International Journal of Clinical Medicine Research
2014; 1(1): 11-17
Published online March 20, 2014 (http://www.aascit.org/journal/ijcmr)

Keywords
Acute Respiratory Distress Syndrome,
Lung Recruitment Maneuvers,
Hypoxemia

Received: February 09, 2014
Revised: February 25, 2014
Accepted: February 26, 2014

Volume controlled ventilation mode is better than pressure controlled ventilation in lung recruitment maneuvers

Daihua Yu*, Xude Sun, Lilong Yao

Department of Anesthesiology, Tangdu Hospital of the Fourth Military Medical University, Xian, China

Email address
yudaihua@hotmail.com (Daihua Yu)

Citation
Daihua Yu, Xude Sun, Lilong Yao. Volume Controlled Ventilation Mode is better than Pressure Controlled Ventilation in Lung Recruitment Maneuvers. *International Journal of Clinical Medicine Research.* Vol. 1, No. 1, 2014, pp. 11-17.

Abstract
Purpose: This study evaluated the effects of lung recruitment maneuvers (RMs) on oxygenation and cardiac function in patients with acute respiratory distress syndrome while based on pressured controlled ventilation compared to the same treatment based on volume controlled ventilation. Methods: Patients with acute respiratory distress syndrome were enrolled and randomly divided into two groups (A, B). RMs were performed by stepwise increasing positive end-expiratory pressure. In group A, pressure controlled ventilation (PCV) mode was used for baseline readings. In group B, volume controlled ventilation (VCV) mode was used for baseline readings. Respiratory system mechanics and hemodynamic parameters were monitored before RMs and during the 2-h follow-up. PaO_2/FiO_2 and Qs/Qt were calculated from recorded blood gas analysis data. Levels of tumor necrosis factor-α (TNF-α), interleukin (IL-1β, IL-6, IL-8), and von Willebrand factor (vWF) in plasma and bronchoalveolar lavage fluid (BALF) were measured using ELISA. Results: Sixty-six patients with ARDS were enrolled. RMs based on VCV significantly increased PaO_2/FiO_2 and SPO_2 and reduced Qs/Qt compared to these indicators based on PCV. RMs with patients both VCV and PCB significantly increased heart rate, while simultaneously reducing cardiac indices and stroke volume. All of these returned to basal level by the 2-h follow-up. The mean arterial pressure and peripheral systemic vascular resistance remained stable throughout the procedures for both kinds of ventilation. Neither VCV nor PCV RMs ventilation mode during RMs had any effect on the plasma or BALF levels of TNF-α, IL-1β, IL-6, IL-8, or vWF. Conclusion: Lung RMs based on VCV may improve hypoxemia effectually than PCV, by increasing oxygenation and reducing intrapulmonary shunt, with little side effect on hemodynamics, having no effect on inflammatory factor production.

1. Introduction

Lung recruitment maneuvers (RMs) are a voluntary means of reopening poorly or nonaerated alveolar units by transiently increasing transpulmonary pressure, with the ultimate goal of improving gas exchange. This strategy has been proposed as an adjunct to mechanical ventilation in anesthesia and acute respiratory distress

syndrome (ARDS) [1]. syndrome have normally or partially aerated upper lobes and nonaerated lower lobes [2]. Thus the number of normally aerated lung units in acute respiratory distress syndrome patients is dramatically reduced, which leads to alveolar flooding and poor- or non-aeration. Concomitantly, an increase in alveolar fluid reduces diffusion of oxygen into capillaries, resulting in a pulmonary shunt.

Currently, mechanical ventilation and lung recruitment are the principle therapeutic strategies for the treatment of hypoxemia. However, mechanical ventilation alone can not completely reopen collapsed lung units [3, 4]. A study evaluating different lung recruitment strategies demonstrated variable efficacy, with normal lung hyperinflation leading to barotrauma or hemodynamic compromise [5]. On the other hand, the response to RMs in acute respiratory distress syndrome patients likely depends on previous respiratory system mechanics, the nature of the lung insult, or the type of ventilator setting [6-9]. For acute respiratory distress syndrome patients with hypoxemia, if collapsed alveolar units are to be effectively reopened with improved oxygenation and without causing severe adverse effects, it is critical to choose the appropriate maneuver strategy.

RMs in ARDS patients is widely practiced, but until now ,there is no coincident mode. Whether RMs based on VCV or PCV is different remain unknown. In the current study, we assessed the effects of lung RMs on oxygenation and intrapulmonary shunt, based on VCV and PCV in the treatment of hypoxemic ARDS patients by analyzing ventilation changes, oxygenation, hemodynamics, and secretion of inflammatory factors in plasma and bronchoalveolar lavage fluid (BALF). We found that, compared with PCV, lung RMs conducted with ARDS patients based on VCV is considered a safe and reliable means of improving oxygenation, significantly reduced intrapulmonary shunt, thereby enhancing reaeration of the impaired lung.

2. Materials and Methods

2.1. Patients

Patients diagnosed as ARDS were enrolled between January 2011 and January 2012 at the intensive care unit in Tangdu Hospital affiliated to the fourth military medical university, according to the criteria for ARDS issued by Infectious Diseases Society of America/American Thoracic Society in 2007. Each patient's Arterial oxygen saturation (SaO_2) was <90% when the fraction of inspired oxygen (FiO_2) was 0.60. The ratio of arterial oxygen concentration to the fraction of inspired oxygen (P/F ratio) was less than 200. Patients with unstable hemodynamic status were excluded. The hospital's ethics review board (No. 2010069) approved the study's protocol. All guardians of the subjects signed a written informed consent before the tests.

2.2. Measurements

During the entire procedure, routine continuous monitoring included electrocardiogram, blood pressure, and arterial oxyhemoglobin saturation via pulse oximetry (SpO_2). A peripheral intravenous rehydration system was established by placing a double-lumen central venous catheter through the right subclavian vein. A swan-ganz catheter was placed in internal jugular vein, central venous pressure (CVP) was monitored and maintained between 8 and 12 cm H_2O. An arterial catheter was placed in the radial artery for continuous invasive blood pressure monitoring and for arterial blood gas analysis.

Hemodynamic indices were monitored using thermodilution technique, which were performed by injecting 15 mL of iced saline solution via swan-ganz catheter after CVP measurement. The average of three subsequent measurements were recorded for each of the following: heart rate (HR), mean arterial pressure (MAP), cardiac index (CI), stroke volume index (SVI), peripheral systemic vascular resistance index (SVRI). Mixed venous oxygen were measured by collecting blood samples via swan-ganz catheter.

2.3. Protocol for RMs

Patients were positioned supine, sedated and spontaneous breathing was controlled by an intravenous infusion of 5 mg total dose midazolam hydrochloride and 2 mg vecuronium bromide. The airway was cleared before RMs began. Patients were mechanically ventilated (Puritan Bennett 840 ventilator, USA) via endotracheal intubation or tracheotomy. All the patients were divided into two groups ramdomly. In group A, pressure control ventilation (PCV) + PEEP ventilation (pressure control 10-20 cmH_2O, PEEP 5 cmH_2O, respiratory rate 15 times/min, FiO_2 50-100%) mode was used for baseline readings. In group B, volume control ventilation (VCV) + positive end-expiratory pressure (PEEP) ventilation mode (tidal volume 6-8 mL/kg, PEEP 5 cmH_2O, respiratory rate 15 times/min, FiO_2 50-100%) mode was used for baseline readings. Before RMs, we collected PEEP, FiO_2, and arterial blood gas analysis data. During the procedure, FiO_2 was kept constant at 100%. RMs were performed as stepwise increments of PEEP [10]. The RMs were performed with consecutive, simultaneous stepwise increases in PEEP of 2 cm H_2O every 2 min, until the arterial partial pressure of O_2 in arterial blood (PaO_2) + partial pressure of CO_2 in arterial blood ($PaCO_2$) reached 400 mmHg. Then stepwise decrease PEEP 2 cmH_2O until $PaO_2 + PaCO_2 < 400$ mmHg. Usually alveoli remain opening at the lowest PEEP level when $PaO_2 + PaCO_2 >$ 400 mmHg, which is considered as the best PEEP. Then, PEEP was kept at the best level after RMs (Figure 1).

The criteria for canceling the RMs were a 20% reduction in SaO_2 for 2 min or a drop in blood pressure (systolic pressure <90 mmHg or a 30% reduction of basal blood

pressure for 2 min). Bedside chest X-rays were obtained to monitor the occurrence of pneumothorax or mediastinal emphysema.

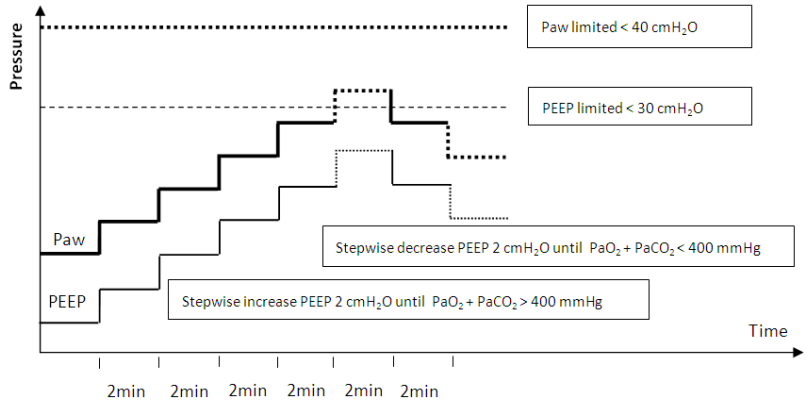

Figure 1. *Diagram of RMs with stepwise increases in PEEP applied in the study.*

The RMs were performed by continuous stepwise increases in PEEP of 2cm H_2O every 2 min until arterial PaO_2 + $PaCO_2$ was higher than 400 mmHg. Then stepwise decrease PEEP 2 cmH_2O until PaO_2 + $PaCO_2$ < 400 mmHg. After RMs, ventilation mode was adjusted back to prior to RMs but kept PEEP at the best level. Paw: Airway pressure. PEEP: Positive end-expiratory pressure.

Arterial and venous blood samples were collected from zero hours (the start of RMs) until 2 h after RMs to characterize pH, PaO_2, SaO_2, $PaCO_2$, oxygen saturation of mixed venous blood (SvO_2), and to calculate the oxygenation index (PaO_2/FiO_2) and intrapulmonary shunt [(Qs/Qt: (Cc02-CaO2)/(CcO2-CvO2)].

2.4. Measurement of Inflammatory Factors in Serum and BALF of Patients with ARDS

Arterial blood samples (3 mL) were collected before and 2 h after RMs. Obtained plasma was stored at -80 °C for future ELISA assays, to detect the concentrations of tumor necrosis factor-α (TNF-α), interleukin (IL-1β, IL-6, IL-8), and von Willebrand factor (vWF). ELISA assays were performed according to the manufacturer's instructions (Puer Biotech, China). BALF was collected before, and 2 or 4 h after, RMs using a bronchoscope (Olympus BFP40, Japan). The bronchoscope was advanced into a subsegmental bronchus and 20 mL 37 °C saline was instilled and then removed by negative pressure suction. The procedure was repeated twice and the recovery rate was 30-50%. Ten milliliters of BALF was centrifuged and supernatant was stored at -80 °C for ELISA assays.

2.5. Statistical Analyses

All statistical analyses were performed using SPSS13.0 software. Data were expressed as mean ± standard division (SD). *P*-values between two groups were calculated using the chi-squared (χ^2) test. The results within one group were analyzed with one-way analysis of variance (ANOVA) for the repeated measures model. The Pearson's correlation coefficient was used to assess the association between plasma and BALF levels of inflammatory factors. A *P*-value < 0.05 was considered significant.

3. Results

Sixty-six patients diagnosed as ARDS with hypoxemia were recruited for this study. There were 30 men and 36 women, between 17 and 76 years old (54.2 ± 22.5 years). The value of their Acute Physiology and Chronic Health Evaluation II (APACHE II) was 18.4 ± 4.2. All patients finished the tests without signs or symptoms of pneumothorax or mediastinal emphysema. Table 1 displays the mean oxygenation and intrapulmonary shunt values during the procedure. We found that, compared to baseline, PaO_2/FiO_2 increased significantly during RMs and remained significantly high throughout the follow-up period whether PCV group or VCV group ($P < 0.05$). However, the increase in PaO_2/FiO_2 at 30 min and 2 h after RMs in VCV group was more dramatic than that for RMs in PCV group ($P = 0.02$). Similarly, the SpO_2 during and after RMs was significantly enhanced compared to the SpO_2 before RMs for both groups ($P < 0.05$). The increase in SpO_2 after RMs was greater in VCV group compared to PCV group ($P < 0.05$). For both groups, the Qs/Qt during and after RMs was significantly decreased compared to the Qs/Qt before RMs ($P < 0.05$). Our results suggest that RMs based on VCV improve oxygenation and decrease intrapulmonary shunt better.

Regarding hemodynamic measurements, MAP remained stable throughout the entire RM procedure for patients in both groups. HR increased significantly during RMs but returned to the basal level by 30 min afterwards in both groups ($P < 0.05$). The CVP, CI and SVI during RMs were significantly decreased compared to starting (basal) values, and returned to basal 30 min after RMs ($P < 0.05$). However, there were no changes in SVRI throughout the experiment. Altogether, we found that RMs in both groups caused little change in most hemodynamic measurements

(Tables 2 and 3).

To evaluate whether RMs influenced lung inflammatory responses in these patients, we measured the secretion levels of TNF-α, IL-1β, IL-6, IL-8, and vWF in plasma using ELISA and found no significant differences between pre- and post- lung RM concentrations. Furthermore, there was no difference in inflammatory factor secretion between two groups ($P > 0.05$, Table 4). Similar results for inflammatory factors were observed in BALF (Table 5). Of note, we found that plasma concentrations of TNF-α, IL-1β, IL-6, and IL-8 were strongly correlated with their respective concentrations in BALF ($P < 0.05$, Table 6). The data suggests that RMs and ventilation mode had no effect on inflammatory response in acute respiratory distress syndrome patients.

Table 1. *Oxygenation and intrapulmonary shunt before, during, and after RM based on PCV or VCV.*

		PaO_2/FiO_2	Qs/Qt (%)	SpO_2 (%)
Group A (PCV)	Pre-RM	251.4 ± 35.3	16.6 ± 1.4	88.5 ± 2.5
	Max-RM	419.2 ± 44.8 [a]	11.8 ± 3.6 [a]	95.5 ± 3.8 [a]
	30 min-RM	335.6 ± 38.2 [a]	12.2 ± 2.2 [a]	95.0 ± 3.2 [a]
	120 min- RM	317.0 ± 36.9 [a]	14.6 ± 1.8 [a]	92.8 ± 2.6 [a]
Group B (VCV)	Pre-RM	275.4 ± 45.7	15.4 ± 2.2	91.6 ± 3.9
	Max-RM	441.6 ± 43.1 [a,b]	9.5 ± 4.7 [a,b]	98.2 ± 1.8 [a,b]
	30 min-RM	398.3 ± 38.0 [a,b]	9.9 ± 3.5 [a,b]	97.0 ± 1.5 [a,b]
	120 min-RM	356.6 ± 36.5 [a,b]	10.0 ± 3.0 [a,b]	95.1 ± 1.6 [a,b]

[a] $P < 0.05$ compared to pre-RM, [b] $P < 0.05$ compared to group A.

Table 2. *The hemodynamic parameters before, during, and after RM based on PCV.*

	Pre-RM	Max-RM	30 min-RM	120 min-RM
HR (beats/min)	80.3 ± 5.5	86.6 ± 8.0[c]	80.9 ± 6.2	83.5 ± 5.2
MAP (mmHg)	71.2 ± 4.7	70.5 ± 5.0	70.6 ± 5.1	72.4 ± 4.3
CVP (mmHg)	8.5 ± 2.5	5.4 ± 1.5[c]	8 ± 2.2	8.1 ± 2
CI ($L/min/m^2$)	3.8 ± 0.6	3.5 ± 0.4 [c]	3.7 ± 0.7	3.7 ± 0.5
SVI ($mL/beat/m^2$)	38.8 ± 6.5	32.4 ± 5.6[c]	36.5 ± 7.1	38.2 ± 6.6
SVRI ($dyn{\cdot}sec{\cdot}cm^{-5}{\cdot}m^2$)	1550 ± 174	1588 ± 166	1560 ± 152	1556 ± 156

[c] $P < 0.05$ compared to pre-RM.

Table 3. *The hemodynamic parameters before, during, and after RM based on VCV.*

	Pre-RM	Max-RM	30 min-RM	120 min-RM
HR (beats/min)	81.5 ± 4.9	88.7 ± 6.6[d]	83.7 ± 5.8	82.3 ± 6.2
MAP (mmHg)	68.2 ± 3.5	65.7 ± 3.2	66.9 ± 4.4	67.8 ± 3.0
CVP (mmHg)	6.1 ± 2.5	3.3 ± 1.8[d]	5.8 ± 1.6	6 ± 1.5
CI ($L/min/m^2$)	3.6 ± 0.4	3.1 ± 0.5[d]	3.5 ± 0.5	3.5 ± 0.6
SVI ($mL/beat/m^2$)	37.3 ± 5	31.2 ± 5.8[d]	37.1 ± 6.6	37 ± 5.1
SVRI ($dyn{\cdot}sec{\cdot}cm^{-5}{\cdot}m^2$)	1562 ± 159	1574 ± 156	1570 ± 161	1568 ± 166

[d] $P < 0.05$ compare to pre-RM.

Table 4. *Plasma concentrations of inflammatory cytokines before and after RM based on PCV or VCV.*

		TNF-α (ng/L)	IL-1β (ng/L)	IL-6 (ng/L)	IL-8 (ng/L)	vWF (ng/L)
PCV	Pre-RM	28.2 ± 3.2	131.5 ± 36.3	3.4 ± 2.7	64.8 ± 7.8	94.4 ± 9.3
	2 h-RM	26.5 ± 3.9	136.2 ± 29.5	3.7 ± 2.0	65.0 ± 6.7	96.0 ± 7.5
	4 h-RM	27.6 ± 2.4	132.6 ± 32.1	3.3 ± 1.5	66.4 ± 8.2	95.2 ± 8.7
VCV	Pre-RM	27.4 ± 2.8	138.8 ± 40.0	3.8 ± 2.6	68.1 ± 8.4	92.5 ± 7.4
	2 h-RM	26.8 ± 3.5	136.7 ± 34.4	4.1 ± 2.3	66.3 ± 6.0	96.0 ± 7.7
	4 h-RM	27.2 ± 2.2	139.5 ± 27.9	3.9 ± 2.2	60.9 ± 5.5	91.4 ± 6.5

Table 5. *BALF concentration of inflammatory factors before and after RM based on PCV or VCV.*

		TNF-α (ng/L)	IL-1β (ng/L)	IL-6 (ng/L)	IL-8 (ng/L)
PCV	Pre-RM	8.3 ± 3.7	32.5 ± 15.9	1.4 ± 2.3	13.5 ± 5.5
	2 h-RM	6.6 ± 2.5	35.2 ± 12.3	1.8 ± 1.8	12.7 ± 4.0
	4 h-RM	8.5 ± 3.3	36.0 ± 17.6	1.5 ± 2.8	12.0 ± 6.4
VCV	Pre-RM	7.7 ± 2.9	32.4 ± 14.6	1.5 ± 1.5	13.2 ± 4.2
	2 h-RM	7.8 ± 3.1	32.6 ± 18.2	2.0 ± 2.9	12.6 ± 5.8
	4 h-RM	8.4 ± 3.4	36.1 ± 15.5	1.3 ± 1.6	12.1 ± 4.3

Table 6. *The association between plasma and BALF concentrations of corresponding inflammatory factors.*

		Plasma							
		TNF-α		IL-1β		IL-6		IL-8	
		r	*P*	r	*P*	r	*P*	r	*P*
BALF	TNF-α	0.73	0.00[e]	—	—	—	—	—	—
	IL-1β	—	—	0.31	0.04[e]	—	—	—	—
	IL-6	—	—	—	—	0.47	0.01[e]	—	—
	IL-8	—	—	—	—	—	—	0.61	0.01[e]

4. Discussion

Acute respiratory distress syndrome is associated with very high mortality. In the present study, we found that the RM strategy applied based on VCV significantly improved oxygenation and lung mechanics in acute respiratory distress syndrome patients with hypoxemia, compared to PCV. More importantly, RMs performed ARDS patients based on VCV had no aggravating effect on hemodynamic status or lung inflammatory responses.

Acute respiratory distress syndrome usually combined with various pathological characteristics and diverse reactions to therapeutic maneuvers [11]. Lung pathology includes alveolar flooding, chronic interstitial inflammation, and edema. Moreover, lung nonaeration, which mainly occurs in the caudal and juxtadiaphragmatic regions, contributes to differing levels of hypoxemia in ARDS patients. Mechanical ventilation with PEEP is one of the most important strategies to reduce this symptom in ARDS patients, but unfortunately the lung protective modes of mechanical ventilation could further increase lung nonaeration or even lead to lung injury [12].

Recently, postural drainage and lung RMs have become widely used in ARDS patients. RMs were found to increase lung volume by enhancing the airway pressure in a short period, thereby promoting the opening of collapsed lung units and preventing secondary atelectasis caused by low tidal volume [13]. Although effective in recruiting the lung and reversing hypoxemia, the use of RMs has not shown consistent outcomes in patients with ARDS [14].

Many studies focusing on the efficacy and adverse effects of RMs in ARDS patients showed variable results and that RMs could be a possible cause of hemodynamic instability [15,16]. In view of this, RMs performed as routine ventilatory protective treatment remain controversial [17,18]. To address the issue, we examined whether stepwise increases in PEEP during RMs could improve hypoxemia without affecting hemodynamics. Our results clearly indicate that stepwise increase in PEEP with the ARDS patient significantly improved oxygenation and lung mechanics. Consistent with this, Borges et al. [19] reported that an incremental stepwise PEEP could obtain nearly full lung recruitment (i.e., $PaO_2 + PaCO_2 \geq 400$ mmHg) in 92% of ARDS patients. In addition, previous studies showed that certain transient hemodynamic variables were compromised after RMs [1, 5]. We found that CVP, CI and SVI decreased, and HR increased, during lung RMs based on PCV or VCV mode. However, the adverse effects were transient and hemodynamic parameters returned to the basal level within 2 h after RMs. We reasoned that RMs induced higher intrathoracic pressure, and a reduction of the amount of blood in the inferior vena cava could be a possible cause.

Interestingly, in the present study RMs were associated with fewer adverse effects when performed based on VCV, indicating that this mode is to be preferred over the PCV for these patients undergoing RMs. ARDS patients have widespread inflammatory lung edema which increases the weight of lung tissues 2- to 3-fold compared to normal subjects; thus, the compression forces involved are strikingly increased in these patients [20, 21].

Cytokine measurements in the BALF of patients with ARDS have provided valuable insights into the complexity of inflammatory responses that occur in the lung. Hyperinflation increased the secretion of proinflammatory cytokines, causing fluid extravasation from the capillaries, and impaired endothelial function [22]. In order to assess the effect of stepwise increases of PEEP on lung vascular endothelia, we measured the concentrations of the inflammatory factors TNF-α, IL-1β, IL-6, IL-18, and vWF in plasma and BALF. TNF-α and IL-1β are early response cytokines which stimulate the production of other cytokines by lung epithelial and mesenchymal cells. Both are present in BALF at the onset of ARDS and could regulate other inflammatory factors. IL-6 and IL-18, markers of the early stage of severe lung injury, are major chemokines in ARDS and are upregulated in different lung injuries. vWF is a biomarker reflecting damage of the vascular epithelia and a prognostic factor of ARDS.

Sustained hypoxia leads to the development of a complex, pulmonary arteries-specific, proinflammatory microenvironment [23]. In patients with ARDS, acute hypoxemia represents one of potentially several proinflammatory stimuli responsible for the development of ARDS [24]. Our results showed that, while there was a

correlation between the levels of inflammatory factors in both serum and BALF in patients with ARDS, RMs and the two ventilation mode had no influence on the secretion of inflammatory factors. This suggests that RMs and ventilation mode have no role in either diminishing or exacerbating lung inflammatory responses in these patients. Consistent with this, one report showed that a single RM had no effect on systemic levels of pro-inflammatory and anti-inflammatory cytokines in mechanically ventilated patients [25]. However, in another studies RMs have been reported to reduce lung inflammatory and fibrogenic responses in patients with ARDS [26]. The reason for this discrepancy remains unclear, although differences in population sizes and methods might contribute. More studies are needed to elucidate this.

In summary, our results suggest that RMs performed while hypoxemic ARDS patients are based on VCV rather than PCV significantly improve oxygenation and reduces intrapulmonary shunt, without inducing adverse side effects such as hemodynamic instability or increases in lung inflammatory responses. Thus, RMs based on VCV can be considered a reliable and effective adjunct to mechanical ventilation strategies for ARDS patients with hypoxemia.

Abbreviations

VCV, volume controlled ventilation;
PCV, pressure controlled ventilation;
ARDS, acute respiratory distress syndrome ;
APACHE II, Acute Physiology and Chronic Health Evaluation II;
BALF, bronchoalveolar lavage fluid;
CI, cardiac index;
CVP, central venous pressure;
HR, heart rate;
IL, interleukin;
MAP, mean arterial pressure;
PaO2, partial pressure of O2 in arterial blood;
PaCO2, partial pressure of CO2 in arterial blood;
PEEP, positive end-expiratory pressure;
Qs/Qt, intrapulmonary shunt;
RM, recruitment maneuver;
SaO2, arterial oxygen saturation;
SpO2, arterial oxyhemoglobin saturation via pulse oximetry;
SVI, stroke volume index;
SvO2, oxygen saturation of mixed venous blood;
SVRI, systemic vascular resistance index;
TNF-α, tumor necrosis factor;
vWF, von Willebrand factor

References

[1] Fan E, et al (2008) Recruitment maneuvers for acute lung injury: a systematic review. Am J Respir Crit Care Med 178(11): 1156-1163.

[2] Bernard GR, et al (1994) The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. Am J Respir Crit Care Med 149(3 Pt 1): 818-824.

[3] Brunner JX, Wysocki M (2009) Is there an optimal breath pattern to minimize stress and strain during mechanical ventilation? Intensive Care Med 35(8): 1479-1483.

[4] Rouby JJ, et al (2004) Mechanical ventilation in patients with acute respiratory distress syndrome. Anesthesiology 101(1): 228-234.

[5] Kacmarek, RM, Villar J (2011) Lung recruitment maneuvers during acute respiratory distress syndrome: is it useful? Minerva Anestesiol 77(1): 85-89.

[6] Guerin C, Debord S, Leray V.et al (2011) Efficacy and safety of recruitment maneuvers in acute respiratory distress syndrome. Ann Intensive Care 19;1(1):9.

[7] Arnal JM, Paquet J, Wysocki M, et al (2011) Optimal duration of a sustained inflation recruitment maneuver in ARDS patients. Intensive Care Med 37(10):1588-1594.

[8] Rival G, Patry C, Floret N, et al (2011) Prone position and recruitment manoeuvre: the combined effect improves oxygenation. Crit Care 15(3):125.

[9] Kacmarek RM, Villar J (2011) Lung recruitment maneuvers during acute respiratory distress syndrome: is it useful? Minerva Anestesiol 77(1):85-89.

[10] Moran I, et al (2011) Acute physiologic effects of a stepwise recruitment maneuver in acute respiratory distress syndrome. Minerva Anestesiol 77(12): 1167-1175.

[11] Valenza F (2010) Do recruitment maneuvers simply improve oxygenation? Crit Care 14(4): 173.

[12] Esteban A, et al (2008) Evolution of mechanical ventilation in response to clinical research. Am J Respir Crit Care Med 177(2): 170-177.

[13] Marini J (2008) How best to recruit the injured lung? Crit Care 12(3): 159.

[14] Villagra A, et al (2002) Recruitment maneuvers during lung protective ventilation in acute respiratory distress syndrome. Am J Respir Crit Care Med 165(2): 165-170.

[15] Guerin C, Debord S, Leray V, et al (2011) Efficacy and safety of recruitment maneuvers in acute respiratory distress syndrome. Ann Intensive Care 19 (1):9.

[16] Iannuzzi M., et al (2010) Different patterns of lung recruitment maneuvers in primary acute respiratory distress syndrome: effects on oxygenation and central hemodynamics. Minerva Anestesio l76(9): 692-698.

[17] Kacmarek RM, Villar J (2011) Lung recruitment maneuvers during acute respiratory distress syndrome: is it useful? Minerva Anestesiol 77(1):85-89.

[18] Park KJ, Oh YJ, Chang HJ, et al: Acute hemodynamic effects of recruitment maneuvers in patients with acute respiratory distress syndrome. J Intensive Care Med. 2009,24(6):376-382.

[19] Borges JB, Carvalho CR, Amato MB (2006) Lung recruitment in patients with ARDS. N Engl J Med 355(3): 319-320

[20] Ware LB (2006) Pathophysiology of acute lung injury and the acute respiratory distress syndrome. Semin Respir Crit Care Med 27(4): 337-349.

[21] Burke DL, et al (2009) Sustained hypoxia promotes the development of a pulmonary artery-specific chronic inflammatory microenvironment. Am J Physiol Lung Cell Mol Physiol 297(2): 238-250.

[22] Hirani N, et al (2001) The regulation of interleukin-8 by hypoxia in human macrophages--a potential role in the pathogenesis of the acute respiratory distress syndrome (ARDS). Mol Med 7(10): 685-697.

[23] Santiago V.R, et al (2010) Recruitment maneuver in experimental acute lung injury: the role of alveolar collapse and edema. Crit Care Med 38(11): 2207-2214.

[24] Halbertsma F.J, et al (2010) A single recruitment maneuver in ventilated critically ill children can translocate pulmonary cytokines into the circulation. J Crit Care 25(1): 10-15.

[25] Ko S.C, et al (2008) Effects of PEEP levels following repeated recruitment maneuvers on ventilator-induced lung injury. Acta Anaesthesiol Scand 52(4): 514-521.

[26] Chan M.C, et al (2007) Effects of prone position on inflammatory markers in patients with ARDS due to community-acquired pneumonia. J Formos Med Assoc 106(9): 708-716.