Asploro Journal of Biomedical and Clinical Case Reports
(ISSN: 2582-0370)
Review Article
DOI: https://doi.org/10.36502/2024/ASJBCCR.6366

# Driving Pressure-guided Ventilation in the Intensive Care Unit and Operating Room

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**Received date**: 24 July 2024; **Accepted date**: 10 August 2024; **Published date**: 17 August 2024

**Citation:** Jiang JL, Li XF, Yu H. Driving Pressure-guided Ventilation in the Intensive Care Unit and Operating Room. Asp Biomed Clin Case Rep. 2024 Aug 17;7(3):216-25.



## Abstract

Mechanical ventilation is the cornerstone of management for critically ill patients and those undergoing general anesthesia. Currently, lung protective ventilation strategies primarily include low tidal volume, positive end-expiratory pressure, and limited pressure, combined with certain recruitment maneuvers. Recently, driving pressure has been proposed as a key parameter to optimize mechanical ventilation. This study reviewed the relevant literature and suggests that driving pressure may be correlated with improved survival in patients with acute respiratory distress syndrome, enhanced intraoperative pulmonary mechanics, reduced postoperative atelectasis, and better gas exchange and oxygenation, even in normal lungs. However, the correlation between driving pressure and postoperative pulmonary complications has also been described as controversial. These findings could serve as a reference for future clinical practice.

## Keywords

Mechanical Ventilation, Driving Pressure, Mortality, Postoperative Pulmonary Complications

## Introduction

Mechanical ventilation (MV) is the cornerstone of management for critically ill patients and those undergoing general anesthesia. However, MV may aggravate pre-existing lung injury or even cause lung injury in healthy lungs, a phenomenon frequently referred to as ventilator-induced lung injury (VILI) [1]. An increased incidence of pulmonary complications can lead to a prolonged duration of postoperative tracheal intubation and a higher infection rate (ventilator-associated pneumonia) [2]. Importantly, lung injury may have systemic consequences, potentially inducing remote organ injury and even multisystem organ failure through the release of inflammatory factors or other mediators, ultimately increasing the death rate. Therefore, optimizing ventilation strategies to reduce lung injury may contribute to protecting systemic organ function [3,4].

## The Mechanism of Lung Injury

Firstly, it is important to elaborate on the mechanism of lung injury. The concepts of stress and strain have been applied to enhance the understanding of lung injury mechanisms [5-7]. Stress is defined as the force divided by the area over which it is applied. More stress on a smaller area of lung tissue is expected to increase the risk of injury. Strain measures the change in the dimension of a structure from its original dimension, with the most pertinent strain in ventilation being the volumetric strain created by

inspiration and expiration. Volumetric strain is defined as the change in volume divided by the initial volume [5]. However, the change in lung volume is represented by VT. The administration of larger tidal volumes requires higher airway positive pressure, which is preferentially distributed in more compliant lung zones. As a result, alveoli in these more compliant zones may become overdistended, leading to stretching and shear forces on the alveolar wall, and possibly even disruption of the alveolar wall, with air diffusing into the extra-alveolar tissues (barotrauma) [2]. Currently, lung-protective ventilation (LPV) strategies, which often include low tidal volume (VT), controlled airway pressures, positive end-expiratory pressure (PEEP), and recruitment maneuvers (RM), are recommended to reduce VILI and improve patient outcomes [8].

The initial lung volume is related to the volume of aerated lung available for ventilation ("functional lung size") [9]. In general, "functional lung size" is smaller than expected in patients with lung pathologies such as atelectasis, consolidation, bullae, effusion, or fibrosis [10]. Thus, VT/ "functional lung size" is more important than VT/kg and deserves more attention from practitioners [9]. Simply controlling VT is insufficient to diminish injurious lung strain in this context. This may be explained by the fact that the effects of VT on outcomes are mediated by a variable associated with lung strain [11]. Recently, driving pressure has been proposed as an important mediating variable.

In 2015, the significance of driving pressure was first described in a post hoc analysis of various randomized trials by Amato et al. [10], which showed that driving pressure was the best variable correlated with survival compared with VT and PEEP in patients with acute respiratory distress syndrome (ARDS). In an analysis of 4,549 patients from a pooled database of patients with ARDS [12], the authors found that only driving pressure and respiratory rate (RR) had significant associations with mortality among ventilator variables. The impact of decreasing driving pressure on reducing mortality was four times stronger than the effect of decreasing RR. In addition, several studies [11,13] have suggested that higher driving pressure is also associated with an increased risk of developing postoperative pulmonary complications (PPCs) during general anesthesia. Therefore, probing driving pressure is clinically relevant.

## The Concept of Driving Pressure

Driving pressure is defined as ΔP = P_plat - PEEP, where P_plat is the plateau pressure, and PEEP is the positive end-expiratory pressure. It is generated by the elastic forces developed during tidal inflation. Driving pressure is therefore affected by the magnitude of tidal inflation and the elastances of the lung and chest wall, and it can be expressed as the ratio between VT and the compliance of the respiratory system (Crs) (driving pressure = VT/ Crs) [10]. In general, driving pressure is easily measured during mechanical ventilation under the application of a muscle relaxant. However, consensus on the measurement of driving pressure during spontaneous breathing or assisted ventilation has not yet been reached.

How does driving pressure act as a positive or negative element in mechanical ventilation? What progress has been made in related research fields? How can driving pressure be minimized when adjusting ventilation parameters? This review outlines answers to these questions.

## Clinical Advances in Driving Pressure

*Mortality*:

Mortality in ICU Patients with ARDS:

The association between driving pressure and outcomes was first described in 2002 [14], which showed that driving pressure was one of the risk factors that differentiated survivors from non-survivors. A decade later, robust evidence came from Amato et al. [10] Their 2015 meta-analysis of ARDS patients analyzed nine prospective trials involving 3,562 patients and demonstrated that higher driving pressure was most strongly associated with worse survival and was linearly associated with outcomes. This association existed even in lung-protective settings (VT ≤ 7 mL/kg predicted body weight (PBW), plateau pressures ≤ 30 $cmH_2O$). Individual changes in VT or PEEP were not independently associated with survival unless they influenced the driving pressure. In addition, a safe driving pressure is likely < 15 $cmH_2O$ in ARDS patients.

A similar conclusion was verified in subsequent studies. The LUNG SAFE study, the largest epidemiologic study of patients with ARDS in 50 countries, recorded the driving pressure parameters of 742 patients [15]. The study showed that potentially modifiable factors associated with increased hospital mortality in multivariable analyses included lower PEEP (<12 $cmH_2O$), higher plateau pressures (≥25 $cmH_2O$), and higher driving pressures (≥ 14 $cmH_2O$). Meanwhile, a secondary analysis of data from two randomized controlled trials (RCTs) [16] showed that driving pressure is a risk factor for death in ARDS patients, even when ventilating patients with low VT (6 ml/kg PBW). They analyzed 787 patients in total and found that each 1 $cmH_2O$ increase in driving pressure was associated with a 5% increased risk of mortality, and survival was significantly higher in patients with a driving pressure ≤ 13 $cmH_2O$ on day 1. However, the results lack generalizability, as more than 60% of patients meeting the criteria for ARDS were excluded from enrollment. Subsequently, in a similar study, a secondary analysis of data from previous observational studies [17], investigators analyzed 778 samples with moderate to severe ARDS. They identified a risk threshold for Pplat (≥ 30 $cmH_2O$) and for driving pressure (≥ 19 $cmH_2O$), above which the risk of death significantly increases. Another observational cohort study reached similar conclusions [18].

As evidence gradually accumulated, the first meta-analysis of driving pressure in mechanically ventilated ARDS patients [19] demonstrated that an increase in driving pressure of 7 $cmH_2O$ was associated with increased mortality (relative risk, 1.41). This analysis, which included four studies (3,252 patients), was published by Aoyama's group in 2017. In addition, the analysis suggested that a target driving pressure for ventilated ARDS patients could exist between 13 and 15 $cmH_2O$. Another meta-analysis reached similar conclusions [20]. Notably, although all included studies had a low risk of bias, no RCTs were included in those meta-analyses. More recently, Urner et al. [21] have made important contributions to this work. They emulated pragmatic trials using observational data, first designing a pragmatic RCT and then using observational data to emulate it. This approach has been reported to generate similar results to a contemporaneous RCT and is an attractive option when a conventional RCT is not feasible [22]. They investigated whether ventilation strategies limiting daily driving pressure reduce mortality compared with usual care in adult patients who received ventilation for more than 24 hours—12,865 patients in total. This study showed that limiting either static or dynamic driving pressure (≤ 15 $cmH_2O$) can further reduce mortality in patients, in addition to traditional lung protection. The study included both ARDS and non-ARDS patients.

In general, driving pressure as a key parameter appears to reduce mortality in patients with ARDS. This is significant, as almost a quarter of ventilated patients in the ICU have ARDS. However, its risk threshold cannot be disregarded. The "functional lung size" would be smaller in ARDS patients. Regrettably, we cannot infer causation, and it is difficult to effectively reduce deterioration in driving pressure.

## Mortality in ICU Patients without ARDS

Whether higher driving pressures are associated with worse outcomes in patients without ARDS is still unclear. Recently, using data collected during a prospective, observational cohort study of 1,132 critically ill participants [23], researchers used multivariable logistic regression to determine that higher driving pressures and Pplat are associated with increased mortality in participants without ARDS. In contrast, a predefined secondary analysis of an international, multicenter, prospective cohort study assessed factors associated with mortality [24]. In this analysis, only higher peak pressure, but not driving pressure, was a potentially modifiable ventilatory variable associated with in-hospital mortality in multivariable analyses, despite approximately 50% of patients without ARDS receiving a VT higher than 8 mL/kg PBW. In addition, reliable values for driving pressure were available for only 343 patients, so the study results should be viewed with caution. This finding was similar to another retrospective analysis that examined 622 ventilated adult patients without ARDS [25]; in this study, driving pressure was not independently associated with hospital mortality.

It is worth noting that there is very limited evidence linking driving pressures to mortality in non-ARDS

patients. One possible reason for this is that the driving pressures in non-ARDS patients are often below the harmful threshold value (13–15 $cmH_2O$) [19]. Additionally, most non-ARDS patients receive assisted ventilation or spontaneous breathing. It is commonly believed that the estimation of Pplat or driving pressure is unreliable in these cases since a sufficiently stable inspiratory hold cannot be achieved [26]. Moreover, these studies carry the limitations of retrospective data collection.

## Mortality in Surgical Patients

In surgical patients, a multicenter RCT published in 2022 compared receiving alveolar recruitment/ individualized PEEP to deliver the lowest driving pressure with protective ventilation (fixed PEEP of 5 $cmH_2O$) during lung resection surgery [27]. They analyzed 1,170 patients and reported that mortality rates were similar between the two groups (0% vs. 0.2%). The mean driving pressure in the two groups (7.1 $cmH_2O$ vs. 9.2 $cmH_2O$) was far below the damage threshold related to mortality. Another study reached a similar conclusion [28]. However, these studies had important limitations, as the primary outcome was not mortality. Taken together, the available evidence is not sufficiently robust to conclude that driving pressure does not affect the mortality rate in surgical patients.

## Postoperative Pulmonary Complications

*Oxygenation, Pulmonary Mechanics, Postoperative Lung Atelectasis*:

In recent years, driving pressure has been considered a tool to optimize mechanical ventilation during surgery to improve outcomes. One study [29] assessed ventilation homogeneity based on electrical impedance tomography and showed that driving pressure–guided PEEP led to more homogeneous ventilation, as well as improved gas exchange and Crs for patients undergoing gynecological laparoscopy. Recently, Li et al. [30] analyzed seven studies with a total of 640 patients; the primary outcome was the $PaO_2/FiO_2$ ratio during one-lung ventilation (OLV). They reported that driving pressure-oriented ventilation during OLV in patients undergoing thoracic surgery was associated with better perioperative oxygenation and improved Crs. Additionally, a study that recruited 82 adult patients undergoing major abdominal surgery found that the primary objective was lung ultrasound scores [31]. They concluded that driving pressure reduced postoperative lung atelectasis. A similar conclusion was drawn in another study on laparoscopic surgery [32]. In general, driving pressure-guided ventilation almost certainly improved gas exchange and oxygenation [29,30], enhanced pulmonary mechanics intraoperatively [27,32], and reduced postoperative lung atelectasis [31,32].

## PPCs in Non-Cardiothoracic Surgery

However, it is unknown whether driving pressure affects clinical outcomes like PPCs in surgical patients. In 2015, a retrospective study of 69,265 patients who underwent non-cardiac surgical procedures showed that higher driving pressure was associated with an increased risk of PPCs in a secondary analysis [13]. Subsequently, a meta-analysis involving 17 clinical studies and 2,250 patients was the first to assess the relationship between driving pressure and PPCs (postoperative lung injury, pulmonary infection, or barotrauma) in surgical patients (including cardiothoracic surgery) [11]. After both multivariate and mediation analyses, driving pressure, but not VT or PEEP, appeared to be the only parameter associated with the development of PPCs. Additionally, the meta-analysis [11] showed that the odds ratio for PPCs is 1.16 for each 1 cm $H_2O$ increase in driving pressure, indicating that even a small increase in driving pressure can affect clinical outcomes. The research methodology in this study was similar to another high-quality study by Amato and colleagues, which focused exclusively on non-critically ill patients with healthy lungs undergoing surgery, whereas Amato et al. focused mainly on critically ill patients with ARDS [10]. These observational data are very encouraging.

Gradually, driving pressure has become a hotspot in mechanical ventilation research. In non-cardiothoracic surgery, a posthoc retrospective propensity score–weighted cohort analysis included 1,128 and 906 patients undergoing open or closed abdominal surgery based on a 10-year-old data set [33]. This analysis showed that driving pressure is associated with PPCs and intraoperative adverse events. Another multicenter retrospective observational cohort study investigated 14,218 patients undergoing major abdominal surgery and showed that dynamic airway

driving pressure, but not tidal volume or PEEP, was associated with PPCs [34]. An RCT conducted in 2018 included 1,012 patients undergoing abdominal surgery expected to last more than two hours [35]. It compared three different lung-protective ventilatory strategies (individually set to achieve the highest dynamic compliance) with a standard lung-protective mechanical ventilation approach. Although driving pressure was not specifically targeted, the intervention reduced this variable (10.4 cm $H_2O$ vs 13.2 cm $H_2O$). In this study, the incidence of PPCs was lower in the individual strategies group (39% vs 48%; P=0.047). However, this potential benefit may be attributable to the use of postoperative CPAP, and multiple comparison adjustments were not performed in the four-group study design. Additionally, a publication by Kranz et al. [28] on the application of driving pressure–guided PEEP titration suggests it may improve oxygenation and effectively reduce the incidence of clinically significant PPCs and the overall severity of PPCs within the first 7 postoperative days after open upper abdominal surgery (n = 148). In this study, the incidence of PPCs was still relatively high (38.8% vs 62.7%). Differences in definition, types of surgery, perioperative management, and accuracy of measurements may all contribute to the varying incidences of PPCs.

The RCT evidence for the relationship between driving pressure and outcomes in non-cardiothoracic surgical patients is limited. In the future, the results of an international, multicenter, two-group, double-blind randomized clinical superiority trial (n=1,468) are eagerly awaited and would be a valuable addition [36]. This trial has adequate power to compare the effects of driving pressure-guided individualized high PEEP with RM versus fixed low PEEP without RM on the occurrence of PPCs after open abdominal surgery.

## PPCs in Cardiothoracic Surgery

In cardiothoracic surgery, an RCT demonstrating the benefits of driving pressure in thoracic surgery was published in 2019 by Park et al. [37]. The study analyzed 292 patients and showed that the application of driving pressure–guided ventilation during OLV was associated with a lower incidence of PPCs within the first 3 postoperative days (5.5% vs 12.2%). However, the median difference in driving pressure between the two groups was only 1 cm $H_2O$ (9 cm $H_2O$ vs. 10 cm $H_2O$). In this study, each intervention was applied only during the period of one-lung ventilation, and an incremental PEEP strategy was used to determine the optimal PEEP. Another study by Yu et al. [38] (n = 222) demonstrated a similar conclusion. The definition of the primary outcome was the same as in Park et al. [37], but the types of interventions were different. The findings showed that the PEEP titration group (using the decremental PEEP trial) significantly reduced PPCs within the first 3 postoperative days rather than within the first 7 postoperative days. Interestingly, they showed that the PEEP titration group did not show a benefit in patients with FEV1/FVC less than 70 in the subgroup analysis, which may be due to the lack of consideration of intrinsic PEEP.

Recently, a multicenter RCT [27] compared receiving alveolar recruitment/individualized PEEP to deliver the lowest driving pressure with protective ventilation (recruitment/fixed PEEP of 5 $cmH_2O$) in lung resection surgery. They analyzed 1,170 patients and reported that driving pressure-guided ventilation improved pulmonary mechanics intraoperatively, but did not reduce the incidence of PPCs within postoperative day 7 (40.5% vs 42.8%). The result was unexpected. The study was well-conducted with appropriate randomization, blinding, dropout management, and handling of missing data. The authors concluded that different definitions of PPCs and titration protocols may have influenced the treatment results. Their definitions of PPCs were more expansive. Several decremental PEEP titrations instead of a single incremental PEEP were performed in their study. Additionally, the effects of the intervention on PPCs might have diminished by postoperative day 7. Another large study including 694 cardiac surgery patients with cardiopulmonary bypass also suggested that a driving pressure-guided ventilation strategy did not reduce the risk of PPCs within the first 7 postoperative days (40.3% vs 40.9%) [39]. The reasons for the contradictory results from different studies may be related to the heterogeneity of the study population, differences in surgery types, interventions (such as incremental or decremental PEEP titration), and outcome definitions.

Regrettably, only a limited number of RCTs could be included in the meta-analyses in this field, and high-quality RCT studies are rare. Recently, fourteen RCTs with 1,105 patients were included in a meta-analysis [40], which compared personalized PEEP based on respiratory mechanics (driving pressure and Crs) with constant PEEP to prevent PPCs in adults. The authors showed that personalized PEEP can reduce the incidence of PPCs. However, conclusions from this study are limited due to high clinical heterogeneity and the small sample size of some included studies. In general, definitive conclusions regarding the efficacy of driving pressure in improving clinical outcomes remain uncertain. More large, well-designed studies are needed to explore the pros and cons of driving pressure-oriented ventilation in the future.

## How Do We Measure Driving Pressure and Minimize It Numerically?

The question then is how can we measure driving pressure? Driving pressure = Pplat – PEEP = VT/Crs. During controlled mechanical ventilation, driving pressure can be calculated by performing a short inspiratory pause of 0.2–0.3 s to measure Pplat, allowing for its calculation. In spontaneously breathing mechanically ventilated patients, the same measurement can be performed by administering short-acting sedatives or myorelaxants. Other alternative approaches, which are more complex, have been thoroughly described by Oriol Roca et al. [41].

However, definitive conclusions regarding the efficacy of driving pressure reduction for outcome improvement are limited by the size and scope of available studies and the lack of standardized techniques for driving pressure reduction. There is no well-established technique to minimize driving pressure yet. According to the formula driving pressure = Pplat – PEEP = VT/Cstat, the common practice is titrating VT or PEEP to obtain the lowest driving pressure during controlled MV.

Typically, the first step is to perform recruitment, which is more common in the literature. When selecting the recruitment method and the magnitude of pressure, the patient's pulmonary conditions and hemodynamic risks need to be considered. Most commonly, such approaches are performed by "bag squeezing" using the airway pressure-limiting valve of the anesthesia ventilator. However, recruitment maneuvers are better controlled if performed during tidal ventilation, such as using a stepwise increase in PEEP, tidal volumes, or a combination of these [42]. For example, a stepwise increase in PEEP at a fixed pressure of 15 to 20 $cmH_2O$ in pressure-controlled ventilation. The PEEP is progressively increased in steps of 5 $cmH_2O$ (30 to 60 s per step) up to 20 $cmH_2O$ [42]. Noteworthy, lung recruitment is not mandatory. Permissive atelectasis may be more protective than an aggressive effort to keep the lung open [43]. Therefore, the best technique for recruitment in various functional lung sizes is unknown.

Next, the question arises of how to perform PEEP titration. For now, either the decremental or the incremental PEEP trial can be selected. Investigators seem to favor the decremental PEEP trial [27,36,43]. This approach may help keep alveoli open at lower driving pressures and improve oxygenation [27,44]. Common specific practice measures include starting PEEP at 10-12 $cmH_2O$ and then decreasing it to 0 $cmH_2O$ in 1-2 $cmH_2O$ intervals [27,45]. Driving pressure is measured at each PEEP level after 5 respiratory cycles. The lowest PEEP should be selected if multiple levels of PEEP show the same lowest driving pressure. Additionally, the incremental PEEP trial is similar to the approaches mentioned above. Regarding VT titration, recent LPV strategies employ small VT, so the adjustable range of VT is small. A study [45] recommends that if driving pressure is higher than 15 $cmH_2O$, VT should be decreased by 1 ml/kg of predicted body weight until it falls below 15 $cmH_2O$. In contrast, if driving pressure increases with VT reduction, a progressive increase in VT is desirable.

Regrettably, fewer studies focus on PEEP titration. A randomized physiological trial [44] comparing incremental with decremental driving pressure-oriented PEEP titration during OLV demonstrated that only the decremental strategy improved oxygenation and lowered intraoperative driving pressure (8 $cmH_2O$ vs 10 $cmH_2O$). The optimal approach for PEEP titration has still not been identified.

## Conclusions

Driving pressure is defined as the distending pressure above the applied PEEP required to generate VT and is influenced by the magnitude of tidal inflation and the elastance of the lung and chest wall. Recently, it has been proposed as a key parameter to optimize mechanical ventilation. The study suggested that driving pressure may be correlated with survival in patients with ARDS and improved intraoperative pulmonary mechanics, reduced postoperative atelectasis, and improved gas exchange and oxygenation even in normal lungs. However, the correlation between driving pressure and PPCs has also been described as controversial. More scientific research is needed to demonstrate these linkages in the future. This study could provide references for clinical practice in the future.

## Competing interests

All authors declare that they have no conflict of interest.

## Funding

There was no funding received for this paper.

## Conflict of Interest

The authors have read and approved the final version of the manuscript. The authors have no conflicts of interest to declare.

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