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Driving Pressure in Mechanical Ventilation: A Review

Driving Pressure & Mechanical Ventilation

Syeda Farheen Zaidi, Asim Shaikh, Daniyal Aziz Khan, Salim Surani, Iqbal Ratnani

Abstract

Driving pressure is a core therapeutic component of mechanical ventilation (MV). Varying levels of driving pressure have been employed during MV depending on the type of underlying pathology and severity of injury. However, driving pressure levels have also been shown to closely impact hard endpoints such as mortality. Considering this, conducting an in-depth review of driving pressure as a unique, outcome-impacting therapeutic modality is extremely important. There is a need to understand the subtleties involved in making sure driving pressure levels are optimized to enhance outcomes and minimize harm. We performed this narrative review to further explore the various uses of driving pressures, the different parameters that can affect its use, and how outcomes vary in different patient populations at different pressure levels. To better utilize driving pressure in MV-requiring patients, additional large-scale clinical studies are needed.

Key Words: Driving Pressure; ARDS; Mortality; PEEP; Ventilator Induced Lung Injury; Mechanical Ventilation

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Core Tip: Driving pressures of <15 have demonstrated the greatest benefit in mortality. It is most utilized in patients with ARDS. Some large-scale randomized controlled trials are currently underway; their results will dictate the outcomes of certain driving pressures under specialized conditions, such as the feasibility of reducing driving pressure in ARDS patients on MV and the impact of lateral positioning on driving pressure. It is clear, however, that careful implementation of driving pressures can greatly improve outcomes.

INTRODUCTION

INTRODUCTION

Driving pressure (ΔP) is a fundamental element employed in mechanical ventilation. Its primary function is to overcome the elastic forces of the pulmonary system. It is derived from the difference between end-inspiratory airway pressure, commonly known as the plateau pressure (Pplat), and positive end-expiratory pressure (PEEP) in the absence of spontaneous respiration. [1–4]

Driving pressure is derived from the ventilator and serves as a function of respiratory compliance and tidal volume. It reflects the pressure difference within a singular breath and is one of the major parameters implicated in lung stress. [5,6] Recent studies have shown a plausible association between driving pressure and improved survival in patients with acute respiratory distress syndrome. [7–16] Even though it is commonly used across critical care centers around the globe, it is a measure that requires further introspection to harness its predictive potential and guide safe and effective ventilation.

This review article discusses the dynamics of mechanical ventilation and explores the role of driving pressure, its significance in recent studies, and the resulting implications for future research.

PHYSIOLOGY AND MECHANICS OF MECHANICAL VENTILATION

Mechanical ventilation allows gas exchange and attenuates increased work of breathing in the setting of an acute compromise of the respiratory system. The mechanics are expressed through indices such as pressure, flow, volume, resistance, work of breathing, and compliance – all of which directly influence lung volumes, functional residual capacity, and the resulting gas exchange. [17]

Physiologically, the respiratory circuit works as a negative pressure system. On inspiration, the diaphragm is pushed down, and negative pleural cavity pressure is generated. A net negative pressure in the airway serves as a suction for air to be brought into the lungs. The negative pressure then, in turn, decreases the right atrial pressure and generates a similar suction effect in the inferior Vena Cava (IVC), which results in an increase in venous return. [17]

During mechanical ventilation, however – this physiology is altered, and a positive pressure is transmitted into the pulmonary system instead. This leads to a more positive pressure in the pleural space and less of that suction effect. This positive pressure is also exerted on the right atrium, which leads to a decrease in venous return and preload. The net impact is a reduced cardiac output due to the underfilling of blood in the left heart and low mean arterial pressures.[18] An understanding of the effects of artificial ventilation is important to guide management in patients and adjust for the consequences.

The baby lung concept [19] was coined by Gattinoni and Pesenti after they observed CT scans of patients with acute respiratory distress syndrome (ARDS) or acute lung injury. It was defined as the fraction of lung parenchyma that, in ARDS, still maintains normal inflation. They noticed that the total aerated tissue of these patients held dimensions of 300-550 g, similar to a 5–6-year-old child. They proposed that the ARDS lung is not stiff but, in fact, functionally small – suggesting that the elasticity of the lung is most likely intact and that the lung tissue may change dimensions after recruitment maneuvers such as prone positioning. They highlighted that gentle lung treatment should thus be employed to avoid baro-volutrauma through standard aggressive resuscitative strategies. This theory has gained traction as further research on ARDS has supported

their findings, and the discovery and application of driving pressure in research has improved outcomes.[20] In general, a tailored approach to ventilation is required to match a patient's variable physiology to reduce the chances of ventilator-induced lung injury.

A) FACTORS THAT INFLUENCE THE MECHANICS OF ARTIFICIAL VENTILATION

Impedance

The forces that impede ventilation include non-elastic or respiratory system resistance, which occurs when gas flows within the airway circuit, and elastic resistance, which occurs in the absence of gas flow in the circuit.[21] Examples of non-elastic resistance include frictional resistance to gas flow, viscoelastic resistance from the deformation of thoracic tissues, and finally, the inertia of gas flow and tissue movement.[21] While small levels of impedance do not always mean underventilation of lung tissues, higher levels of impedance require higher driving pressures for effective ventilation. These forms of resistance can be reflected in the equation below:

(Resistance R = Δ pressure/flow)

The elastic resistance comprises resistance exerted by the chest wall and lung tissue, along with resistance exerted by the surface forces at the alveolar gas-liquid interface. The elastic resistance can be used to derive total compliance of the lung and chest wall. [21] [22]These forms of resistance can be reflected in the equations below:

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(Compliance Crs = Δ volume/Δ pressure)

(Elastance ELrs = Δ pressure/Δ volume = 1/C)

As a rule, high levels of compliance, and therefore lower levels of elastance, allow for less effective mechanical ventilation at lower driving pressures. Hence, in certain conditions that alter these mechanics, such as emphysema which leads to higher compliance, higher levels of driving pressure are required to maintain adequate levels of ventilation.

PRESSURE

Airway pressure

Airway pressure is equal to alveolar pressure in the resting state and depicts the pressure generated to overcome the retractive elastic forces of the pulmonary system. It is reflected below in the following equation. [23,24]

(airway pressure = flow x resistance + alveolar pressure)

Airway pressure dictates the driving pressures required for adequate ventilation in all patients. Higher alveolar pressures and general airway resistance require increasing levels of driving pressure to maintain effective ventilation.

Plateau pressure

Plateau pressure is the pressure exerted by the ventilator into the alveoli and small airways of the lung. Calculated during an inspiratory pause of 0.5-1 s on the ventilator when the respiratory muscles are relaxed. This pressure approximates the mean peak alveolar pressure. [25,26] As noted previously, resting high plateau pressures are incorporated in driving pressure calculations in order to identify requirements for overcoming inside pressures.

Transpulmonary pressure

Transpulmonary pressure (PTP) is the distending pressure of the lungs and is derived by calculating the difference between the pressure within the alveoli (PALV) and the pleural pressure (PPL).[27]

(PTP = PALV – PPL)

Driving Pressure

Driving pressure (ΔP) is derived from the difference between Plateau pressure (Pplat) and Positive end-expiratory pressure (PEEP). It is essentially the pressure required to open the alveolar sacs. Since static lung compliance (Cstat) is derived from Tidal Volume / (Pplat – PEEP), driving pressure is derived as an inverse function of lung compliance (CRS). The higher the driving pressure, the lower the compliance of the lung and, therefore, an increased risk of volutrauma. Driving pressure is the foundational pillar of mechanical ventilation. Adequate driving pressure levels are needed for effective air delivery in order to overcome resistances, high inner pressures, and losses during delivery. It is depicted in the equations below. [28]

(ΔP =Pplat – PEEP)

(ΔP = VT/CRS)

Transpulmonary driving pressure

Transpulmonary driving pressure (ΔPpL) can be defined as the difference between the transpulmonary pressures at end inspiration and end-expiration.

Peak pressure

Peak pressure is the maximum recorded pressure at the end of inspiration in the presence of airflow. Peak pressure depends on tidal volume, respiratory rate, and airflow. [17,24]

Intrinsic PEEP

Intrinsic peak expiratory pressure (IPEEP) reflects the pressure exerted by the residual volume in the lung due to incomplete exhalation. It can be calculated by doing an expiratory pause and measuring the end-expiratory pressure. [17]

Stress

Lung stress refers to the pressure required to distend the lung against the counterforce exerted by the chest wall. Stress is depicted best by transpulmonary pressure, which is the difference between airway pressure (Paw) and pleural pressure (PPL). Its formula is depicted below:

(Paw- PPL)

Despite its high predictability, transpulmonary pressure is not frequently used due to the difficulty of calculation, and plateau pressure is thus used as an alternative. Plateau pressure is reflective of alveolar pressure when the airflow is zero and is calculated during an inspiratory pause on the ventilator when the respiratory muscles are relaxed.

Strain

Lung strain is directly related to lung stress and refers to the change in lung volume when compared to its volume during regular respiration. [24,27,29]

B) MODIFIABLE INPUTS IN ARTIFICIAL MECHANICAL VENTILATION

Tidal volume

Tidal volume is the amount of air exchanged during ventilation at rest and is matched by ideal body weight or approximations based on the patient's disposition. [17] Tidal volume follows a proportional relationship with driving pressure in mechanical ventilation. Higher tidal volumes increase driving pressures. This can be modified as needed.

Positive end-expiratory pressure

Peep or extrinsic peep is the end-expiration pressure that is delivered by mechanical ventilation to prevent the lung from collapsing. It is important to maintain the patency of the small airways and alveoli. This, in turn, increases lymphatic flow and allows adequate drainage of the lung. Therefore, lower levels of PEEP increase driving pressures.

Respiratory rate

The rate of ventilation is set to achieve target levels of carbon dioxide according to the patient's metabolic demands. [17] Respiratory rate is a component of mechanical power along with driving pressure. These levels can be changed depending on ventilation requirements and desired mechanical power metrics.

C) MEASURES OF PATIENT-MACHINE INTERACTION

Mechanical energy

Mechanical energy (EnergyL) refers to various forms of energy transferred after each ventilatory cycle and can be derived simply through plateau pressure (ΔPL) and the elastance (EL) of the lung. It is described in the following formula(s):

$$(EnergyL = \Delta PL\ 2/EL)$$

$$(EnergyL = \Delta V2 \times [(0.5\times ERS + RR \times (1+ I:E)/60\times I:E \times Raw) + \Delta V \times PEEP])$$

Mechanical power and intensity

Mechanical power (MP) refers to the mechanical energy multiplied by the rate of respiration, thus reflecting the mechanical energy transferred per minute from artificial ventilation. This value captures both static and dynamic metrics that influence respiration. [30] Mechanical power has recently emerged as a novel and promising predictor of ventilator-induced lung injury VILI. While its incorporation clinically is yet to be widened, it has shown promise. Maintaining lower rates of mechanical power by considering the dynamic metrics it incorporates can reduce rates of VILI.

$$MP = (EnergyL\ x\ RR)\ or\ RR\cdot\ W=RR\cdot\ \int 0\ VT\ PawdV$$

CLINICAL RELEVANCE OF DRIVING PRESSURE

In recent years, the understanding behind VILI has rapidly expanded from a limited perspective of pressures, volumes, and tidal cycles to an understanding of forces and their interplay in periods of stress and strain while being subjected to different forms of energy and power. The value of driving pressure has recently gained traction in research and practice due to key findings demonstrating the impact of high driving pressures, resulting in low compliance and increased risk of volutrauma. Ultimately

leading to higher morbidity and mortality in patients requiring artificial ventilation – particularly in cases of ARDS.

A meta-analysis by Amato *et al* analyzed 9 randomized controlled trials and demonstrated that in intensive care settings, ARDS patients with elevated driving pressures of 15cm H2O were positively associated with higher mortality (relative risk, 1.41; 95% confidence interval [CI], 1.31 to 1.51; P<0.001), (relative risk, 1.36; 95%CI, 1.17 to 1.58; P<0.001).

After every 1 standard increment in ΔP (approximately 7 cm of water), this result was despite the protective range of tidal volumes and plateau pressures. [14] A driving pressure less than 15 cm H20 was considered to be a safe threshold to guide ventilation in ARDS patients and decrease mortality.[14] This study, despite its limitations, provided a significant understanding of the delicate role driving pressures can play in the management of ARDS and the intricate and precise difference the slightest of modifications can make.

In addition, the Large observational cohort study to understand the Global impact of Severe Acute Respiratory failure (LUNG-SAFE) STUDY, a multicenter, international study, was conducted to identify the incidence of ARDS in intensive care units but also to collect information about the associated ventilatory management, therapies, and outcomes. The multivariate analyses concluded that high peak pressures, higher plateau pressures, high driving pressures of >14cm h20, and low peep were associated with increased mortality in these patients. [31]

This notion gained additional strength when Bellani *et al*, in their retrospective study, also demonstrated that a higher driving pressure was associated with higher mortality rates. [32]

Chiumello *et al* revealed that ARDS patients with higher than threshold values of driving pressure experienced higher lung stress and thus were likely to experience more ventilator associated lung injury (VALI) due to increased cyclic stretch. It can, therefore, be inferred that the driving pressure reflects the stress on the lungs and that outputs like tidal volumes should be adjusted for driving pressure instead of traditional measures.[2]

Similarly, PEEP can be adjusted to accommodate the loss of airway recruitment, increased levels of stress and strain, and the resulting increase in driving pressure. A higher peep will improve lung compliance and attenuate the high driving pressures resulting from lung inhomogeneity. [33,34]

Villar *et al* provided evidence that driving pressure was related to an increase in hospital mortality despite optimized protective ventilation. [35]

Urner *et al* assessed the dose-effect relationship between driving pressure and survival. A hazard ratio of 1.064 (95% confidence interval 1.057-1.071) was seen with a daily increment of driving pressure. An increased mortality was noted with driving pressure levels of >= 15 cm H20, even if present for brief periods, and had a greater increase in mortality when compared to PaO_2/FiO_2 or other metrics of oxygenation. [36]

While it has emerged as a promising metric to help moderate VILI, despite reliable estimation of lung pressures, driving pressure alone may not provide an accurate measure of risk. The process of VILI is still multifactorial and contains a complex interplay between various forces and entities that need to be accounted for.

MONITORING, MEASUREMENT, AND PATIENT CHARACTERISTICS

Driving pressure is measured in two ways. Firstly, in the setting of an absence of spontaneous breathing, an end-inspiratory hold of a few seconds on the ventilator

provides the value of Pplat. The driving pressure can be derived from the following formula;

(Pplat-PEEP)

This method can be vulnerable to oversimplification and bias when auto-PEEP is significant and not accounted for. It can also be erroneous when clinical leaks such as bronchopleural fistulas or micro leaks are found in the apparatus or tubing. These errors can result in second-by-second variability in Pplat values. A way to counter this discrepancy is to shift the ventilator to volume control mode and set a shorter inspiratory pause of 0.3 s. This method will provide consistent measures of Pplat and thus more reliability due to shorter occlusion periods[37]

Foti *et al* described the method of calculating driving pressure in static conditions with pressure support ventilation. The derivation of Pplat is performed after an end-inspiratory hold and respiratory muscle relaxation (when the pressure generated by the ventilator (Paw) reaches a plateau).[38] This method was proven by Akoumianaki *et al* to overestimate Pplat and driving pressure due to confounding by expiratory muscle activity. [39]

Another potential problem that distorts an accurate read of the Pplat is reverse triggering, wherein a patient initiates inspiratory effort during the middle or end of a passive inspiration by the ventilator. This is a form of ventilator desynchrony that tends to occur when a patient is weaning off sedation or paralysis. This results in an underestimation of Pplat due to a misleading drop in end-inspiratory pressures.[40]

In the case of spontaneous breathing, the derivation of driving pressure becomes slightly more complex, as the patient component of respiratory effort needs to be accounted for, which is essentially driving the breath. Therefore, the pressure applied

by the ventilator (Pplat-PEEP) needs to be added to the pressure generated by the respiratory muscles; i.e., pleural pressure. The pleural pressure can be accurately estimated through esophageal manometry, and this dynamic measurement is called the PL swing. The swing describes the driving pressure for insufflation of the lung and generation of flow. – thus representing the overall change in pleural pressure. [41]

The formula changes as the following:

(Pplat-PEEP + Δpleural pressure)

Another value Bertoni *et al* investigated was the ΔPocc (occluded inspiratory airway pressure), also known as the Pes swing. This value emerged from performing an expiratory hold to ascertain the patient's inspiratory effort. The deflection shows the change in pleural pressure. This was described as a dynamic pleural pressure. [42]

(Predicted dynamic DPL= (Ppeak – PEEP) – 0.66 x ΔPocc)

Telias *et al* also showed the value of the airway occlusion pressure (P0.1) metric that is measured in the first 100 ms. of an occlusion. This metric was used to accurately detect inspiratory effort and low ventilatory drive. P0.1 can also be used to ascertain high values of dynamic DPL. [43]

The driving pressure is shown to be reduced by high PEEP, low Tidal volume, increased alveolar recruitment, and low plateau pressures. [44]

A study by Di Mussi *et al* demonstrated there may be an increase in the neuro-ventilatory drive during pressure support ventilation. This can lead to variations in various respiratory drives and effort – which can also influence driving pressure and other metrics during measurement. [45]

DRIVING PRESSURE IN SPECIAL POPULATIONS

ARDS

In ARDS, the lung becomes less compliant, resulting in a reduced proportion of recruitable tissue that can be ventilated. This was best illustrated by the previously described baby lung concept. [19,46] These alterations thus require modulation of ventilatory techniques to account for the loss of lung volume, such as adjusting tidal volume with compliance and increasing PEEP to target driving pressures essentially. [14] As discussed earlier, there are many studies that have described the role of driving pressure in patients with ARDS. The strong association of cyclical stretch and lung stress correlates with driving pressure and overall survival in ARDS.

Blondonnet *et al* analyzed driving pressure at baseline and at 24 h in patients who had developed ARDS. The analysis showed that both baseline driving pressure and respiratory rate were significantly lower. Driving pressure greater than 16.5 cm H2O was predictive for ARDS development and vice versa.[47]

Haudebourg *et al* demonstrated that driving pressure-targeted ventilation in patients with moderate to severe ARDS improved ventilatory parameters such as increased tidal volumes, lower mechanical power requirement, and reduced respiratory rate. [48]

Guerin *et al*, in their study, showed that driving pressure was more strongly associated with survival as compared to PEEP and tidal volume in ARDS patients.[7]

While many studies have highlighted the role of driving pressure and its influence on outcomes, some studies suggest otherwise.

One such study by Romano *et al* compared limiting driving pressure with standard lung protective measures during ventilation of patients with ARDS. The tidal volume was set according to ideal weight – 4-8 mL/kg and a driving pressure of 10 or the lowest possible was applied, while the comparison group was ventilated according to the ARDSNet protocol with adjustments made in tidal volume based on Plateau pressures. It was seen that both the driving pressure and tidal volumes were lower in the driving pressure-limited group as opposed to the conventional group, although there was no effect on outcomes.[49]

ECMO

Extracorporeal membrane oxygenation (ECMO), an external circuit to directly oxygenate the blood and remove carbon dioxide, was unveiled in the 1970s, but its use took off in more recent years, increasing a whopping 433% since 2006[50]. ECMO is used to rest the lung, decreasing stress, strain, and intensity experienced in mechanical ventilation and providing cardiac, respiratory, or cardiorespiratory when needed. [51] Ultra-low tidal volumes are employed, and various strategies are used to achieve this.

A study by Gupta *et al* analyzed driving pressures pre and post-ECMO initiation to compare how high and low driving pressures influence mortality and outcomes. In this study, 46% of patients had increased driving pressures and higher drops in PEEP post-ECMO initiation. The study also showed a significantly longer length of ECMO stay in patients, perhaps due to poor parameters influencing clinician decision of weaning. High driving pressure in ECMO was seen as a strong predictor of 30-day mortality in both adjusted and unadjusted analyses of patients receiving ECMO in both groups. [52]

Magunia *et al* showed in their study of patients receiving VV-ECMO that survivors had increased compliance levels and lower driving pressures as compared to non-survivors.

Chiu *et al*, in their study of patients with severe ARDS on ECMO, showed that the cut-off point between survivors and non-survivors was a 33% change in driving pressure within the first 12 h with a sensitivity of 78% and a specificity of 67.9%.[53]

In the study by Sorbo *et al*, the effects of changing driving pressure were correlated with various variables. A linear relationship was demonstrated between the change in driving pressure and the concentration of certain inflammatory mediators that correlate with ventilator-induced lung injury in lung epithelial cells. [54]

Current guidelines for mechanical ventilation of ECMO target plateau pressure and tidal volumes corrected for ideal body weight.[55]

Surgical

In the surgical setting – there is a high likelihood of pulmonary complications, particularly in thoracic surgery, due to direct injury of lung tissues and open ventilation of one lung. This results in a heightened immune response and increased pulmonary vascular permeability, resulting in ARDS. [56]

Blank *et al* analyzed the driving pressure and tidal volumes of patients undergoing thoracic surgery with two or one-lung ventilation and found that driving pressure was a risk factor for overall postoperative morbidity with an odds ratio of 1.034 (97.5% CI. 1.001 to 1.068). [57]

In a meta-analysis of surgical patients, Neto and colleagues demonstrated a positive correlation between postoperative respiratory complications in patients with higher driving pressures with an odds ratio of 1.16 for each 1 cm H_2O increase in driving

pressure. No such associations were found with tidal volume, and PEEP was only influential if it altered the driving pressure.[58]

In a cohort study conducted by Mathis *et al* of cardiac patients undergoing surgery, modified driving pressure was independently associated with decreased pulmonary complications. However, it was not clear whether active control of driving pressure would result in improved outcomes, and the method of controlling or reducing driving pressure was not particularly defined in their study. [59]

Park *et al* randomized patients who were receiving elective thoracic surgery into two ventilatory groups. One group was ventilated with standard measures of low tidal volumes, a peep of 5cm H_20, and tailored maneuvers to increase recruitment were utilized as needed. Low tidal volumes were used in the second group, but PEEP was titrated according to the desired driving pressure. Postoperative pulmonary complications were higher in conventional 12.2% as compared to the 5.5% in the group with accommodation for driving pressure in ventilation. The incidence of ARDS was also elevated in the conventional group (5 patients) as opposed to 0 in the driving pressure group. Despite the impressive findings, there was no impact on the development of ARDS by day 7, nor was there any decrease in the length of ICU and hospital stay. [60]

COPD

In the setting of chronic obstructive pulmonary disease, increased air trapping, obstruction, and airway resistance – there is an increase in end-expiratory lung volume and an increase in end-expiratory alveolar pressure – also referred to as intrinsic peep. Using end expiratory and inspiratory hold is needed to accurately generate compliance and therefore driving pressures. [61] Although specific studies on COPD patients and the

role of driving pressure in their ventilation have not been captured, COPD patients require monitoring to ensure the emptying of lung air. PEEP is thus primarily adjusted.

Obesity

Obese patients typically have higher chest wall elastance, low or more negative transpulmonary pressures, and lower compliance. Due to the variability of these values – a true reflection of driving pressure cannot be obtained accurately. In obese patients, transpulmonary driving pressure is more reliable, but more studies are required to better explain these assumptions. [62]

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Jong *et al* studied the relationship between driving pressure during the first day of ventilation and 90-day mortality in 100 obese patients and 262 non-obese patients with ARDS but found no association between driving pressure and mortality in obese patients. A limitation of the study was the reliance on body mass index as a measure of obesity and body fat percentage was not accounted for. [63]

Pregnancy

In pregnancy, the physiology of the respiratory symptom is altered. Due to the chemical effects of progesterone and prostaglandins E1 and E2, bronchodilation occurs. Prostaglandin F2alpha, however, can increase airway resistance and constrict bronchial smooth muscles.

In addition, due to uterine distension, the diaphragm is elevated, and there is an increase in end-expiratory abdominal pressure (Pga). The pleural pressure also increases, leading to a reduction in expiratory residual volume (ERV) and functional residual capacity (FRC) due to early closure of small airways. The chest height also becomes shorter. ERV is 8-40% lower during the second half of pregnancy. The tidal

volume and occlusion pressure also increase, reflecting a need for adjustment for ventilation.[64,65]

Theoretically, the increase in pleural pressure and resistance should increase driving pressure and plateau pressure.

Respiratory failure in pregnancy is rare, occurring in 1 in 10,000 pregnancies, but its incidence has increased, particularly since COVID-19.[66] A study by Vasquez *et al* showed that respiratory mechanics in pregnant females remained similar to the general population that required ventilation in cases of COVID.[67]

In a study by Lapinski *et al*, they conducted a retrospective analysis of the impact of COVID-19 on mechanical ventilation parameters. In the case of driving pressures, survivors had an average of <14 cm H20, and non-survivors had higher driving pressures. Post-delivery, there was an increase in the PaO_2/FiO_2 ratio, but there was no change in static compliance or driving pressure. [68]

Pediatric

The implication of driving pressure in the pediatric age group has limited data. A retrospective study by Rauf *et al* assessed the effects of driving pressure on morbidity and mortality in children admitted to the ICU with ARDS. The study divided the children into two groups – one with driving pressures of ^{3} 15 cm h20 in the first hour and the other with lower than 15 driving pressures. It was seen that children with lower pressures had significantly lower morbidity in ARDS. [9] A study by Yehya *et al*, however, suggested that driving pressure in children with ARDS was not an independent predictor of mortality. It is worth noting that driving pressure was not accurately defined in either of these studies. [69]

The first pediatric study to assess driving pressure in mechanically ventilated children was conducted by Schelven *et al* In their study, they demonstrated higher disease severity, MV indication, and an increase in extubation time in patients with higher driving pressures.[16]

The pediatric lung is thus similarly influenced by driving pressure during ventilation.

Elderly

Aging can result in an alteration of lung physiology through increased pro-inflammatory and fibrotic factors. Decreased chest wall compliance and higher levels of air trapping due to loss of lung tissue with a reduction in FEV1. [70] No study has specifically explored the effect of aging on driving pressure, but theoretically, it is assumed that it would increase due to the change in compliance. Elderly patients are far more susceptible to higher morbidity and mortality in the ICU setting, and several studies have reported age as a strong predictor for mortality. [71–74]

Heart Failure

Cardiac failure due to structural and functional causes frequently results in pulmonary edema, which requires mechanical ventilation strategies. In a fluid-filled lung, the lung's compliance dramatically decreases, and the resistive forces increase. The lung behaves in a similar way to ARDS due to the pulmonary edema and, therefore, holds the same pathological changes in mechanics. In an observational study by Yang and colleagues, they analyzed 632 patients with heart failure who required invasive ventilation. It was found that higher driving pressures above a threshold of 14.27 cm h_20 were found to be independently associated with increased in-hospital mortality if patients were ventilated over 48 h. With each increment of 1cmh_20 of driving pressure, an increased Odds ratio of 1.12 in the risk of in-hospital mortality was observed.[75]

In contrast, Schmid *et al*'s study showed that there was no association with mortality in non-ARDS patients, including patients with heart failure and other cardiac-related diseases.[10]

Table 1: Findings from clinical studies regarding Driving Pressure. (Insert Table Here)

CLINICAL OUTCOMES

A cohort study by Goodwin *et al* examined electronic health records to ascertain the importance of driving pressure and elastance in influencing clinical outcomes. The study assessed various factors in 2334 homogenous patients with respiratory failure in the ICU. After adjustment for covariates – exposure to driving pressures >15 cm H_20 was associated with a 19% increased risk (1.19; CI 1.07-1.33) of mortality and 1.5 fewer ventilator-free days as compared to controls. Increased respiratory elastance of >2cm H_20/mL/kg was also associated with a 13% increase in the risk of mortality without any impact on the length of stay or ventilatory-free days. This study established a time-weighted averaging method to derive exposure of driving pressure and other metrics to give a consistent reading of driving pressure and its resulting influence.[76]

Driving pressure and elastance have been shown by numerous studies as predictors of reduced lung function, increased stress, and a high likelihood of ventilator-induced lung injury.

Employing lung-safe ventilation strategies has expanded from lowering tidal volume to acceptable thresholds of plateau driving pressures and reducing ventilation frequency. Currently, values of Plateau pressure of 30cm H_20 and driving pressure of 15cm H_20 are considered the upper limit. Intervention is thus necessary to tailor ventilatory care. [77,78]

FUTURE DIRECTIONS AND LATEST RESEARCH

Many studies have provided significant insight into the relevance of driving pressure as a detrimental factor in guiding ventilation. These studies have demonstrated this by showcasing high numbers of adverse events in the setting of elevated driving pressures. It is worth noting that they are not without limitations and lack causality -- therefore, a direct impact may not be demonstrated. There is a need for more comparative analyses to better predict the validity of driving pressure when compared to other parameters such as PEEP, elastance, tidal volume, mechanical power, *etc.* A standardized method of quantifying driving pressure is also crucial to ensure accuracy, and a protocol should be introduced for clinicians to follow if they plan to conduct further research on the impact of driving pressure. The adjunct of additional modalities, such as Electrical Impedance Tomography (EIT) and Ultrasound, will further improve validity and give valuable insight. [79] Driving pressure in ECMO should also be utilized and studied to extract valuable findings.

It is common in studies to derive driving pressures during passive ventilation, but efforts should be made to explore driving pressures in the presence of spontaneous breathing. This will deliver additional comparative data and assess whether there are any shifts in driving pressure while illuminating additional metrics that may directly or indirectly influence results. The newer generation of ventilators should also be introduced when feasible – to guide clinicians in accounting for all the dynamic and static forces at play so that they are able to determine attributable risk.

Further research on ARDS can benefit from using measurements such as esophageal manometry, as transpulmonary driving pressure is a more accurate representation of the force being applied to the lung. An effort should be made to conduct more studies that include different pathologic states that lead to ARDS and clarify any variations in driving pressure and ventilatory parameters.

In addition, more randomized controlled trials are needed to better understand the usefulness of driving pressure in practice, establish causality, and determine its impact on long- and short-term outcomes. Further exploration of the impact of driving pressure in various subsets of populations with varying etiologies is also needed.

Basic science and physiological studies assessing the variability of pressures, lung volumes, oxygenation, and deformation of respiratory cells are needed to gain a more causal, sophisticated glance into cellular stress and strain.[15]

Some up-and-coming trials that may provide further insight into the prospects and usefulness of driving pressure were researched. Upon searching the term 'driving pressure' in clinicaltrials.gov, many promising studies emerged that aim to elaborate on the role of driving pressure in various situations. A few of them are described below.

Driving Pressure Limited Ventilation for Patients With ARDS [ART-2—Trial ID: NCT02365038]; a multicenter pilot randomized control trial that is assessing the feasibility of limiting driving pressure during ventilation of ARDS patients in one arm and employing the standard ventilatory guidance by ARDS Network strategy in the control arm. The tidal volume will be adjusted 3-8 mL/kg PBW to get target values of 13cm H_20 in driving pressures calculated day 1 and day 3 of randomization.

Mechanical Ventilation Based on Driving Pressure in Lateral Position {Trial ID: NCT04455789} A randomized, controlled, double blind study of 60 patients undergoing total hip replacement surgery. The aim is to investigate the effects of different positions on ventilation utilizing traditional lung protective parameters in the control arm and a low driving pressure arm. They aim to assess hemodynamic and respiratory values and overall postoperative outcomes.

Driving Pressure During General Anesthesia for Open Abdominal Surgery. {Trial ID: NCT03884543] A randomized multicenter double-blinded control trial to assess whether the application of high peep during mechanical ventilation to maintain low levels of driving pressure helps prevent complications compared to standard low peep strategies. The study targets patients undergoing abdominal surgery who are at intermediate to high risk of pulmonary complications based on the ARISCAT score.

These studies and many others hold strong promise in showing an appropriate application of driving pressure and its impact in various settings.

CONCLUSION

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Driving pressure has proven to be a highly significant metric when ventilating patients, particularly in ARDS. Adjusting for driving pressure has shown improved clinical outcomes and fewer incidences of VILI. Considerations should be made to improve the accuracy of measurements and monitoring. Ongoing research should enhance our understanding of driving pressure and how to best harness its potential in providing tailored, safe, and effective ventilation.

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