / \textbf{PaCO}_2$$

$PeCO_2$: partial pressure of expired carbon dioxide.

The second half of this equation represents the dead space fraction. The diffusion of gases across the alveolar membrane is so rapid that $PaCO_2$ equals alveolar PCO_2 ($PACO_2$). $PeCO_2$ represents diluted $PACO_2$ with dead-space gases (which are usually inspired gases and devoid of CO_2).

In case of increased physiological dead space in patients on invasive mechanical ventilation, the instrumental dead space can be reduced by removing the number of connections like catheter mount, connectors, and closed suction. Using a heated humidifier instead of HME filter, cut the endotracheal tube without compromising safety, or change to tracheostomy (reduce the dead space by 10–12 mL).

Instrumental dead space may be very high (above 100 mL) with multiple connections like HME, catheter mount, connectors, and endotracheal tube. HME filter has a volume above 50 mL (up to 90 mL), catheter mount (20–60 mL), many connectors may be used in patients (CO_2 cuvette for end-tidal CO_2 monitoring, closed suction and other adaptors for inhalation therapies) and may represent an essential additional dead space [20].

16 Measuring Patient Effort and Work of Breathing

Spontaneous breathing in patients on invasive mechanical ventilation has been shown to induce both positive and negative effects. The patient's spontaneous breathing may help in the recruitment of basal lung fields, prevent disuse atrophy of the diaphragm and other respiratory muscles, reduce sedation requirements, and facilitate earlier weaning. However, the undue high respiratory drive can generate high tidal volume or pressure and may cause harm in the form of patient self-inflicted lung injury (P-SILI) similar to VILI [21]. The positive effect of early use of neuromuscular blocking agents (especially cisatracurium) in patients with ARDS is possibly related to abolishing spontaneous respiratory effort [22]. Thus, the monitoring of the breathing effort might be valuable in better understanding respiratory mechanics and precision-based mechanical ventilation.

Mechanical work is defined as the product of force and distance and is measured in Joules (J).

However, the assessment of breathing effort is difficult without complex diagnostic techniques. The "gold standard" parameters for the assessment of respiratory effort are the work of breathing (WOB) and pressure-time product (PTP), which are more research tools and require esophageal or gastric pressure. Recently, diaphragm electromyography and ultrasound have been tried to assess breathing effort with good results [23–25].

In respiratory physiology, work is the product of pressure (representing the force) and volume (representing the distance). It represents the energy required to move tidal volume at a given pressure (spontaneous, mechanical, or both). WOB is often reported in the work per liter (J/L) unit, obtained by dividing the work per breathing cycle by tidal volume.

The patients on neuromuscular blocking agents and invasive mechanical ventilation, and plots of airway pressure versus tidal volume, indicate the total amount of work needed to inflate the respiratory system. It represents the work done by the ventilator and not the work performed by the respiratory muscles.

The WOB calculation can be used to evaluate weaning failure, effects and titration of different modes, therapeutic interventions, and ventilator performance (like triggering and flow delivery).

Different components contribute to the total WOB: elastic, resistive, and intrinsic PEEP.

Elastic work: WOB to overcome the elastic recoil of the lung or chest wall.

Resistive work: Work done to overcome the airway, chest wall, or lung parenchyma resistance.

The total WOB in a healthy adult is from 0.3 to 0.6 J/L. In patients with either severe obstructive or restrictive lung disease, WOB is increased by two to three times at rest, and a marked increase is seen during exertion.

The pressure-time product (PTP) is the time integral of the pressure performed by the respiratory muscles (P_{MUS}) during inspiration.

The PTP is calculated as the time integral of the P_{MUS}:

$$\mathbf{PTP} = \mathbf{P}\left(\mathbf{cmH_2O}\right) \times \mathbf{t}\left(\mathbf{s}\right) = \int \mathbf{Pdt}\left(\mathbf{cmH_2O^*s}\right)$$

The PTP for global respiratory muscles can be calculated using this equation if esophageal pressure is available. The PTP will help to calculate effort for all three forces: elastic, resistive, and intrinsic PEEP (threshold). The PTP of the diaphragm needs gastric pressure measurement. The PTP is independent of volume and flow, helpful to calculate effort during isovolumic contractions. This is also a limitation of PTP as the effort for inefficient muscle contractions generated during higher flows and volume cannot be calculated [26].

17 Airway Occlusion Pressure (P0.1)

Airway occlusion pressure (P0.1) is the pressure generated in the occluded airway 100 milliseconds (ms) after the onset of inspiration to monitor the respiratory drive during mechanical ventilation.

P0.1 was first described by Whitelaw et al., who found decreased airway pressure during the first 100 ms after end-expiratory occlusion, and it correlates to end-tidal CO_2. There is also a good correlation between P0.1 and inspiratory effort compared to measured either by WOB or PTP. There is no effect of the patient's effort, lung or thoracic wall recoil, or airway resistance on inspiratory effort calculation as flow is interrupted, so resistance disappears.

The normal value of P0.1 in healthy subjects varies between 0.5 and 1.5 cmH_2O. However, a significant breath-to-breath variability is seen with P0.1 calculation, and an average of 3–4 values is taken.

The ventilators use different methods to measure P0.1, breath-to-breath estimation (using a trigger window), or a temporary end-expiratory occlusion only when a measurement is required.

P0.1 can be helpful in the precision-based adjustment of ventilatory support due to its close correlation with inspiratory effort. The higher values of P0.1 imply inadequate ventilatory support, while lower values correspond to excessive assistance (using a cutoff of $\leq$1.6 cmH_2O) both during control and spontaneous modes of ventilation. Recently, ventilator modes using a target P0.1 and closed-loop algorithm to automatically adjust the level of support have been developed.

P0.1 can also be used to adjust PEEP in patients with dynamic hyperinflation. Application of an external PEEP less than intrinsic PEEP is one of the recommended measures for dynamic hyperinflation. The decrease in P0.1 after the addition of external PEEP indicates a decreased intrinsic PEEP and WOB. P0.1 has extensively been tried during weaning. An increase in P0.1 along with other variables during spontaneous breathing trial can be taken as a surrogate of failure [27].

18 Mechanical Power

Mechanical power represents the energy transformed from a mechanical ventilator to the respiratory system over a given time. It includes all parameters (pressures, volume, flow, respiratory rate) associated with VILI. Different complex mathematical equations are available to calculate mechanical power. This includes the area under the quasi-static pressure-volume curves to more complex equations based on the static and dynamic components [28]. A simple equation to calculate the mechanical power on volume-controlled ventilation is given below:

$$\textbf{Mechanical Power} = \textbf{VE} \times \left(\textbf{Peak Pressure} + \textbf{PEEP} + F/\textbf{6}\right)\textbf{20}$$

VE: Minute ventilation, F: inspiratory flow.

Mechanical power is expressed in Joules/minute.

Studies showed that mechanical power above 12 J/min was associated with reduced survival [29].

19 Conclusion

19.1 Stress Index

A simple and reliable approach to assess SI at the bedside is to examine the pressure-time curve on the ventilator screen. This simplification may aid in implementing SI in clinical practice in order to personalize mechanical ventilation. In constant

flow-volume ventilation, the stress index is used to assess the pressure-time curve. A linear increase in pressure (constant compliance, stress index = 1) indicates adequate alveolar recruitment without overdistention. During inflation, compliance may worsen (progressive decrease in compliance, upward concavity, stress index > 1), suggesting overdistention, for which it is recommended to lower the PEEP or VT. A progressive increase in compliance (downward concavity, stress index < 1), along with the potential for additional recruitment, suggesttidal recruitment, and PEEP should be increased [30].

The knowledge of respiratory mechanics is crucial for the safe application of mechanical ventilation; it reduces VILI risk, helps in troubleshooting, and may improve outcome. The equation of motion and calculation of Pplat, driving pressure, resistance, compliance, and TCexp is helpful during LPV. The calculation of respiratory effort using airway occlusion pressure, ultrasound, or PTP is helpful to diagnose various conditions, weaning failure, and personalized mechanical ventilation settings. Mechanical power is a new tool in the armamentarium to monitor the risk of VILI and reduced survival.

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Principles of Mechanical Ventilation

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1 Less Is More in Mechanical Ventilation

1.1 History of Ventilation

The management of patients with respiratory failure has undergone a constant transformation throughout the history of medicine; technological advances in recent decades have made it possible to better adapt ventilators to the needs of the patient and monitor the changes that occur in real time.

From the first records in ancient Egypt in the Papyrus of Ebers, one of the oldest medical treatises, it is mentioned how Isis, the goddess of mystery and wisdom, resurrected Osiris with a breath of life pushing air inside with her wings.

There are several mentions of ventilation in the Bible, where healing properties are attributed to air; in the Old Testament, it is narrated how the prophet Elisha performs a mouth-to-mouth resuscitation maneuver on a child. Hippocrates known as the father of medicine describes in his treatise about air tracheal intubation as a method to artificially ventilate the lungs of a human being.

In 175 BC, Galen, the prominent Greek physician and scientist, promoted the study of anatomy to understand the interaction of the lung and the heart, describing

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how the physical act of breathing causes the heart to beat. Andreas Vesalius, a medical researcher, published in 1543 a treatise on anatomy where he makes the first reference to positive-pressure ventilation: “But that life may be restored to the animal, an opening must be attempted in the trunk of the trachea, into which a tube of reed or cane should be put; you will then blow into this, so that the lung may rise again and take air.”

Paracelsus in the years 1493 and 1541 carried out numerous experiments reviving a patient by placing a tube in the mouth and blowing air through a bellows. Robert Hooke in 1667 kept a dog alive by supplying a continuous flow of oxygen by applying positive pressure.

Mechanical ventilation began in the 1700s with the discovery of oxygen and subsequently the importance of respiration in the delivery of oxygen. William Tossach reported in 1774 the first case where mouth-to-mouth resuscitation was applied in a miner rescued from a coal mine.

The first mechanical apparatus used to provide noninvasive mechanical ventilation was introduced by Chassier in 1780, a bag-and-mask manual ventilator [1]. In 1827, Leroy demonstrated that positive-pressure ventilation had its hazards and that damage could be caused to the lungs by overinflation.

The first description of a negative-pressure ventilator was of a full-body-type ventilator. This “tank ventilator” was first described by the Scottish physician John Dalziel in 1838. It consisted of an airtight box, with the patient maintained in the sitting position, and negative pressure was established by manually pumping air into and out of the box [2].

Marshall Hall and Silverten, in 1857 and 1858, respectively, disclosed the method of chest pressure and arm lift used to fill the lungs of a suffocated person with fresh air. In the nineteenth century, ventilation was provided using subatmospheric pressure applied around the patient to replace or increase the work done by the respiratory muscles. The first viable iron lung was introduced in 1876 by the Frenchman Woillez and was called a manually operated spirophore.

In 1904, Sauerbruch even developed a negative-pressure operating chamber. The patient’s body, except for the head, was maintained inside the chamber [3]. The chamber was large enough so that the surgeon was able to perform surgery while also in the chamber. The patient’s lower body was encased in a flexible sack so that positive pressure could be applied to this part of the body, preventing blood from accumulating in the abdomen and lower extremities, causing what was referred to as “tank shock” [4].

Another approach to providing noninvasive mechanical ventilation was introduced by Green and Janeway in 1910 [1]. They referred to their device as a “rhythmic inflation apparatus.” The patient’s head was placed into the apparatus, and a seal was secured around the patient’s neck with positive pressure applied to the patient’s head.

In 1911, Dräger had already created a positive-pressure ventilation device, which became known as the Pulmotor, which used a cylinder of oxygen or compressed air as a source of energy for its operation and delivered a mixture of these gases and ambient air to the patient, through a nasobuccal mask.

In 1929, Drinker and McCann built an electric cabinet fan; later developed models of the iron lung were used extensively in the treatment of polio for nearly 30 years. Negative-pressure ventilation became a much greater clinical reality with the development of the iron lung; this approach to ventilatory support reached its pinnacle during the worldwide poliomyelitis epidemic from 1930 to 1960. The first ICUs were set up to manage in some cases dozens of patients, of all ages, requiring negative-pressure ventilation [5].

Although mechanical ventilators are generally classified as negative- and positive-pressure ventilators, negative-pressure ventilators are rarely used today. Available engineering advancements made it possible to switch from first-generation devices that initially were only volume controlled, had no alarms or monitors, and could not detect the breaths triggered by the patient.

In the second-generation devices, the trigger of the patients was possible, and some parameters such as respiratory rate could be monitored. Intermittent mandatory ventilation (IMV) began to be used, and pressure-controlled and pressure-assisted ventilation was used in clinical practice.

The third-generation devices have microprocessors. Flow triggering was introduced, and gas delivery and monitoring were possible. Synchronized intermittent mandatory ventilation (SIMV) was applied, and pressure support could be given. Today's complex and modern devices are known as fourth-generation devices, and the most important feature of these devices is the wide variety of modes and options they have [6].

The modern ventilator devices have made it possible to perfect the art of ventilation and provide patients with increasingly complete support, which has gone through several changes and has evolved until reaching the great technological advances that critical medicine currently has at its disposal.

1.2 Definition

Respiration is a fundamental biological function in the life of a human being; the gaseous exchange of oxygen and carbon dioxide takes place in the pulmonary alveoli and has as an indispensable requirement the correct functioning of each element of the respiratory system.

The ability to provide enough oxygen to the body and preserve gas exchange can be affected by multiple life-threatening medical conditions. With the development and evolution of mechanical ventilation, it is possible to provide artificial support to patients with loss of respiratory function, which can potentially save their lives.

Mechanical ventilation is a procedure that allows a mechanical device to help or replace the respiratory function, preserving lung mechanics and gas exchange. This respiratory assist machine integrates volume, pressure, time, and flow to deliver a tidal breath under positive pressure to replace the respiratory process during the time it takes to recover the patient's hemodynamics and respiratory autonomy.

Ventilatory support in critically ill patients is one of the most widely used life support strategies in intensive care units around the world. Its routine application has improved the quality of care for these patients and has had a significant impact on the survival. In recent years, the implementation of protective mechanical ventilation has improved the care of patients with acute respiratory failure, making ventilatory support safer and more effective.

One of the medical conditions where the benefits and applications of mechanical ventilation have been most demonstrated is in patients with acute respiratory distress syndrome (ARDS); 50 years after its initial description, this disease continues to be a common and lethal form of respiratory insufficiency.

Acute respiratory distress syndrome is defined as acute hypoxemia, noncardiogenic pulmonary edema, reduced lung compliance, increased work of breathing, and need for ventilation; mortality remains high even in highly specialized centers.

ARDS most often develops in the context of pneumonia (bacterial, viral, and fungal), nonpulmonary sepsis, aspiration of gastric contents, and trauma. Several other causes are also associated with the development of ARDS, including acute pancreatitis, transfusions, hemorrhagic shock, or reperfusion injury and smoke inhalation.

In the global COVID-19 pandemic and ARDS secondary to a lung infection, ventilatory support became the cornerstone of currently available therapy. Given the rapid spread of COVID-19 and the lack of targeted medical therapy, the only globally accepted therapy is protective ventilation in any of its modalities.

1.3 Epidemiology

Mechanical ventilation is one of the most common interventions employed in critical patients. Annually, over 240,000 patients in the USA needs mechanical ventilation [7]. The number of patients requiring mechanical ventilation is expected to increase substantially. In the United States, approximately 310 persons per 100,000 adults undergo invasive ventilation for nonsurgical indications [8].

The mortality in intensive care unit from ARDS is 35.3%, and hospital mortality is 40% [9]. COVID-19 ARDS appears to have worse outcomes than ARDS from other causes. The mortality ranged between 26 and 61.5%, and in patients who received mechanical ventilation, the mortality can range between 65.7 and 94% [10].

In patients with COVID-19, it is estimated that 14% will develop a severe disease that requires oxygen and 5% require admission to intensive care and mechanical ventilation [11]. Although noninvasive ventilation has been used more frequently in intensive care units in recent years, it is not always available. It has been suggested that helmet NIMV may decrease intubation and improve mortality in ARDS patients; [12] however, its use in patients with COVID-19 has not yet been sufficiently studied.