Progress in the relationship between mechanical ventilation parameters and ventilator-related complications during perioperative anesthesia

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Abstract

Background: Mechanical ventilation, as an important respiratory support, plays an important role in general anesthesia and it is the cornerstone of intraoperative management of surgical patients. Different from spontaneous respiration, intraoperative mechanical ventilation can lead to postoperative lung injury, and its impact on surgical mortality cannot be ignored. Postoperative lung injury increases hospital stay and is related to preoperative conditions, anesthesia time, and intraoperative ventilation settings.

Method: Through reading literature and research reports, the relationship between perioperative input parameters and output parameters related to mechanical ventilation and ventilator-related complications was reviewed, providing reference for the subsequent setting of input parameters of mechanical ventilation and new ventilation strategies.

Results: The parameters of inspiratory pressure rise time and inspiratory time can change the gas distribution, gas flow rate and airway pressure into the lungs, but there are few clinical studies on them. It can be used as a prospective intervention to study the effect of specific protective ventilation strategies on pulmonary complications after perioperative anesthesia.

Conclusion: There are many factors affecting lung function after perioperative mechanical ventilation. Due to the difference of human body, the ventilation parameters suitable for each patient are different, and the deviation of each ventilation parameter can lead to postoperative pulmonary complications. Inspiratory pressure rise time and inspiratory time will be used as the new ventilation strategy.

Keywords: mechanical ventilation; ventilation parameters; postoperative pulmonary complications; ventilator-associated pneumonia

Introduction

Mechanical ventilation (MV) is a kind of life support system. The complications related to MV are affected by the input and output parameters of ventilator. Correct setting of ventilator parameters can not only improve the ventilation quality of patients but can also reduce the complications related to MV. MV involves patients in many clinical departments, including not only patients after anesthesia surgery but also patients in need of respiratory support such as severe trauma, burn, and infection. The medical personnel who understand and master MV are not only anesthesiologists but also intensive care physicians and respiratory therapists. In addition, the department of MV is not only the operating room or intensive care medicine but also involves other departments related to the intensive care unit (ICU), such as cardiac surgery, general surgery, and so on. The effects of MV parameters on lung function and respiration-related complications, which are discussed in this article, are important for health-care workers using MV.

Mechanical ventilation-related complications

Ventilator-induced lung injury

Ventilator-induced lung injury (VILI) may be caused by incorrect MV, and its progression is mainly related to inflammation, apoptosis, and oxidative stress. Wnt/β-catenin pathway modulates inflammation and apoptosis [1]. There is evidence that loss of endothelial barter function plays a major role in the development of VILI and acute respiratory distress syndrome (ARDS) [2]. VILI is characterized by vascular barrier dysfunction and inhibition of alveolar fluid clearance [3]. There are two common causes of VILI: one is alveolar collapse at the end of expiration, which occurs...
repeatedly during ventilation and produces shear force, and the other is alveolar hyperinflation at the end of inspiration [4].

Ventilator-related vascular injury
MV may induce or amplify local inflammation and activate inflammatory cells, resulting in injury of alveolar capillary endothelium, exposure of alveolar capillary basement membrane, and loss of pulmonary vasoconstriction and relaxation regulation function, resulting in decreased compliance of pulmonary vessels and increased resistance of pulmonary vessels. In experimental atelectasis with minimum tidal volume re-expansion, MV redistributes blood volume away from well-ventilated areas and worsens PaO2/FIO2 [5].

Ventilator-associated immune damage
Ventilator-induced lung injury (VILI) is caused by stretch stimulation and other factors associated with MV. NOD-like receptor protein 3 (NLRP3) is an important natural immune component and is closely related to VILI [6]. MV upregulates the expression of NLRP3 messenger RNA in alveolar macrophages and induces NLRP3 inflammasome dependent pulmonary inflammatory response [7, 8]. In addition, upregulation of mir-127 expression may promote VILI by regulating lung permeability, inducing histopathological changes, and enhancing inflammatory responses involving NF-κB- and p38 MAPK-related signaling pathways [9].

Ventilator-associated mental stress
MV can cause postoperative mental stress, such as postoperative delirium, posttraumatic stress disorder, etc. The lung–brain interaction theory of MV focuses on the increase of blood–brain barrier permeability, the migration of peripheral inflammatory factors to the center, and the activation of microglia; peripheral mechanical stimulation through the vagus nerve to the nucleus of the solitary tract increased impulse, and neurotransmitter release abnormalities lead to delirium [10, 11]. A prospective longitudinal study found that psychologists diagnosed 12% of patients with PTSD 3 months after ventilator withdrawal [12]. MV is a known risk factor for delirium, a cognitive disorder characterized by frontal cortex and hippocampal dysfunction, and VILI induces potentially reversible neuronal damage and inflammation in the frontal cortex and hippocampus of mice [13].

Effects of local anesthesia and perioperative analgesia on pulmonary complications
In thoracic surgery, the front, side, and back of the chest and abdomen can be successfully anesthetized with paravertebral nerve block and can effectively block sensory, motor, and sympathetic nerve fibers in the thoracic segment, thereby reducing postoperative pain and lung complications [14, 15]. In patients undergoing thoracoscopic lobectomy/segmental resection, thoracic paravertebral nerve block can effectively reduce the occurrence of postoperative pulmonary complications and improve the long-term prognosis of patients [16]. In addition to good analgesic effect, thoracic epidural analgesia can alleviate perioperative stress, control postoperative blood sugar well, reduce inflammatory indicators, reduce postoperative acute kidney injury, and reduce pulmonary complications [17]. Patients with existing lung diseases face the risk of perioperative complications and increased morbidity. Compared with regional anesthesia, patients with general anesthesia may be more prone to barotrauma, postoperative hypoxemia, and pneumonia. New regional anesthesia techniques provide effective analgesia and surgical anesthesia while greatly reducing the incidence of phrenic nerve paralysis, thereby maintaining lung function [18]. In conclusion, local anesthesia and perioperative analgesia can effectively reduce postoperative pulmonary complications.

Role of ventilation parameters in ventilator-related complications
During MV, the ventilation parameters of ventilator include respiratory rate (RR), tidal volume (Vt), peak inspiratory pressure (Paw), plateau pressure (Pplat), inspiratory/expiratory ratio (I/E ratio), Fraction of inspiration O2 (FiO2), positive end-expiratory pressure (PEEP), etc. Do mechanical ventilation parameters affect postoperative pulmonary complications? Studies have reported that in patients undergoing noncardiac and nonthoracic elective surgery requiring general anesthesia with tracheal intubation, decreased tidal volume, decreased compliance, increased mechanical power, and decreased ETCO2 are independently correlated with postoperative complications [19].

Input parameters
Tidal volume
In earlier studies, the benefits of high tidal volumes were the opening of distal airways, stimulation of surfactant production, and subsequent improvement in oxygenation [20]. However, ventilation management changed over time and lung injury from high tidal volumes increased. Higher tidal volume, Pplat, and lower PEEP are associated with ARDS and acquired pneumonia during ICU hospitalization [21]. In an observational cohort study of the acute phase after spinal cord injury, patients receiving high tidal volume ventilation were more likely to develop ventilator-associated pneumonia and require tracheotomy than those receiving standard tidal volume [22]. Ventilation at high tidal volumes increases vascular filtration pressure; causes stress fractures of capillary endothelium, epithelium, and basement membrane; and leads to lung rupture, mechanical damage, leading to leakage of fluid, protein, and blood into tissue and air space, or leakage of air into tissue space [23]. In a study of 28 patients scheduled for video-assisted thoracoscopic esophagectomy, it was found that high tidal volume ventilation was performed during one-lung ventilation (Vt = 10 ml/kg); or low tidal volume ventilation (Vt = 5 ml/kg); low tidal volume ventilation decreased peak airway pressure (Ppeak) during one-lung ventilation (Ppeak); Pplat and driving pressure (ΔP) inhibit lung infiltration and inflammation induced by MV and also inhibit the activation of NLRP3 inflammatory bodies in alveolar lavage fluid, thus playing a protective role in VILI [24]. Low tidal volume also has an impact on lung function. In the MV model of aged rats, relatively short-term low tidal volume and hyperoxia have the greatest impact on aged rats, reducing diaphragm contraction function and increasing lung inflammation [25], which has an important significance in general anesthesia MV. Giving appropriate tidal volume to patients in a short period has protective effect. However, how to optimize tidal volume settings remains controversial.

Respiratory rate
Hotchkiss et al. found that during MV, low RR has lower probability of perialveolar vascular hemorrhage than high RR. Reducing RR of MV can reduce pulmonary vascular injury and also facilitate the repair of vascular endothelial injury [26]. High intraoperative
ventilation rate is associated with an increased risk of postoperative respiratory complications and increased utilization of postoperative medical care [27]. Therefore, it is very important to select appropriate RR during perioperative anesthesia.

**Inspiratory flow rate**

During MV, high inspiratory flow rate can increase shear stress parallel to airway and alveolar wall surface, leading to deformation of lung parenchyma and bronchial epithelial cells, and release profibrosis and proinflammatory mediators [28, 29]. It has been found that during one-lung ventilation, increasing inspiratory flow rate under pressure controlled ventilation (PCV) mode can increase tidal volume, reduce dead space rate, promote CO2 exchange, and improve lung dynamic compliance (Cdyn), but cannot improve oxygenation and intrapulmonary shunt and, while inspiratory flow rate of 50 ml/l can achieve the above improvement of respiratory function and respiratory mechanics under the condition of less inflammatory response [30]. Using MV for ARDS patients, we found that on the basis of small tidal volume, reducing inspiratory flow rate can play a certain protective role on damaged lung tissue, which is more conducive to maintaining human–machine coordination [31].

**Inspiratory/expiratory ratio or inspiratory time**

Volume-controlled ventilation and PCV are commonly used in general anesthesia patients. In the PCV ventilation mode, when the inspiratory pressure is constant, the form of deceleration wave is adopted, and the preset pressure level is reached through a high initial inspiratory flow rate at the beginning of the inspiratory flow. As the inhalation process progresses, the airflow waveform decreases exponentially, so that the inhaled gas is dispersed in the lung tissue in the form of laminar flow until the end of the inhalation. This method of ventilation can reduce the airway pressure and has a certain lung protection effect. Prolonged inspiratory time makes gas diffuse more evenly and improves lung Cdyn. However, if the velocity of deceleration wave does not decrease to “0” at the end of inspiration, the airway pressure and uniform gas distribution cannot be reduced to the maximum extent. In this case, the tidal volume can be increased by prolonging the inspiration time, and the inspiration velocity will decrease further until it reaches “0”, that is, “zero velocity at the end of inspiration.” Compared with the inhalation/exhalation ratio (I:E 1:2) commonly used during surgery, the prolonged Inhalation/exhalation ratio (I:E 1:1) can provide “balanced stress-time product,” and this ratio increases inspiration time and mean airway pressure, while reducing Ppeak, and increases PaO2, reduces alveolar–arterial oxygen gradient, and inflammatory factors, thus reducing postoperative lung injury [11]. However, there is currently no evidence that specific I:E ratio has obvious benefits. The previous study of this research group found that pressure control ventilation targeting end-inspiratory flow rate can reduce pulmonary complications and inflammation level after percutaneous nephrolithotomy in prone position under general anesthesia by adjusting the inhalation–exhalation ratio to make the end-inspiratory flow rate close to zero [32]. This shows that under the condition of PCV mode ventilation, targeting end-inspiratory velocity can reduce postoperative pulmonary complications.

**Inspiratory pressure**

During MV inhalation, the airway pressure increases and the alveolar capillary wall tension (stress) increases, resulting in ultrastructural changes that lead to leakage of plasma and even red blood cells from the alveolar vessels into the alveolar cavity, resulting in alveolar hemorrhage [33].

**Inspiratory pressure rise time**

Inspiratory pressure rise time (IRT, also known as slope time) is the point from when pressure begins to rise to peak pressure. The duration of IRT affects the shape of the pressure waveform. In PCV, shortening IRT increases peak flow at the beginning of inspiration. The shorter IRT, the greater the amount of airflow entering the lungs within a short period of inspiration, and the turbulence in the airflow may cause lung injury. When PAW is reached, airflow redistributes in the lungs for the rest of the inspiration time. A study of sheep found that short IRT can cause lung damage [34]. In a study using IngMar ASL 5000 to construct a passive two-compartment lung model, adding IRT balanced inspiratory pressure (IP), chamber-specific tidal volume, and volume balance [35]. In a crossover study, 12 infants weighing >2 kg were treated with synchronized intermittent volume assurance positive pressure ventilation (SIPPV-VG) and volume assurance pressure support ventilation (PCV-VG) using a Dräger Babylog VN 500 ventilator by using different IRT during SIPP-VG or PCV-VG. The use of short or long IRT affects some ventilation parameters, but this does not significantly affect oxygenation and carbon dioxide emission [36].

**Positive end-respiratory pressure**

The main effects of PEEP are [37-39]: promoting distal alveolar expansion to prevent collapse and preventing opening and closing of distal small airways and alveoli. However, excessive PEEP can lead to excessive alveolar expansion and increase pulmonary circulation resistance [40, 41], and it is generally believed that PEEP setting >12 cmH2O is likely to lead to pulmonary circulation damage. PEEP may protect against pulmonary circulation damage by reducing surface membrane collapse and subsequent membrane rupture upon re-inflation and/or by reducing surfactant displacement into the airways, but PEEP may also downregulate surfactant release [42]. High PEEP (12 cmHg) may be used in open surgery during MV under general anesthesia. In MV under general anesthesia, high PEEP (12 cmH2O) and lung re-expansion during open surgery cannot prevent postoperative pulmonary complications. Intraoperative protective ventilation strategies should include low tidal volume and low PEEP and lung re-expansion should not be performed [43]. Individualized PEEP settings can reduce postoperative atelectasis (as measured by computed tomography), while improving intraoperative oxygenation and drive pressure, to minimize side effects [44]. Lung protective MV can significantly improve lung and lung compliance in patients undergoing abdominal laparoscopic surgery, but this has no significant effect on early postoperative atelectasis and pulmonary oxygen function on the first day after surgery [45]. Therefore, how to set the appropriate PEEP level is a problem that needs attention in clinical anesthesia work. In terms of PEEP, determining the optimal PEEP level requires titration based on a patient’s drive pressure [46] or PV curves [47], which vary from patient to patient and have also been reported in recent studies.

**Fraction of inspiration O2 (FiO2)**

In healthy patients, most patients develop atelectasis after pre-oxygenation and anesthesia induction, and moderate PEEP alone is sufficient to minimize atelectasis and maintain oxygenation [48]. The development of atelectasis after preoxygenation and anesthesia induction is oxygen- and time-dependent, with the benefit of using 80% oxygen during anesthesia induction to reduce atelectasis diminishing over time [49]. Atelectasis and free
radical oxygen can lead to postoperative complications such as infection, prolonged respiratory support, and increased hospital stay. High FiO2 has a greater impact on the development of atelectasis in obese patients than low FiO2 [50]. Retrospective analysis of different oxygen concentrations (mild: PaO2 100–199 mmHg, moderate: PaO2 200–299 mmHg, and severe: PaO2 > 300 mmHg) found that the severe hyperoxia exposure group is prone to more infectious complications, prolonged hospital stay, and prolonged MV time after cardiac surgery [51]. In clinical anesthesia, it is important to adjust ventilator parameters according to oxygenation index and blood gas analysis. In a noninvasive randomized trial, the intraoperative high oxygen uptake score of 0.8 was compared with the standard oxygen uptake score of 0.3–0.4 in adult patients undergoing major elective or emergency surgery, and the results showed that there was no significant difference in the incidence of postoperative pulmonary complications between the two groups [52], indicating that the optimal level of FiO2 is still worth exploring.

Output parameters
The output parameters of the ventilator can be obtained after MV through the input parameters of the ventilator, including pressure–volume (P–V) curve, dynamic lung compliance (Cdyn), airway resistance, Fpeak, Pplat, ΔP, etc.

Pressure–volume curve
The respiratory static P–V curve is a classical method used to describe the mechanical properties of a patient’s respiratory system and to guide MV [53]. Studies have confirmed that P–V curve-oriented MV lung recruitment strategy can improve the lung ventilation and reduce lung injury for ARDS patients, and through the inflection point of P–V curve, it can determine the best level of positive end-expiratory pressure and find the best PEEP for effective ventilation [54]. During low tidal volume ventilation, the PEEP-level ventilation determined by the P–V curve low turning point pressure + 2cmH2O can reduce the release of pulmonary inflammatory mediators and reduce the mortality of ARDS patients [55]. P–V curves and lung recruitment–expansion ratio (R/V ratio) can be used to assess the lung recruitment capacity and individualized PEEP at the bedside [56]. However, there is little research on MV guided by P–V curve.

Dynamic lung compliance
Lung compliance can be divided into static lung compliance (Cst) and dynamic lung compliance (Cdyn). Through Cdyn-guided PEEP titration, individual PEEP can be found for each patient, which can be used for intraoperative MV to reduce the incidence of postoperative atelectasis in obese patients [57].

Airway resistance, peak airway pressure, and plateau pressure
At the beginning of the end-inspiratory operation, the pressure measured in the airway (PAW) is at its highest value and is called PAW (PIP or Ppeak), followed by a rapid drop in pressure (P1), and then slowly decays to a plateau (Pplat); the pressure drop from PIP to P1 represents the pressure lost by the gas flowing in the airway resistance, while the smaller drop from P1 to Pplat is due to gas oscillation and redistribution of tissue internal forces (viscoelastic forces); the overall respiratory system resistance is determined by the pressure drop (PIP – P1) divided by the flow at end-inspiratory occlusion, i.e. airway resistance at inspiration = (Fpeak – Pplat)/end-inspiratory flow rate. The resistance due to opposing tissue deformation (viscoelastic forces), which we call as the “late resistance to breathing” system can be expressed as follows: Airway resistance at expiration = (P1 – Pplat)/maximum expiratory flow rate [58]. During MV, it is beneficial to reduce lung injury by adjusting respiratory parameters and monitoring airway resistance, Ppeak and Pplat.

Driving pressure
ΔP is defined as the difference between Pplat and PEEP (ΔP = Pplat – PEEP). ΔP is an important parameter for optimizing MV during operation. The study found that setting tidal volume with ΔP as guidance is better than setting tidal volume with small tidal volume or control. The tidal volume with Pplat <30 cmH2O has less risk of ventilator-related lung injury, and the ΔP setting tidal volume is more reasonable [59].

Conclusion
During perioperative MV, many factors affect postoperative pulmonary function. Because of the difference of human body, the ventilation parameters suitable for each patient are different, and the deviation of each ventilation parameter can lead to postoperative pulmonary complications. During the inspiratory phase, tidal volume, IP, IRT, inspiratory time, and other parameters can make the distribution of gas entering the lung, gas flow rate, pressure on the airway, and so on change accordingly, and these changes can cause certain effects on the lung, or good, or bad. By adjusting the input parameters, the output parameters reflect whether the input parameters are set reasonably. Unlike spontaneous breathing, spontaneous breathing is regulated by the patient himself, and the airflow is evenly distributed in the lungs. MV can only ensure that airflow enters the lungs for gas exchange, but its airflow distribution in the lungs cannot be evenly distributed, which leads to uneven damage to the alveoli in all parts of the lungs, resulting in various postoperative pulmonary complications. Optimizing PEEP according to respiratory mechanics (ΔP or respiratory system compliance) is a simple and straightforward strategy. During the perioperative period, anesthesiologists should not only ensure the oxygenation of patients but should also pay attention to the influence of airflow on lung tissue. Turbulence created by fluid flow can damage adjacent lung tissue.

IRT reflects the change of inspiratory flow velocity. The shorter the IRT, the easier it is to reach the required IP. However, the more turbulent the air flow is, the greater the lung damage. Therefore, prolonging the IP rise time can reduce the airway damage caused by the turbulent air flow. However, the longer the IRT is, and the longer the time is, the longer the time affects oxygenation. Therefore, it is necessary to adjust the IRT according to the patient’s condition. It can be used as a prospective intervention to study the effect of specific protective ventilation strategy on pulmonary complications after perioperative anesthesia.

Postoperative physical therapy also plays an important role in the recovery of postoperative lung function. Preoperative respiratory muscle training can reduce the risk of pulmonary complications and pneumonia after cardiac surgery, increase the maximum IP, and shorten the length of hospital stay [60]. In addition, transcutaneous acupoint electrical stimulation can significantly shorten the length of postoperative ICU stay and stay and reduce the incidence of postoperative pulmonary complications, and it is an effective postoperative physical therapy [61]. In addition to drugs, the combined application of drug therapy and pulmonary rehabilitation exercise training can promote the recovery of cardiopulmonary function and respiratory muscle of lung cancer.
patients after thoracoscopic lobectomy and improve lung capacity and autonomous ventilation [62].

Conflict of interest
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Key References

Answers: 1.c; 2.c; 3.c; 4.e; 5.a

Self-assessment questions
1. What are the correct input parameters of mechanical ventilation ()
   a. respiratory rate, tidal volume (VT), peak inspiratory pressure (Paw)
   b. plateau pressure, inspiratory/expiratory ratio (I/E ratio)
   c. Fraction of inspiration O2 (FiO2)
   d. positive end-expiratory pressure (PEEP)
2. What are the correct output parameters of mechanical ventilation ()
   a. pressure–volume (P–V) curve, dynamic lung compliance (Cdyn), respiratory rate
   b. peak inspiratory pressure (Paw), tidal volume (VT)
   c. peak airway pressure (Ppeak), plateau pressure (Pplat), driving pressure (∆P)
   d. Fraction of inspiration O2 (FiO2)
3. What does lung compliance mean ()
   a. static lung compliance (Cst)
   b. dynamic lung compliance (Cdyn)
   c. static lung compliance (Cst) and dynamic lung compliance (Cdyn)

4. What are the complications related to mechanical ventilation ()
   a. ventilator-induced lung injury
   b. Ventilator-related vascular injury
   c. ventilator-associated immune damage
   d. ventilator-associated mental stress
   e. all
5. What is drive pressure(ΔP) ()
   a. ∆P = Pplat – PEEP
   b. ∆P = Ppeak – PEEP
   c. ∆P = P1 – PEEP

References


