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Mechanical Ventilation

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Summary

Mechanical ventilation is a revolutionary technology that has been a critical lifesaving measure in many conditions. Mechanical ventilation is a therapeutic method in which respiration is artificially stimulated. A device, which is responsible for moving gas into and out of the lungs, is connected to the patient. This therapeutic method has recently become more relevant in society and media in the setting of the COVID-19 pandemic. Uses of mechanical ventilation may be beneficial for a vast and diverse array of cases. However, mechanical ventilation, itself, does not reverse any underlying disease and can potentially harm the patient on it. Mechanical ventilation is a very complex technology, and it requires a well-trained and knowledgeable team of physicians, nurses, and technicians to ensure effective use and patient safety. The purpose of this review paper is to provide the reader with a simplified and brief explanation of important topics within the very complex concept of mechanical ventilation. This review paper will explore general concepts of mechanical ventilation, including the definitions of various pressures, mechanical breath generation, the types of ventilation, ventilator modes, positive-end expiratory pressure, monitoring a ventilated patient, the process of weaning, indications, complications, and finally, mechanical ventilation and its relation to the COVID-19 pandemic.

Keywords: Mechanical ventilation, Ventilator Modes, Weaning, Positive-end expiratory pressure, COVID-19

Sažtak

Mehanička ventilacija je revolucionarna tehnologija koja je bila kritična mjera spašavanja života u mnogim uvjetima. Mehanička ventilacija je terapijska metoda u kojoj se umjetno stimulira disanje. Uređaj, koji je odgovoran za premještanje zrak u pluća i iz njih, povezan je s pacijentom. Ova terapijska metoda nedavno je postala relevantnija u društvu i medijima u okruženju pandemije COVID-19. Upotreba mehaničke ventilacije može biti korisna za širok i raznolik niz slučajeva. Međutim, mehanička ventilacija, sama po sebi, ne preokreće nijednu temeljnu bolest i potencijalno može naškoditi pacijentu na njoj. Mehanička ventilacija vrlo je složena tehnologija i zahtijeva dobro obučen i obrazovan tim liječnika, medicinskih sestara i tehničara kako bi se osigurala učinkovita uporaba i sigurnost pacijenata. Svrha ovog pregleda je pružiti čitatelju pojednostavljena i kratka objašnjenja važnih tema unutar vrlo složenog koncepta mehaničke ventilacije. Ovaj pregledni rad istražit će opće koncepte mehaničke ventilacije, uključujući definicije različitih pritisaka, mehaničku kratku generaciju, vrste ventilacije, načine ventilacije, tlak pozitivnog izdisaja, praćenje ventiliranog pacijenta, proces odvikavanja, indikacije, komplikacije i na kraju, mehaničku ventilaciju i njezin odnos s pandemijom COVID-19.

Respiratory Physiology

The respiratory system consists of muscles and organs which are responsible for ventilation. Ventilation is defined as a physiological process in which air is inhaled into and exhaled out of the lungs and delivered to the alveoli for gas exchange (2). The respiratory tract consists of the nose, mouth, pharynx, larynx, trachea, bronchi, bronchioles, and lungs. The muscles involved in respiration include the diaphragm, which is the principal muscle, and the intercostal muscles (2).

The respiratory tract can be anatomically subdivided into the upper respiratory tract (this includes the nose, mouth, pharynx, and larynx) and the lower respiratory tract (this includes trachea, bronchi, bronchioles, alveolar duct, and alveoli) (3). The respiratory tract can also be functionally divided into the conducting zone and the respiratory zone. The conducting zone forms a pathway for the passage of inhaled gases and consists of nose, pharynx, larynx, trachea, bronchi, and bronchioles. The respiratory zone is where gas exchange occurs and consists of the alveolar ducts and alveoli (3).

Respiration, itself, can be separated into an active inspiratory phase and a passive expiratory phase. During the active inspiratory phase, inspiratory muscles contract against the elastic resistance of the lungs and chest wall and the frictional resistance resulting from organ displacement during breathing and resistance to the flow of gas in the airways (2, 10). The contraction of the inspiratory muscles increases the volume of the chest cavity. The increase in volume reduces intrathoracic pressure and creates a pressure gradient. The pressure gradient causes air to move into and down the respiratory tract (2). During the passive expiratory phase, the inspiratory muscles relax,

and the elastic tissues of the chest wall passively return to a resting position which results in expiration (2).

Gas exchange is a dependent on the ventilation and perfusion of the lungs. Lung ventilation (V) is described as the flow of air into and out of the alveoli (5). Lung perfusion (Q) is the term which describes the blood flow through alveolar capillaries (5). The degree of ventilation and perfusion is variable amongst different alveoli in different regions of the lungs. A major factor affecting ventilation of the lungs is gravity. In a standing or upright position, the lung base is more ventilated than the apex. In a supine position, the posterior part of the lung is better ventilated, and in a lateral position the lower lung is ventilated more (2). Lung perfusion is determined by the circulation of blood to the lungs which is controlled by pulmonary vascular resistance (PVR). The PVR is influenced by factors such as gravity, transmural pressure, lung volume, and vascular architecture (2). Ventilation to perfusion ratios (V/Q) are a clinical measurement used to interpret the efficiency and adequacy of gas exchange. Optimal gas exchange occurs when there is an even distribution of ventilation and perfusion (when $V/Q \approx 1.0$) (2).

Diffusion of oxygen and carbon dioxide occurs due to various pressure gradients. The partial pressure of oxygen in alveolar air is 100 mmHg, and the partial pressure of the venous blood in pulmonary circulation is 40 mmHg (5). The oxygen readily defuses down the pressure gradient from the higher pressure towards the lower pressure. The partial pressure of carbon dioxide in alveolar air is 47 mmHg, while the partial pressure of carbon dioxide in pulmonary circulation is 46 mmHg (5).

History of Mechanical Ventilation

The first documented attempt at mechanical ventilation occurred in the year 1530 when Swiss physician Paracelsus inserted a tube connected to fire bellows into a patient's mouth (6). Later, in the 1880s, Fell and O'Dwyer developed the foot pump. The Fell-O'Dwyer foot pump was comprised of air bellows, tubing, an intralaryngeal cannula, and an exit port in which the operator could control the inspiratory-expiratory cycling with his or her thumb (7). The foot pump was the first known device that was specifically designed to deliver mechanical ventilation (6).

In 1929, Philip Drinker and Louis Shaw designed the iron lung (8). This ventilator consisted of a large cylindrical chamber that encompassed the patient from the neck down (8). The cylindrical chamber would create negative pressure surrounding the patient and would result in lung expansion (6). The iron lung was critical for treating patients in poliomyelitis epidemics of the 1930s and 1940s (6,8).

Today, the use of negative pressure mechanical ventilation has been widely replaced with positive pressure ventilation using an artificial airway (6). In the late 1960s, positive end-expiratory pressure (PEEP) was introduced (8). During PEEP, a positive pressure greater than atmospheric pressure remains inside the airways during the end of exhalation (9). PEEP will be discussed in greater detail later in this review paper. Advances in technology have allowed better patient monitoring and the creation of ventilation modes such as intermittent mandatory ventilation and synchronous intermittent mandatory ventilation. Modern microprocessors can make automatic adjustments to delivery of mechanical breath (6).

Basic Concepts of Mechanical Ventilation

Units of Pressure, Definition of Pressures and Pressure Gradients

Units of Pressure

The standard unit used to express pressure in ventilation is centimeters of water pressure (cm H_2O). Atmospheric pressure is used as a reference and assigned a baseline value of 0 cm H_2O (10). Therefore, normal atmospheric pressure which is 760 mm Hg (or 1034 cm H_2O) at sea level is set to be equal to zero. Conversion values of various units of pressure will be placed in table below.

Table 1: Pressure Equivalents

1 mm Hg = 1.36 cm H_2O
1 kPa = 7.5 mm Hg
1 Torr = 1 mm Hg
1 atm = 760 mmHg = 1034 cm H_2O

Defined Pressures

Important defined pressures that need to be measured and known include airway opening pressure, body surface pressure, intrapleural pressure, and alveolar pressure.

Airway opening pressure (P_{awo}) is the pressure surrounding the mouth and, it is equivalent to atmospheric pressure or 0 cm H_2O, unless an additional pressure is applied (10). Other terms used to describe airway opening pressure includes mouth pressure, airway pressure, upper-airway pressure, mask pressure, and proximal airway pressure (10).

Body surface pressure (P_{bs}) is equivalent to atmospheric pressure or 0 cm H_2O (10).

Intrapleural pressure (P_{pl}) is the pressure found in the space between the layers of parietal and visceral pleurae (10). Normal values for intrapleural pressure include -10 cm H_2O at the end of inspiration and -5 cm H_2O at the end of expiration (10). Since it is difficult to measure intrapleural pressure, esophageal pressure (P_{Es}) is often measured as a substitute (10, 14). Esophageal manometry is used to measure esophageal pressure (14).

Alveolar pressure (P_{alv}) is the pressure measured at the level of the alveoli. Normal values of alveolar pressure are -1 cm H_2O during inspiration and +1 cm H_2O during exhalation (10). Other terms used to reference alveolar pressure include intrapulmonary pressure and lung pressure (10). Plateau pressure (P_{plat}) can be used as a surrogate for alveolar pressure (10). Plateau pressure is a measurement made on mechanical ventilation during the phase of inspiration where there is no flow is present (15).

Pressure Gradients

Pressure gradients are necessary within the respiratory system to create air flow. Normal ventilation is described using four pressure gradients. These gradients include

trans-airway pressure, transthoracic pressure, transpulmonary pressure, and trans-respiratory pressure (10).

Trans-airway pressure (P_{TA}) is defined as the pressure gradient that is required to produce airflow inside the conductive airways (10). It is calculated by taking the difference between the airway opening pressure and alveolar pressure (10).

Transthoracic pressure (P_w or P_{TT}) is the pressure needed to inflate or deflate the lungs and chest wall (10). Transthoracic pressure is calculated by subtracting alveolar pressure from body surface pressure (10).

Transpulmonary pressure (P_L or P_{TP}) is the pressure needed to maintain alveolar inflation (10). This pressure gradient is calculated by subtracting alveolar pressure and intrapleural pressure. Transpulmonary pressure can also be referred to as alveolar distending pressure (10). During inspiration, transpulmonary pressure is increased in all modes of ventilation (10).

Trans-respiratory pressure (P_{TR}) is pressure required to expand the lungs during positive pressure ventilation (10). It is calculated by taking the difference between airway opening pressure and body surface pressure (10). Table 2, below, will express the equations for each of the pressure gradients mentioned above.

Table 2: Pressure gradients and formulas

Pressure gradient	Equation	Description
Trans-airway Pressure	$P_{TA} = P_{awo} - P_{alv}$	Airway pressure – alveolar pressure
Transthoracic Pressure	P_W (or P_{TT}) = $P_{alv} - P_{bs}$	Alveolar pressure – body surface pressure
Transpulmonary Pressure	P_L (or P_{TP}) = $P_{alv} – P_{pl}$	Alveolar pressure – pleural pressure
Trans-respiratory Pressure	$P_{TR} = P_{awo} – P_{bs}$	Airway opening pressure – body surface pressure

Compliance and Resistance

The characteristics of the lungs are described in terms of compliance and resistance. Compliance is defined as the relative ease at which a structure expands (10). Pulmonary compliance which is a measure of lung expansion can be determined by dividing the change of volume over the change in pressure (11). The units used in the measurement of compliance is typically litters or millilitres per centimetres of water (10). Pulmonary compliance is inversely related to elasticity, in which elasticity is defined as the tendency for a structure to return to its original form after being acted upon by an external force (10). Pulmonary compliance is comprised of the sum of the compliances of lung

parenchyma and adjacent thoracic structures (10). Normal compliance values for spontaneously breathing individual range from 50- 170 ml/cm H_2O (10). For an individual that is intubated and mechanically ventilated the compliance value ranges form 40-50 mL/ cm H_2O up to 100 mL/ cm H_2O for males and 35-45 mL/ cm H_2O up to 100 mL/ cm H_2O for females (10). Factors that affect the elasticity of the lungs or a change within the condition of the lungs and/ or chest wall can result in changes in compliance values (10, 11). Examples of medical conditions that reduce pulmonary compliance include acute respiratory distress syndrome and kyphoscoliosis (10). Emphysema, on the other hand, is a pathological condition in which compliance is increased due to the decrease of lung elasticity (10). For a patient on mechanical ventilation, compliance can be measured directly (11). This measured compliance is known as static compliance or static effective compliance (10). Static compliance is calculated by dividing tidal volume by the difference between end-expiratory alveolar pressure and end-inspiratory alveolar pressure (11).

Pulmonary resistance is a measurement of the frictional forces needed to be overcome during respiration (10). The frictional forces involved in respiration are derived from the anatomical structure of the respiratory system and the flow of air through the airways. The resistance from the anatomical structure results from the displacement of involved organs and structures and from tissue viscous resistance (10). Resistance to the flow of air depends on multiple factors including the density and viscosity of the gas, the length and diameter of the tube, and the flow rate of the gas (10). Poiseuille's law, which is used to define the flow rate of a gas, states that the flow of a fluid depends on the length and radius of the tube, pressure gradient, and fluid viscosity (13). For a mechanically ventilated patient, tube length, density, and viscosity remain constant (10). The diameter

of the airway lumen can significantly vary due to a multitude of factors and causes. Examples of conditions that can affect lumen diameter include bronchospasm, increased secretions, and mucosal edema (10). Airway resistance is calculated by dividing trans-airway pressure (peak pressure subtracted by plateau pressure) by the gas flow (10). The typical unit used to describe resistance is centimetres of water per liter per second (cm H_2O/ [L/s]) (10). Upon insertion of an artificial airway, airway resistance can be increased by 5-7 cm H_2O/ [L/s] (10).

Time Constants

Time constant is used to describe the amount of time required for the lungs to inflate and deflate to a certain volume (10). Time constants are measured in units of seconds. The value for a time constant is derived by multiplying compliance and resistance together. One time constant represents 63% of the lung tidal volume being inflated or being deflated (10). Five time constants represent 100% of the tidal volume being inflated or being deflated (10). Time constant calculation is vital for setting inspiratory and expiratory times on ventilators. Typically, inspiratory time is set to five time constants, and expiratory time is set to three to four time constants (10). It is important to keep in mind the respiratory rate and the individual patient's condition when setting inspiratory and expiratory times on the ventilator.

Mechanical Breath Generation

Mechanical breath generation can be divided into four separate phases: initiation phase, inspiratory phase, cycling phase, and expiratory phase.

The initiation phase follows the expiratory phase and is regulated by a trigger variable (25). The mechanical ventilator sets a specific threshold as the trigger, and upon reaching the specific threshold mechanical breath is initiated. The trigger variable can be time, pressure, or flow (25). A common setting for a pressure trigger value is -2 to -1 cm H_2O (6). When choosing an appropriate threshold for a trigger, it is important to select a value that does not have too low sensitivity, or the mechanical breath can be delivered too easily and very frequently (6). If the sensitivity is too high, the patient will need to work much harder to overcome the threshold and to trigger a breath (6).

Following the trigger, the inspiratory phase begins. During this phase, air flows into the patient (25). The operator of the mechanical ventilator sets a limit variable to control and terminate this phase. Limit variables can be set values of volume, pressure, and flow (25).

After reaching the limit variable, the cycling phase of mechanical breath generation begins. The cycling phase is a short period of time between the inspiratory and expiratory phases. In the cycling phase, the expiratory valve opens for an instant during which airflow ceases (25). A cycling variable is used to control the cycling phase. This variable can include time cycling, pressure cycling, and flow cycling (25).

The final phase of mechanical breath generation is the expiratory phase. The expiratory phase describes when air flows out of the patient (25). In this phase, the expiratory valve

is opened, and the patient passively exhales (25). A positive end expiratory pressure (PEEP) variable is set to control the expiratory phase. This PEEP variable describes the pressure that will remain after the cessation of the expiratory airflow (25).

Types of Ventilators and Ventilator Modes

Types of Ventilators

Types of ventilators van be subdivided into the following categories: negative pressure ventilation, positive pressure ventilation, and high frequency ventilation.

Negative Pressure Ventilation

With negative pressure ventilation (NPV), a negative pressure is created around the patient's thorax. This initiates inspiration by expanding the lungs (17). Exhalation is initiated by the passive recoil of the lungs when the negative pressure surrounding the thorax is removed or replaced with positive pressure that causes the torso to compress (17). Examples of negative pressure ventilators include iron lungs, traditional cuirass, jacket ventilators, and Hayek oscillators (17).

NPV has many benefits and limitations. One major benefit to NPV is that endotracheal intubation is unnecessary, and its side effects are avoided (17, 18). Another advantage with NPV is that speech, cough, swallowing, and feeding functions are preserved. Additionally, therapeutic and diagnostic procedures such as bronchoscopy can be performed on a patient during NPV (18). However, NPV also has some limitations. One

limitation is that in NPV the upper airway is not protected which can result in aspiration, especially in neurological and/or unconscious patients (18). Another limitation is the risk of upper airway obstruction in neurological and/or unconscious patients (18). With NPV, there might be limitation to the physician's ability to access their patient for monitoring or treatment purposes (17). Additional side effects reported with NPV include upper airway collapse, back pain, esophagitis, rib fractures, tiredness and/or depression, and poor compliance (18).

Indications for the use of NPV include severe respiratory acidosis, severe hypercapnic encephalopathy, excessive airway secretion, facial deformity, inability to properly fit a mask, and mask intolerance (18). NPV is also indicated in the use of pediatric and neonatal cases in the intensive care unit, during surgeries involving the airways, and for at home or in hospital medium to long term ventilation (17).

Contraindications for the use of NPV include sleep-apnea syndrome, severe obesity, severe kyphoscoliosis, claustrophobia, rib fractures, and recent abdominal surgery (18).

Positive Pressure Ventilation

Positive pressure ventilation (PPV) is used to describe the process of using a mechanical ventilator to deliver air or oxygen combined with other gases directly into the lungs via positive pressure (10, 19). PPV can be administered in two ways: non-invasively or invasively (19). Non-invasive positive pressure ventilation (NIPPV) involves the use of a mask. On the other hand, invasive positive pressure ventilation (IPPV) is performed using an endotracheal tube or a tracheostomy tube (19).

There are many indications for the use of PPV. Some major indications include airway protection, hypercapnic respiratory failure, hypoxic respiratory failure, and circulatory failure (19). Indications for NIPPV include chronic obstructive pulmonary disease (COPD) exacerbations, acute cardiogenic pulmonary edema, and acute hypercapnic respiratory failure (19). NIPPV is contraindicated in conditions where emergency endotracheal intubation is required or cases of encephalopathy, altered mental status, hemodynamic instability, defects or trauma to the face, airway obstruction secondary to a mass, gastrointestinal bleeding, and when prolonged mechanical ventilation is expected. (19). Contraindications for IPPV include cases where the patient is against mechanical ventilations and situations in which NIPPV would be an effective alternative (19).

Many complications are associated with PPV. It should be noted that these complications are more commonly associated with IPPV, though very rare, these complications are still possible with NIPPV (19). Common complications of PPV include ventilator- induced lung injury (VILI), barotrauma, reduction of cardiac preload secondary to increased intrathoracic pressure (can lead to a cardiac arrhythmia or myocardial ischemia), ventilator-associated pneumonia, oxygen toxicity, and neuromuscular complications like atrophy of the diaphragm or critical illness myopathy (19). A complication of NIPPV that occurs in about thirteen percent of patients includes facial ulcers and lacerations associated with the seal around the mask being too tight (20).

High Frequency Ventilation

High frequency ventilation (HFV) is a condition in which a mechanical ventilator delivers high ventilating rates with low ventilating volumes (10). The respiratory rate is set to values greater than sixty breaths per minute, and the tidal volume lower than the volume of autonomic dead space (21). There are three strategies when using HFV. These strategies include high- frequency positive pressure ventilation (HFPPV), high-frequency jet ventilation (HFJV), and high- frequency oscillatory ventilation (HFOV) (10). HFPPV is a strategy that uses respiratory rates of 60 – 100 breaths per minute and can be achieved with a conventional positive pressure ventilation (10). HFJV uses respiratory rates of 100 – 600 breaths per minute and is achieved through use of a specifically designed endotracheal tube adaptor (10). HFOV utilized respiratory rates 1000 – 4000 breaths per minute (10). A piston or specialized device is needed to achieve HFOV (10).

HFV is indicated in both adults and neonates. Adult indications of HFV include the prevention of ventilator-induced lung injury in cases of severe acute respiratory distress syndrome (ARDS), bronchopleural fistula, pneumothorax, pulmonary interstitial emphysema, refractory hypoxemia, and in cases where conventional mechanical ventilation fails (22). Neonatal indications include persistent pulmonary hypertension, ARDS, pulmonary interstitial emphysema, pulmonary hypoplasia, and meconium aspiration (22).

Complications associated with HFV include air trapping, barotrauma, decreased venous return, decreased cardiac output, decreased clearance of secretions, and a higher risk of secondary sepsis (22).

Ventilator Modes

Ventilator modes describe various settings on a mechanical ventilator. These ventilator modes define how the mechanical ventilator controls volume, pressure, and gas flow within a breath and the sequence of the breaths (23). Factors that are considered when choosing a ventilator mode include a patient's history, physical assessment, patient interface, control variable, and type of breath.

There are countless different modes. Currently, there is no standardized classification or categorization used when describing ventilator modes. Yuan Lei, author of *Medical Ventilator System Basics: A Clinical Guide,* uses three categories to describe ventilator modes: conventional, adaptive, and biphasic (35).

Lei describes conventional ventilation modes as a mode in which the ventilator follows all the settings selected by the operator, and no settings are automatically controlled (35). These conventional modes are the most frequently used and serve as a foundation for modes in the following two categories.

Adaptive ventilation modes include modes in which one or more of the control settings are automatically adjusted (35).

Finally, biphasic ventilation modes are modes in which the baseline pressure fluctuates between two positive pressure levels intermittently corresponding to the operator's settings, and ventilated patients are able to spontaneously breath at both levels (35).

The specific ventilator modes that will be discussed in this review paper include continuous mandatory ventilation, assist control ventilation, synchronized intermittent mandatory ventilation, pressure-controlled ventilation, and dual control modes.

Continuous Mandatory Ventilation

Continuous mandatory ventilation (CMV) is a ventilator mode in which the patient has no effect on the mechanical ventilation and all breaths are delivered based on controlled and set variables (6). The operator of the ventilator sets a parameter, for example time, and the ventilator delivers generated breaths based upon the set parameters (6). The patient has no interaction with the ventilator, and all breaths are mechanically generated.

Assist- Control Ventilation

Assist- control (AC) ventilation is similar to CMV, and some sources use AC ventilation or CMV interchangeably. AC ventilation, unlike CMV, does allow the patient to take spontaneous breaths and adjusts to the patient's breathing. This mode is one of the most used mechanical ventilation modes in the intensive care unit (36). The operator selects a tidal volume that the ventilator will deliver at set period of time or if the patient initiates a spontaneous breath (36). In AC mode, the selected tidal volume will be the same. Parameters that can be set in AC mode include tidal volume, respiratory rate, fraction of inspired oxygen, and positive end expiratory pressure (36).

AC ventilation is commonly use in patients with respiratory or metabolic acidosis and patients with acute respiratory distress syndrome. In fact, AC mode was utilized in the groundbreaking study, "Ventilation with Lower Tidal Volumes as Compared with Traditional Tidal Volumes for Acute Lung Injury and the Acute Respiratory Distress Syndrome". This study found using a lower tidal volume during mechanical ventilation resulted in a decreased mortality and an increase in the number of days without

ventilator use (37). The findings of this study helped to establish the ARDSNET protocol which is the current guidelines for patients with acute respiratory distress syndrome (38). Therefore, AC ventilation is the mode of choice for cases with acute respiratory distress syndrome because it permits operators to provide low tidal volumes and adjust PEEP as needed (36). Other benefits of AC ventilation include patient comfort and low work on breathing (36).

AC ventilation mode has some disadvantages including risk for barotrauma, intrinsic PEEP, and hyperventilation (36).

Synchronized Intermittent Mandatory Ventilation

Synchronized intermittent mandatory ventilation (SIMV) is a ventilation mode in which the ventilator operator sets a required number of breaths at a preset volume while simultaneously permitting spontaneous breathing (39). In SIMV mode, the ventilator seeks to synchronize the supply of set breaths with the patient's voluntary efforts (39). Unlike AC mode, SIMV delivers breaths at various volumes that are entirely determined by the patient's effort (39).

SIMV is widely used for weaning patients from mechanical ventilators. In fact, a national survey conducted in the United States concluded that 90.2% of surveyed hospitals preferred to use SIMV mode as a weaning technique (40).

SIMV is contraindicated in patients who are unable to take spontaneous breaths (39).

Pressure-controlled Ventilation

Unlike the modes discussed above in which a mandatory tidal volume is selected, pressure-controlled ventilation is a mode the operator controls the maximal peak pressure (41). The operator selects an inspiratory pressure and PEEP, thereby controlling peak pressure (41). With this mode, the patient can be protected from developing barotrauma (41).

Pressure- controlled ventilation mode can be delivered as continuous mandatory ventilation (PC-CMV) or as intermittent mandatory ventilation (PC-IMV) (41).

It is important to note that although the patient is at low risk of developing barotrauma, if the pressure is too high the patient is at risk of volutrauma due to excessive tidal volume (41). The opposite effect may occur if the tidal volume is extremely low causing an increase in dead space ventilation and eventually ventilatory failure (41). Ventilatory failure is a condition in which the mechanical ventilator is unable to supply enough oxygen to support the metabolic demands of the patient (43).

Dual Control Ventilation

Dual control mode is a specific method of ventilation which allows the operator to control volume or control pressure. It is impossible to control volume and pressure simultaneously, so dual control mode can control either volume or pressure and can operate during a breath or between breaths (42). The operator is therefore able to alternate from pressure to volume control within the middle of a breath (42).

Definitions of Pressures in Positive Pressure Ventilation

A manometer is a pressure gauge connected to the mechanical ventilator. The operator of the mechanical ventilator can check the pressure values at any point of the respiratory cycle and these various pressure measurements can be graphed in a pressure over time curve (10). These pressure measurements can produce information about the mode of ventilation, can calculate various parameters, and be used to monitor a ventilated patient (10). The pressure values that will be discussed below include baseline pressure, peak pressure, plateau pressure, and pressure at the end of exhalation.

Baseline Pressure

Baseline pressure serves as the reference point in which the other airway pressures are measured relative to (10). Baseline pressure is usually equivalent to atmospheric pressure or zero, except in cases where positive end expiratory pressure (discussed in more detail later) is added (10).

Peak Pressure

Peak pressure refers to the measurement of the highest recorded pressure at the end of inspiration. Peak pressure can also be referred to as peak inspiratory pressure (PIP) or peak airway pressure (10). Measurements of pressure during the inspiratory phase are the results of the sum of the pressure of the gas filling the alveoli and the pressure required to overcome the airway resistance (10).

Plateau Pressure

Plateau pressure is the value measured right after the delivery of a breath and before the start of the exhalatory phase (10). The operator of the mechanical ventilator selects a control marked “inspiratory pause” or “inflation hold”. This control prevents exhalation for 0.5 to 1.5 seconds and stimulates breath holding (10). The plateau pressure is obtained during this breath holding. Plateau pressure is the measurement of pressure applied to the small airways and alveoli by the ventilator, and it is reflective of alveolar pressure (34).

Pressure at the End of Exhalation

Pressure at the end of exhalation should be equal to the baseline pressure unless positive end expiratory pressure (PEEP) is present (10). PEEP can be present due to being set by the ventilator operator (extrinsic PEEP) or because of air trapping (intrinsic PEEP) (10). PEEP will be discussed in more detail in the next section of this paper.

Positive End-Expiratory Pressure

Positive end-expiratory pressure (PEEP) is the positive pressure which remains in the airways at the end of exhalation, and this pressure is higher than the atmospheric pressure of the patient on a mechanical ventilator (27). Extrinsic PEEP is when PEEP is set as a parameter on the ventilator for therapeutic purposes (9). Intrinsic PEEP or auto-PEEP, on the other hand, describes the complication of PEEP resulting from air trapping (9).

Extrinsic PEEP is beneficial to ventilated patients because it increases oxygenation, improves ventilation-perfusion mismatches, and decreases the work of breathing (9). Extrinsic PEEP increases oxygenation by utilizing the principal of Henry's law. Henry's law states that amount of gas which dissolves into a liquid is directly proportional to the pressure of the gas applied to the liquid (28). When applying this principal to mechanical ventilation, extrinsic PEEP increases the pressure in the alveoli which then increases the ease in which oxygen crosses the alveolocapillary membrane (9). This ultimately increases the oxygenation of blood for a patient on mechanical ventilation with PEEP (9). Extrinsic PEEP decreases ventilation-perfusion mismatches by opening collapsed airways, decreasing atelectasis, and improving alveolar ventilation (9, 29). It has been observed that extrinsic PEEP significantly decreases the amount of work a patient needs to preform, especially in cases with low lung compliance (9). A study performed by Smith and Marini found that the addition of PEEP improved the trigger sensitivity of the mechanical ventilator, reduced ventilator drive, and decreased the mechanic work of breathing during the mechanically assisted ventilatory cycle (30). Smith and Marini concluded that low PEEP levels can improve lung mechanics and decrease the amount of work required for ventilated patients with severe airway obstructions without increasing the risk of hyperinflation (30). Another study performed by Glérant, Leleu, Rose, Mayeux, and Jounieaux followed the oxygen consumption of nine mechanically ventilated patients and concluded that oxygen consumption decreases with extrinsic PEEP (31).

Examples of complications associated with extrinsic PEEP include decreasing cardiac preload and therefore decreasing cardiac output, barotrauma, and interference of hemodynamic measurements in patients with right-heart catheters (9).

A complication associated with mechanical ventilation includes intrinsic PEEP (9, 32). During normal exhalation, the lungs empty the air until the pressure within the lungs is equivalent to the atmospheric pressure. Intrinsic PEEP is a phenomenon in which during passive exhalation the lungs do not completely deflate. This results in air trapping which creates a positive pressure during the end of expiration (32). When this phenomenon occurs repeatedly with each breathing cycle, the amount of air trapped increases the positive pressure at the end of expiration (9). This increased intrathoracic pressure can become pathological, and the ventilated patient becomes at risk of developing hypotension or barotrauma and the work of breathing increases (9). Risk factors for developing intrinsic PEEP includes, inflammation of the airway, high lung compliance (for example in COPD patients), high tidal volume ventilation, high respiratory rate, and a slow inspiratory flow (9). Signs of intrinsic PEEP include exhalation continuing into the next respiratory cycle, increased plateau pressure, use of accessory breathing muscles during exhalation, hypotension, prolonged expiratory times, or respiratory distress (9). If a ventilated patient develops intrinsic PEEP, it is important to ensure the patient has enough time to exhale (33). This can be accomplished by decreasing the respiratory rate, increasing inspiratory rate, using the square wave form, decreasing tidal volume, and decreasing respiratory demand by decreasing the work of breathing (9). In emergency cases where respiratory distress and shock is present, the patient should be

disconnected from the ventilator and given enough time for exhalation, the patient should be manually bagged (9).

Indications for Mechanical Ventilation

Mechanical ventilation is commonly used in intensive care units (ICU) globally, and the general use of mechanical ventilation is growing. In fact, a population-based study performed in North Carolina, found that the prevalence of mechanical ventilation for adults grew 11% in the years 1996 to 2002 (44). Theoretically, mechanical ventilation is indicated whenever the lung's ability to be ventilated or the exchange of gases is compromised to the point where injury to the patient is very probable (45). The three underlying pathophysiological process that contribute to compromise of lung ventilation or gas exchange include the loss of proper ventilatory control, imbalance between ventilatory muscle demand and capability of the ventilatory muscles, and/ or the loss of patency in the alveoli (45). The main indications to mechanically ventilate a patient include airway protection, respiratory arrest, hypercapnic or hypoxemic respiratory failure, cardiovascular distress, severe respiratory acidosis, and in cases where it is expected that the patient will need mechanical ventilation (45, 46).

Before beginning mechanical ventilation, it is imported to take a thorough and integrative assessment of the patient. It is important to assess the patient's mental status, the ability to protect his or her airway, their spontaneous ventilatory pattern, the tolerated load of ventilatory muscles, and any signs of organ damage or dysfunction (45). It is also very

important to assess whether the indication for mechanical ventilation justifies the possible risks associated with mechanical ventilation (45).

Monitoring and Maintaining Support of the Ventilated Patient

Monitoring a Ventilated Patient

During mechanical ventilation, it is critical to closely monitor the patient to ensure the patient's safety. Vital signs including heart rate, respiratory rate, oxygen saturation, blood pressure, and body temperature are vital parameters to monitor on a ventilated patient.

Hemodynamically monitoring patients is very important, and continuous arterial blood pressure monitoring is standard in most ICUs (6). Arterial cannulation is indicated in cases where continuous blood pressure monitoring and recurrent blood gas measurements are required (48). Complications to consider with arterial cannulation include risk of hemorrhage, infection, and ischemia resulting from embolus, thrombus, or spasm (47). Additional invasive hemodynamic monitoring methods include central venous catheter placement and pulmonary artery cannulation. Central venous catheters are useful for providing direct measurements of central venous pressure and central venous blood gases, administering fluids, and providing nutritional support (47). Risk factors associated with central venous catheters include infection, embolus formation, thrombus formation, and pneumothorax (47). Pulmonary artery cannulation is indicated to obtain measurements of pulmonary capillary wedge pressure (PCWP), cardiac output, and mixed venous blood gases (47). Pulmonary artery cannulation complications include

infection, embolus formation, thrombus formation, cardiovascular injury, arrythmia, and pneumothorax (47). Additional hemodynamic parameters which can be calculated while monitoring a ventilated patient include stroke volume, systemic vascular resistance, pulmonary vascular resistance, and right and left ventricular stroke work (47).

Oxygen saturation is closely monitored to detect any changes due to ventilation or hypoxemia in the patient (6). This is achieved using a pulse oximeter (6).

In addition, end-tidal carbon dioxide ($ETCO_2$) is an important parameter to monitor in a ventilated patient. $ETCO_2$ is defined as the amount of carbon dioxide which is released at the end of exhalation (49). The value of $ETCO_2$ represents the adequacy with which carbon dioxide is carried in from the blood to the lungs and ultimately exhaled (49). Two non-invasive methods exist that measure $ETCO_2$. These methods include capnometry and capnography. Capnometry gives $ETCO_2$ numbers, and capnography provides comprehensive measurements which can be presented in graphical form, as a wave, or in numerical form (49). Capnography is the recommended method (49).

Ventilator Waveforms

Standard, modern ventilators use ventilator waveforms to provide an assessment of respiratory dynamics and how the mechanical breath is delivered (50). Ventilator waveforms can provide information regarding airway resistance, compliance of the lungs, and synchrony between the patient and ventilator (50). Three waveforms are demonstrated by the ventilator. These three graphs represent pressure over time, flow over time, and volume over time (50). Having a complete understanding of ventilator

waveforms is essential to assess the respiratory dynamics of the patient and his or her interaction with the mechanical ventilator (50). Changes in the waveforms may be indicative of asynchrony, so monitoring ventilator waveforms are essential for ventilated patient safety (50).

Maintaining Support of Ventilated Patient

In order to provide a patient with effective ventilation, it is critical to maintain support and comfort for the patient.

The use of analgesics and sedatives benefit the patient by increasing their comfort and tolerance to mechanical ventilation. These drugs can be beneficial by reducing pain, delirium, anxiety, and other forms of distress (51). There is a high level of variability between medication regimes, monitoring methods, and treatment algorithms among different clinicians around the world (51). To successfully manage a patient with analgesic and sedative medications it is important to have an individualized approach and consider any predisposing and contributing factors (51). Regardless of which medications are selected, close monitoring and the utilization of validated scales should be applied (6). The Richmond Agitation- Sedation Scale (RASS) is commonly used to evaluate the agitation or sedation of a patient (52). Additionally, the use of the Confusion Assessment Method- Intensive Care Unit (CAM-ICU) is useful in assessing the presence of delirium in the patient (53). The daily use of a Spontaneous Awakening Trial (SAT) and Spontaneous Breathing Trial (SBT) should be done to evaluate the patient's readiness to be liberated from the ventilator (6).

In addition to medication, maintaining patient support can be achieved through proper positioning of the patient. There is no gold standard for the correct position to place a mechanically ventilated patient, but a supine position should be avoided (6). Positioning should be based on the individual patient and consider whether the patient has unilateral lung injury or is severely hypoxemic, and adjustments should be made accordingly (6).

Weaning Patient from Mechanical Ventilation

Weaning is the term used to describe the whole process of liberating a patient from mechanical ventilation (54). Weaning is an extremely important process because prolonged ventilation can increase the risk for developing barotrauma, pneumonia, injuries to the trachea, and musculoskeletal deterioration (55). Additionally, a postponement of weaning a patient has been associated with higher levels of morbidity, mortality, and hospital stay (55).

In 2005, an International Consensus Conference in Intensive Care Medicine was held. The main topic of this conference was weaning from mechanical ventilation (54). The conference concluded by the weaning process be divided into six steps. The steps are as follows:

1. Provide the patient with adequate treatment for acute respiratory failure
2. Consider weaning as early as possible
3. Evaluate the patient's readiness to wean
4. Preform a spontaneous breathing test (SBT)
5. Extubation of the patient

6. Possible reintubation, if required (55)

To evaluate a patient's readiness to wean various weaning predictors exist. The weaning predictors vary greatly between various ICUs and between clinicians. The Rapid Shallow Breathing Index (RSBI) is the frequency- to-tidal volume ratio (f/VT) and is a very important weaning predictor (56). A RSBI value which is less than 105 is said to predict a successful weaning. RSBI values of 105 or greater predict an unsuccessful weaning. RSBI is only part of the clinical assessment of a patient's readiness to wean, and the results of an RSBI are not completely indicative of the weaning outcome.

Currently, three methods are used when preforming an SBT. These methods include the use of invasive ventilation with low pressure support, the use of a T-piece, or the use of continuous positive airway pressure (CPAP) (57). Upon selecting the method, the following criteria must be met for a minimum of thirty minutes for the SBT to be successful:

- Respiratory rate less than 35 breaths per minute
- Heart rate less than 140 beats per minute or heart rate variability greater than 20%
- Oxygen saturation greater than 90%
- Systolic blood pressure between 80-180 mmHg or less than 20% change from the baseline
- Good tolerance to the SBT
- No signs of distress or increased work of breathing (57).

Weaning failure describes cases in which the patient fails to discontinue mechanical ventilation or requires reintubation within 24-72 hours following removal of the endotracheal tube (58). Weaning failure is defined by an unsuccessful SBT (58). Cases in which reintubation is required within the first 72 hours of extubation can also be referred to as extubation failure. Extubation failure occurs in 2-25% of patients (59). Extubation failure can be caused by a discrepancy between the capacity of respiratory muscles and work of breathing, an obstruction of the upper airway, excessive secretions, encephalopathies, cardiac dysfunction, and inadequate cough (59). Patients with extubation failure have an increased rates of mortality and morbidity, increased duration of ICU and hospital stay, prolonged mechanical ventilation, and increased necessity for tracheostomy (58, 59). It should be noted that risk factors for extubation failure include pediatric patients, age greater than 70 years, prolonged mechanical ventilation, continuous intravenous setation, and anemia (59).

Complications of Mechanical Ventilation

A multitude of complications can arise from mechanically ventilating patients. This paper will focus specifically on ventilator-induced lung injury, ventilator associated lung injury, ventilator associated pneumonia, and hemodynamic compromise.

Ventilator-Induced Lung Injury (VILI) and Ventilator-Associated Lung Injury (VALI)

Ventilator-associated lung injury (VALI) is an acute lung injury that occurs during mechanical ventilation. If it can be proven that the acute lung injury is directly caused by the mechanical ventilator, it is called ventilator-induced lung injury (VILI).

The four pathophysiological mechanisms in which VILI can occur include barotrauma, volutrauma, atelectrauma, and biotrauma (60).

Barotrauma

Barotrauma is lung injury that results from high transpulmonary pressure caused by elevated lung inflation pressure in ventilated patients (60). This causes the lungs to over expand and results in air leakage (60). Barotrauma can lead to alveolar rupture, pneumothorax, pneumomediastinum, and subcutaneous emphysema (60). Barotrauma can be prevented by carefully controlling the inflation pressure value (60).

Volutrauma

Volutrauma is a term used to describe a condition in which the alveoli are over expanded (60). As over expansion occurs, the connection between alveolar epithelium and vascular endothelium begins to split apart (60). This results in the formation of alveolar and interstitial edema (60).

Atelectrauma

Atelectrauma is defined as damage to the lungs due to shear forces as adjacent alveoli collapse and expand during mechanical ventilation (61). Atelectrauma can be prevented by utilizing PEEP (61). Lung inhomogeneity increases the risk of developing ateletrauma due to the shearing forces and ununiform inflation of alveoli (60).

Biotrauma

Biotrauma describes an adverse inflammatory response to an injury to the lungs (60). This lung injury causes cytokines and other inflammatory mediators to activate. This harmful inflammatory response can spread to other organs in the body and cause multi-organ dysfunction. Biotrauma is associated with an increase in the mortality of the mechanically ventilated patient (60).

Ventilator- Associated Pneumonia (VAP)

Ventilator- associated pneumonia (VAP) is the onset of pneumonia more than 48 hours following the beginning of ventilation (62). In order to diagnose VAP, the patient cannot have been diagnosed with pneumonia before or during intubation (60). VAP is associated with increased mortality and morbidity (60). VAP can be divided into two categories: early-onset VAP and late-onset VAP. Early onset VAP occurs within the first 96 hours and is associated with a better prognosis than late-onset VAP which presents itself after the first 96 hours (60). Late-onset VAP is related to a higher risk of infection caused by a multi-drug resistant pathogen and a higher mortality rate (60).

Hemodynamic Compromise

It is very important to continuously monitor a ventilated patient's blood pressure because hemodynamic compromise is a potential complication of mechanical ventilation. Following endotracheal intubation, right atrial pressure increases and results in a decreased preload which, in turn, worsens hemodynamics within the patient (6). Another cause of hemodynamic compromise can result from the use of sedation and analgesia during ventilation. Sedation and analgesia may decrease the tone of the arterioles (6). Hemodynamic compromise, as a complication of mechanical ventilation, is usually a consequence of an inherent comorbidity of the patient as well as the patient's preload status (6). Upon noticing any change within the hemodynamics of a ventilated patient, a thorough investigation of potential roots of the hemodynamic compromise should be conducted (6).

Mechanical Ventilation and COVID-19

In the past couple of years, mechanical ventilation, as a treatment option, has gained much global notoriety due to the coronavirus pandemic, which began in the year 2020. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 virus) is a respiratory virus which causes the contagious disease known as coronavirus disease or COVID-19. Majority of individuals infected with coronavirus will exhibit mild to moderate symptoms, while some infected individuals will develop severe and even life-threatening conditions.

The virus primarily affects the lungs which can lead to the development of ARDS in which the patient will meet the criteria to be mechanically ventilated (63). ARDS in

Covid-19 infected patients differs from classical non-Covid-19 ARDS (66). The Berlin criteria is used to diagnose classical ARDS. The Berlin criteria is as follows:

- ARDS occurs within one week of a known clinical insult or respiratory symptoms worsen
- Chest x-ray or chest CT reveals bilateral opacities which are not entirely explained by effusions, lobar/lung collapse, and nodules
- Edema originates from respiratory failure which is not entirely explained by cardiac failure or fluid overload
- Oxygenation levels which can be described as mild (200 mmHg < PaO_2 / FiO_2 ≤ 300 mmHg), moderation (100 mmHg < PaO_2 / FiO_2 ≤ 200 mmHg), ore severe (PaO_2 ≤ 100 mmHg). Where PaO_2 represents the partial pressure of oxygen and FiO_2 represents inspiratory oxygen fraction (66)

Differences amongst the presentations of classical ARDS and COVID-19 associated ARDS exist. Firstly, patients with COVID-19 ARDS tend to have severe hypoxemia and more compliant lungs when compared to classical ARDS (66, 67). Various studies have found the onset time of COVID-19 ARDS to be longer than classical ARDS defined by the Berlin criteria (66). The range of onset time between the studies concluded COVID-19 ARDS onset time to range from 8 to 12 days (66). Imaging is also different since patients with COVID-19 ARDS typically present with bilateral ground-glass appearance distributed in the peripheral lung (66).

COVID-19 ARDS has been described as having two phenotypes (67). The first phenotype, known as Type L in which the traits are low elasticities, low lung weights, low

ventilation/ perfusion ratios, and low lung recruitabilities (67). The second phenotype of COVID-19 ARDS is known as Type H (67). Characteristics of Type H includes high elasticities, high lung weights, high right-to-left shunts, and high lung recruitabilities (67). Gattinoni L. et al. proposed that L Type phenotype is the initial presentation of COVID-19 ARDS, and some patients transition to H Type due to worsening of the COVID-19 infection or injury due to high- stress ventilation (67).

Assessing the COVID-19 phenotype of a patient is important in order to select appropriate treatment options. The initial approach should be to attempt to reverse the hypoxemia of the patient by increasing FiO_2, and it should be noted that Type L who are not dyspneic have a positive response to increasing FiO_2 (69). Treatment options for dyspneic Type L patients includes noninvasive ventilation, high-flow nasal cannula, and continuous positive airway pressure (69). If the Type L patient is intubated and sedated and hypercapnic, they can be ventilated with large volumes ranging from 6 to 9 ml/kg (69). This is because Type L phenotype has high compliance (low elasticity) and the risk of developing VILI is low (69). Due to the fact that Type L has low recruitability, PEEP should be low (8-10 cmH_2O), to avoid risking hemodynamic compromise (69). Additionally, it is advised to not use prone positioning in Type L COVID-19 patients (69). Cases with H Type phenotype should be treated the same as severe ARDS. This treatment includes utilizing higher levels of PEEP, the prone position, and support (69). It should also be noted that early intubation can prevent the transition from L Type to H Type (69).

Additional indications for initiating mechanical ventilation in a COVID-19 patient include inefficient gas exchange, respiratory muscle fatigue, tachypnea, bradypnea, or apnea (63).

The frequency of the use of mechanical ventilation as a treatment option for coronavirus afflicted patients varied greatly between different nations. A study preformed in from the United States of America reported 89.9% of COVID-19 patients admitted into an ICU were intubated (64). A Chinese study reported 29.1 % of their patients admitted to the ICU were placed on mechanical ventilation (64). There are many reasons why this variation amongst the incidence of intubation existed. For example, throughout the pandemic, there was also a no standardized criteria for when to provide a COVID-19 patient with mechanical ventilation, so the decision was made on an individual basis by clinicians (64). Another reason for this large variability is also the availability of ventilators and associated resources between different nations (64).

A study entitled “ICU and ventilator mortality among critically ill adults with COVID-19,” followed the outcomes of 217 patients that were admitted to COVID-19 designated ICUs across Atlanta, Georgia (65). The study concluded that the mortality rate of those who required mechanical ventilation was 29.7% (65). It should be noted, because of the small sample size, this is not an accurate representation of the mortality rate for mechanically ventilated patients with coronavirus.

Due to coronavirus’s unpredictable and fast transmissible nature, the demand for ICU beds and mechanical ventilators skyrocketed. The entire world was placed on lockdown in an attempt to slow the spread of the coronavirus and to not exacerbate the ICU

resources. Policies and laws were being enacted to ensure the availability of ventilators. Interestingly, mechanical ventilation and ventilators stood in the epicenter of the unique era of human history known as the coronavirus pandemic.

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