Review

Bench-to-bedside review: Adjuncts to mechanical ventilation in patients with acute lung injury

Jean-Jacques Rouby and Qin Lu

1Professor of Anesthesiology and Critical Care Medicine, Director of the Surgical Intensive Care Unit Pierre Viars, La Pitié-Salpêtrière Hospital, University of Paris, Paris, France
2Praticien Hospitalier, Surgical Intensive Care Unit Pierre Viars, Department of Anesthesiology, Research Coordinator, La Pitié-Salpêtrière Hospital, Paris, France

Corresponding author: Jean-Jacques Rouby, jjrouby.pitie@invivo.edu

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Abstract

Mechanical ventilation is indispensable for the survival of patients with acute lung injury and acute respiratory distress syndrome. However, excessive tidal volumes and inadequate lung recruitment may contribute to mortality by causing ventilator-induced lung injury. This bench-to-bedside review presents the scientific rationale for using adjuncts to mechanical ventilation aimed at optimizing lung recruitment and preventing the deleterious consequences of reduced tidal volume. To enhance CO₂ elimination when tidal volume is reduced, the following are possible: first, ventilator respiratory frequency can be increased without necessarily generating intrinsic positive end-expiratory pressure; second, instrumental dead space can be reduced by replacing the heat and moisture exchanger with a conventional humidifier; and third, expiratory washout can be used for replacing the CO₂-laden gas present at end expiration in the instrumental dead space by a fresh gas (this method is still experimental). For optimizing lung recruitment and preventing lung derecruitment there are the following possibilities: first, recruitment manoeuvres may be performed in the most hypoxaemic patients before implementing the preset positive end-expiratory pressure or after episodes of accidental lung derecruitment; second, the patient can be turned to the prone position; third, closed-circuit endotracheal suctioning is to be preferred to open endotracheal suctioning.

Introduction

Mechanical ventilation is indispensable for the survival of patients with acute lung injury (ALI) and acute respiratory distress syndrome (ARDS). However, inappropriate ventilator settings may contribute to mortality by causing ventilator-induced lung injury. Tidal volumes greater than 10 ml/kg have been shown to increase mortality [1-5]. High static intrathoracic pressures may overdistend and/or overinflated parts of the lung that remain well aerated at zero end-inspiratory pressure [6-8]. Cyclic tidal recruitment and derecruitment experimentally produces bronchial damage and lung inflammation [9]. Although the clinical relevance of these experimental data has been challenged recently [10,11], the risk of mechanical ventilation-induced lung biotrauma supports the concept of optimizing lung recruitment during mechanical ventilation [12]. It has to be mentioned that the two principles aimed at reducing ventilator-induced lung injury may be associated with deleterious effects and require specific accompanying adjustments. Reducing the tidal volume below 10 ml/kg may increase the arterial partial pressure of CO₂ (PaCO₂) and impair tidal recruitment [13]. Optimizing lung recruitment with positive end-expiratory pressure (PEEP) may require a recruitment manoeuvre [14] and the prevention of endotracheal suctioning-induced lung derecruitment [15]. This bench-to-bedside review presents the scientific rationale supporting the clinical use of adjuncts to mechanical ventilation aimed at optimizing lung recruitment and preventing the deleterious consequences of reduced tidal volume.

Adjuncts aimed at increasing CO₂ elimination

Increase in respiratory rate

In patients with ARDS, increasing the ventilator respiratory rate is the simplest way to enhance CO₂ elimination when tidal volume is reduced [5,16,17]. However, an uncontrolled increase in respiratory rate may generate intrinsic PEEP [18,19], which, in turn, may promote excessive intrathoracic pressure and lung overinflation [20]. If the inspiratory time is not decreased in proportion to the increase in respiratory rate, the resulting intrinsic PEEP may even cause right ventricular function to deteriorate [21]. In addition to inappropriate ventilator settings – high respiratory rate together with high inspiratory to expiratory ratio – airflow limitation caused by bronchial injury promotes air trapping [22,23]. Acting in the opposite direction, external PEEP reduces intrinsic PEEP and provides a more homogeneous
alveolar recruitment [24,25], whereas lung stiffness tends to accelerate lung emptying [16,26]. As a consequence, in a given patient, it is impossible to predict intrinsic PEEP induced by a high respiratory rate and no ‘magic number’ can be recommended. At the bedside, the clinician should increase the ventilator respiratory rate while looking at the expiratory flow displayed on the screen of the ventilator: the highest ‘safe respiratory rate’ is the rate at which the end of the expiratory flow coincides with the beginning of the inspiratory phase (Fig. 1).

Decrease in instrumental dead space
When CO₂ elimination is impaired by tidal volume reduction, the CO₂-laden gas present at end expiration in the physiological dead space is readministered to the patient at the beginning of the following inspiration. The physiological dead space consists of three parts: first, the instrumental dead space, defined as the volume of the ventilator tubing between the Y piece and the distal tip of the endotracheal tube; second, the anatomical dead space, defined as the volume of the patient’s tracheobronchial tree from the distal tip of the endotracheal tube; and third, the alveolar dead space, defined as the volume of ventilated and nonperfused lung units. Only the former can be substantially reduced by medical intervention. Prin and colleagues have reported that replacing the heat and moisture exchanger (HME) placed between the Y piece and the proximal tip of the endotracheal tube by a conventional heated humidifier (HH) on the initial part of the inspiratory limb in 11 patients with ARDS (reproduced from [27] with the permission of the publisher); filled circles, reduction of PaCO₂ obtained by combining the increase in respiratory rate (without generating intrinsic end-expiratory pressure) and the replacement of the HME by a conventional HH in six patients with ARDS [16]. ConMV, conventional mechanical ventilation (low respiratory rate with HME); OptiMV, optimized mechanical ventilation (optimized respiratory rate with HH). Published with kind permission of Springer Science and Business Media [27].

Expiratory washout
The basic principle of expiratory washout is to replace, with a fresh gas, the CO₂-laden gas present at end expiration in the

Figure 1

(a) Flow (l/min)

(b) Flow (l/min)

(c) Flow (l/min)

Figure 2

Effect of replacing HME by HH

Effect of replacing ConMV by OptiMV

Optimization of CO₂ elimination in patients with severe acute respiratory distress syndrome (ARDS). Open circles, reduction of arterial partial pressure of CO₂ (PaCO₂) obtained by replacing the heat and moisture exchanger (HME) placed between the Y piece and the proximal tip of the endotracheal tube by a conventional heated humidifier (HH) on the initial part of the inspiratory limb in 11 patients with ARDS (reproduced from [27] with the permission of the publisher); filled circles, reduction of PaCO₂ obtained by combining the increase in respiratory rate (without generating intrinsic end-expiratory pressure) and the replacement of the HME by a conventional HH in six patients with ARDS [16]. ConMV, conventional mechanical ventilation (low respiratory rate with HME); OptiMV, optimized mechanical ventilation (optimized respiratory rate with HH). Published with kind permission of Springer Science and Business Media [27].
instrumental dead space [28]. It is aimed at further reducing 
CO₂ rebreathing and PaCO₂ without increasing tidal volume
[29]. In contrast to tracheal gas insufflation, in which the
administration of a constant gas flow is continuous over the
entire respiratory cycle, gas flow is limited to the expiratory
phase during expiratory washout. Fresh gas is insufflated by a
gas flow generator synchronized with the expiratory phase of
the ventilator at flow rates of 8 to 15 L/min through an
intratracheal catheter or, more conveniently, an endotracheal
tube positioned 2 cm above the carina and incorporating an
internal side port opening in the internal lumen 1 cm above
the distal tip [16, 29]. A flow sensor connected to the inspiratory
limb of the ventilator gives the signal to interrupt the
expiratory washout flow when inspiration starts. At
catheter flow rates of more than 10 L/min, turbulence
generated at the tip of the catheter enhances distal gas
mixing, and a greater portion of the proximal anatomical dead
space is flushed clear of CO₂ permitting CO₂ elimination to
be optimized [30, 31]. Expiratory washout can be applied
either to decrease PaCO₂ while maintaining tidal volume
constant or to decrease tidal volume while keeping PaCO₂
constant. In the former strategy, expiratory washout is used to
protect pH, whereas in the latter it is used to minimize the
stretch forces acting on the lung parenchyma, to minimize
ventilator-associated lung injury.

Two potential side effects should be taken into consideration
if expiratory washout is used for optimizing CO₂ elimination.
Intrinsic PEEP is generated if the expiratory washout flow is
not interrupted a few milliseconds before the beginning of
the inspiratory phase [16, 29]. As a consequence, inspiratory
plateau airway pressure may increase inadvertently, exposing
the patient to ventilator-induced lung injury. If expiratory
washout is to be used clinically in the future, the software
synchronizing the expiratory washout flow should give the
possibility of starting and interrupting the flow at different
points of the expiratory phase. A second critical issue
conditioning the clinical use of expiratory washout is the
adequate heating and humidification of the delivered
washout gas.

Currently, expiratory washout is still limited to experimental
use. It is entering a phase in which overcoming obstacles to
clinical implementation may lead to the development of
commercial systems included in intensive-care-unit ventilators
that may contribute to optimizing CO₂ elimination [30], in
particular in patients with severe acute respiratory syndrome
associated with head trauma [32].

Adjuncts aimed at optimizing lung recruitment
Sighs and recruitment manoeuvres
Periodic increases in inspiratory airway pressure may
contribute to the optimization of alveolar recruitment in
patients with ALI and ARDS. Sighs are characterized by
intermittent increases in peak airway pressure, whereas
recruitment manoeuvres are characterized by sustained
increases in plateau airway pressures. The beneficial impact
of sighs and recruitment manoeuvres on lung recruitment is
based on the well-established principle that inspiratory
pressures allowing reaeration of the injured lung are higher
than the expiratory pressures at which lung aeration vanishes.
At a given PEEP, the higher the pressure that is applied to
the respiratory system during the preceding inspiration, the
greater the lung aeration. In patients with ALI, the different
pressure thresholds for lung aeration at inflation and deflation
depend on the complex mechanisms regulating the removal
of oedema fluid from alveoli and alveolar ducts [33, 34], the
reopening of bronchioles externally compressed by cardiac
weight and abdominal pressure [35], and the preservation of
surfactant properties.

Reaeration of the injured lung basically occurs during
inspiration. The increase in airway pressure displaces the
gas–liquid interface from alveolar ducts to alveolar spaces
and increases the hydrostatic pressure gradient between the
alveolar space and the pulmonary interstitium [36]. Under
these conditions, liquid is rapidly removed from the alveolar
space, thereby increasing alveolar compliance [37] and
decreasing the threshold aeration pressure. Surfactant
alteration, a hallmark of ALI, results from two different
mechanisms: direct destruction resulting from alveolar injury,
and indirect inactivation in the distal airways caused by a loss
of aeration resulting from external lung compression [38]. By
preventing expiratory bronchiole collapse, PEEP has been
shown to prevent surfactant loss in the airways and avoid
collapse of the surface film [38]. As a consequence, alveolar
compliance increases and the pressure required for alveolar
expansion decreases. The time scale for alveolar recruitment
derecruitment is within a few seconds [39, 40], whereas
the time required for fluid transfer from the alveolar space to
the pulmonary interstitium is of the order of a few minutes
[36]. It has been demonstrated that the beneficial effect of
recruitment manoeuvres on lung recruitment is
obtained only when the high airway pressure (inspiratory or incremental
PEEP) is applied over a sufficient period [41, 42], probably
preserving surfactant properties and increasing alveolar
clearance [14].

In surfactant-depleted collapse-prone lungs, recruitment
manoeuvres increase arterial oxygenation by boosting the
ventilatory cycle onto the deflation limb of the pressure–
volume curve [42]. However, in different experimental models
of lung injury, recruitment manoeuvres do not provide similar
beneficial effects [43]. In patients with ARDS, recruitment
manoeuvres and sighs are effective in improving arterial
oxygenation only at low PEEP and small tidal volumes
[44, 45]. When PEEP is optimized, recruitment manoeuvres
are either poorly effective [46] or deleterious, inducing
overinflation of the most compliant lung regions [47] and
haemodynamic instability and worsening pulmonary shunt by
redistributing pulmonary blood flow towards non-aerated lung
regions [48]. However, after a recruitment manoeuvre, a
sufficient PEEP level is required for preventing end-expiratory alveolar derecruitment [49]. Furthermore, recruitment manoeuvres are less effective when ALI/ARDS is due to pneumonia or haemorrhagic oedema [43].

Different types of recruitment manoeuvre have been proposed for enhancing alveolar recruitment and improving arterial oxygenation in the presence of ALI [50]. A plateau inspiratory pressure can be maintained at 40 cmH₂O for 40 s. Stepwise increases and decreases in PEEP can be performed while maintaining a constant plateau inspiratory pressure of 40 cmH₂O [42]. Pressure-controlled ventilation using high PEEP and a peak airway pressure of 45 cmH₂O can be applied for 2 min [51]. The efficacy and haemodynamic side effects have been compared between three different recruitment manoeuvres in patients and animals with ARDS [49,51]. Pressure-controlled ventilation with high PEEP seems more effective in terms of oxygenation improvement, whereas a sustained inflation lasting 40 seconds seems more deleterious to cardiac output [49,51].

Studies reporting the potential deleterious effects of recruitment manoeuvres on lung injury of regions remaining fully aerated are still lacking. As a consequence, the administration of recruitment manoeuvres should be restricted to individualized clinical decisions aimed at improving arterial oxygenation in patients remaining severely hypoxaemic. As an example, recruitment manoeuvres are quite efficient for rapidly reversing aeration loss resulting from endotracheal suctioning [52] or accidental disconnection from the ventilator. In patients with severe head injury, recruitment manoeuvres may cause cerebral haemodynamics to deteriorate [53]. As a consequence, careful monitoring of intracranial pressure should be provided in case of severe hypoxaemia requiring recruitment manoeuvres.

**Prose position**

Turning the patient into the prone position restricts the expansion of the cephalic and parasternal lung regions and relieves the cardiac and abdominal compression exerted on the lower lobes. Prone positioning induces a more uniform distribution of gas and tissue along the sternovertebral and cephalocaudal axis by reducing the gas/tissue ratio of the parasternal and cephalic lung regions [54,55]. It reduces regional ventilation-to-perfusion mismatch, prevents the free expansion of anterior parts of the chest wall, promotes PEEP-induced alveolar recruitment [56], facilitates the drainage of bronchial secretions and potentiates the beneficial effect of recruitment manoeuvres [57], all factors that contribute to improving arterial oxygenation in most patients with early acute respiratory failure [55] and may reduce ventilator-induced lung overinflation.

It is recommended that the ventilatory settings be optimized before the patient is turned into the prone position [35]. If arterial saturation remains below 90% at an inspiratory fraction of oxygen of at least 60% and after absolute contraindications such as burns, open wounds of the face or ventral body surface, recent thoracoabdominal surgical incisions, spinal instability, pelvic fractures, life-threatening circulatory shock and increased intracranial pressure have been ruled out [56], the patient should be turned to prone in accordance with a predefined written turning procedure [56]. The optimum duration of prone positioning remains uncertain. In clinical practice, the duration of pronation can be maintained for 6 to 12 hours daily and may be safely increased to 24 hours [58]. The number of pronations can be adapted to the observed changes in arterial oxygenation after supine repositioning [55]. Whether the abdomen should be suspended during the period of prone position is still debated [56]. Complications are facial oedema, pressure sores and accidental loss of the endotracheal tube, drains and central venous catheters. Despite its beneficial effects on arterial oxygenation, clinical trials have failed to show an increase in survival rate by prone positioning in patients with acute respiratory failure [59,60]. Whether it might reduce mortality and limit ventilator-associated pneumonia in the most severely hypoxaemic patients [59,60] requires additional study.

**Closed-circuit endotracheal suctioning**

Endotracheal suctioning is routinely performed in patients with ALI/ARDS. A negative pressure is generated into the tracheobronchial tree for the removal of bronchial secretions from the distal airways. Two factors contribute to lung derecruitment during endotracheal suctioning: the disconnection of the endotracheal tube from the ventilator and the suctioning procedure itself. Many studies have shown that the sudden discontinuation of PEEP is the predominant factor causing lung derecruitment in patients with ALI [52,61]. During a suctioning procedure lasting 10 to 30 seconds, the high negative pressure generated into the airways further decreases lung volume [15]. A rapid and long-lasting decrease in arterial oxygenation invariably results from open endotracheal suctioning [62]. It is caused by a lung derecruitment-induced increase in pulmonary shunt and a reflex bronchoconstriction-induced increase in venous admixture; both factors increase the ventilation/perfusion ratio mismatch [52]. The decrease in arterial oxygenation is immediate and continues for more than 15 min despite the re-establishment of the initial positive end-expiratory level. A recruitment manoeuvre performed immediately after the reconnection of the patient to the ventilator allows a rapid recovery of end-expiratory lung volume and arterial oxygenation [62]. However, in the most severely hypoxaemic patients the open suctioning procedure itself may be associated with dangerous hypoxaemia [62].

Closed-circuit endotracheal suctioning is generally advocated for preventing arterial oxygenation impairment caused by ventilator disconnection [63,64]. However, a loss of lung volume may still be observed, resulting from the suctioning procedure itself and appearing dependent on the applied
negative pressure [15,63]. Both experimental studies and clinical experience suggest that closed-circuit endotracheal suctioning is less efficient than open endotracheal suctioning for removing tracheobronchial secretions [64,65]. As a consequence, the clinician is faced with two opposite goals: preventing lung derecruitment and ensuring the efficient removal of secretions [66]. Further clinical studies are needed to evaluate an optimum method that takes both goals into account.

In patients with ALI/ARDS, closed-circuit endotracheal suctioning should be considered the clinical standard. In severe ARDS, endotracheal suctioning should be optimized by pre-suction hyperoxygenation and followed by post-suction recruitment manoeuvres. In addition to the methods described above, two other types of recruitment manoeuvre have been proposed to prevent a loss of lung volume and reverse atelectasis resulting from endotracheal suctioning: the administration of triggered pressure-supported breaths at a peak inspiratory pressure of 40 cmH₂O during suctioning [15] and the administration of 20 consecutive hyperinflations set at twice the baseline tidal volume immediately after suctioning [52].

There is as yet no guideline for endotracheal suctioning in patients with severe ARDS. An algorithm is proposed in Fig. 3 aimed at preventing lung derecruitment and deterioration of gas exchange during endotracheal suctioning in hypoxaemic patients receiving mechanical ventilation with PEEP.

**Conclusion**

Mechanical ventilation in patients with ALI/ARDS requires specific adjustments of tidal volume and PEEP. Clinical use of adjuncts to mechanical ventilation allows optimization of alveolar recruitment resulting from PEEP and prevention of deleterious consequences of reduced tidal volume. Appropriate increases in respiratory rate, replacement of heat and moisture exchanger by a conventional humidifier, administration of recruitment manoeuvre in case of accidental episode of derecruitment, prone positioning and closed-circuit endotracheal suctioning all contribute to optimization of arterial oxygenation and O₂ elimination.

**Competing interests**

The author(s) declare that they have no competing interests.

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