Lung-protective strategy of acute respiratory distress syndrome: a comparative study between pressure control and volume control

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Introduction
Acute respiratory distress syndrome (ARDS) constitutes a major phenotype of acute hypoxemic respiratory failure. Pressure control (PC) and volume control (VC) modes are used for the management of moderate and severe ARDS. Each mode has its benefits and drawbacks.

Aim
The aim of this study was to compare lung-protective strategy (LPS) using PC ventilation with LPS using VC ventilation to get the best benefit for those critically ill ARDS patients and to solve the problem of hypoventilation.

Patients and methods
This prospective, randomized controlled trial was carried out at the respiratory intensive care unit of university hospital during the period from October 2017 to December 2018. The study included 30 patients diagnosed as ARDS according to Berlin definition. Those patients were categorized into two groups: group I is the PC group (15 patients) using the LPS and group II is the VC group (15 patients) using the LPS.

Results
The mean age was 48.93 ± 9.91 years for the PC group with female predominance (53.3%), while the mean age was 46.11 ± 7.94 for the VC group with male predominance (53.3%). Arterial blood gases showed a significant higher pH and lower $PaCO_2$ in the VC group. Mechanical parameters showed a significant higher V_T and V_E in the VC group. Weaning and outcome in both groups were successful, while seven of the patients of PC (46.7%) and four of the patients of VC (26.7%) failed extubation and died.

Conclusion
The authors conclude that both modes are equally effective in improving oxygenation in patients of ARDS, who were ventilated with LPS, while VC achieved better ventilation, higher pH, and lower PCO_2 than PC. But it needs strict monitoring of plateau pressure to maintain safety.

Keywords:
acute respiratory distress syndrome, lung-protective strategy, mechanical ventilation, strategies

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Introduction

Acute respiratory distress syndrome (ARDS) constitutes a major phenotype of acute hypoxemic respiratory failure, accounts for one-quarter of cases of acute respiratory failure in ICUs, and a third to half of patients die in the ICU, in hospital or during follow-up [1].

In 1994, the American European Consensus Conference established criteria for the diagnosis of ARDS [2]: acute onset (<7 days), ratio of arterial oxygen tension (PaO_2) to the fraction of inspired oxygen (FiO_2) was chosen to reflect the degree of hypoxemia and measured at different FiO_2, diffuse bilateral pulmonary infiltrates on chest radiograph consistent with pulmonary edema, poor systemic oxygenation, and absence of left heart failure (clinical assessment or wedge pressure ≤18 mmHg).

In 2011, a panel of experts of the American Thoracic Society and the Society of Critical Care Medicine developed the Berlin definition [3]. The New Berlin classification for ARDS categorizes ARDS based on the degree of hypoxemia:

(1) Mild ARDS: (200 mmHg $<PaO_2/FiO_2 \leq 300$ mmHg).
(2) Moderate ARDS: (100 mmHg $\leq PaO_2/FiO_2 \leq 200$ mmHg).
(3) Severe ARDS: ($PaO_2/FiO_2 \leq 100$ mmHg).

The syndrome is characterized by the rapid onset of severe hypoxemia and dyspnea and be caused by a variety of direct and indirect injuries. ARDS occurs as a result of an inflammatory process that occurs at the alveolar–capillary interface in the lungs, the space in which the blood in the capillaries is separated from the gas present in the alveoli. This causes pulmonary infiltrates leading to acute respiratory failure and in other cases death [4].

The management of ARDS is supportive with lung-protective ventilation and fluid-conservative strategy, cardiorespiratory and nutritional support, prevention of further lung injury, and prevention of complications, while waiting for the acute inflammatory response to resolve and to improve lung function [5]. Mechanical ventilation remains the cornerstone of ARDS management.

Respiratory support with a mechanical ventilator is a double-edged sword that can improve oxygenation, more homogeneous aeration, reduced sedative requirements, and lower risk for ventilator-induced diaphragmatic dysfunction, but can exacerbate lung injury and may contribute to non-pulmonary organ failure and mortality in patients with ARDS [6,7].

Lung-protective ventilation strategy is composed of low tidal volumes (6–4 ml/kg IBW), inspiratory pressures (plateau pressure <30 cmH_2O), and positive end-expiratory pressure (PEEP) above the lower inflection point (LIP) on the static pressure–volume curve of the respiratory system in relation with adequate FiO2 [8]. The use of low tidal volume may result in CO_2 retention and respiratory acidosis causing permissive hypercapnia. It can be managed with a higher respiratory rate [9–11]. PEEP is used to improve oxygenation by increasing the functional residual capacity, preventing small airways and alveoli from collapsing, thus improving the ventilation–perfusion (V/Q) matching [6,12]. The aim of this study was to compare lung-protective strategy (LPS) using pressure control (PC) ventilation with LPS using volume control (VC) ventilation to get the best benefit for those critically ill ARDS patients and to solve the problem of hypoventilation.

Patients and methods

Patients

This is a prospective randomized controlled trial carried out at the Respiratory Intensive Care Unit of University Hospital during the period from October 2017 to December 2018. The study included 30 patients diagnosed as ARDS according to Berlin definition. The patients were categorized into two groups [3]. Ethical approval was obtained under 17101036:

(1) Group I: PC group.
(2) Group II: VC group.

Inclusion criteria

Adult patients with moderate or severe ARDS with hypoxemic respiratory failure who were intubated and mechanically ventilated after 2 h of refractory hypoxemia on FiO_2 60%. Patients were ventilated with the Nellcor Puritan Bennett 840 ventilator system (Fridley City, Minnesota State, United States of America (U.S.A)).

Exclusion criteria

Those who fall under the following categories were excluded:

(1) Age more than 60 years old.
(2) Chronic obstructive pulmonary diseases.
(3) Cardiac diseases.
(4) Chronic renal or liver diseases.

All patients were subjected to:

(1) History and clinical examination.
(2) Arterial blood gases (ABG): the sample of arterial blood is withdrawn from radial artery for blood gas analysis using an ABL800 blood gas analyzer (USA).
(3) Complete blood picture.
(4) Liver and renal functions.

Ventilatory settings

Group I

(1) PEEP set at LIP and greater than or equal to 10 cm H_2O.
(2) Pressure limit set at higher inflection point and less than or equal to 30 cm H_2O with target tidal volume (V_T) 6 ml/kg (IBM).
(3) FiO_2 adjusted at 60%.
(4) Respiratory rate 16/–25 breaths/min to obtain minute volume more than 6 l.

Group II

(1) V_T set at 6 ml/kg of IBW and ↓ to a minimal level of 4 ml/kg of IBM provided that the plateau pressure (P_{PLAT}) is not more than 30 cmH_2O.
(2) Respiratory rate 16 up to 25 breaths/min to obtain minute volume greater than 6 l.
(3) Use descending inspiratory waveform.
(4) FiO_2 adjusted at 60%.

Monitoring of mechanical parameters

(1) Peak inspiratory pressure (P_{peak}).
(2) $P_{plateau}$.

(3) Respiratory rate (RR).
(4) Exhaled tidal volume (VT).
(5)Minute volume (VE)

During volume ventilation there is strict monitoring for $P_{plateau}$ every 15 min using inspiratory pause maneuver provided that it is less than or equal to 30 cm H_2O:

(a) Continuous monitoring of vital signs: blood pressure, heart rate, and respiratory rate.
(b) Oxygen saturation (SpO_2) by pulse oximeter.
(c) ABG.

We record the previous parameters at 2, 6, 12, 24, 48, and 72 h interval before weaning and after extubation.

Outcome measures

In each group, success and failure of weaning will be recorded.

Failure is defined as failure of weaning or death during the ventilation period. Weaning of improved patients is done by ↓ PEEP by 5 cmH_2O every 2 h provided that SpO_2 is not ↓ more than 20% of the previous level. When PEEP reaches 5 cmH_2O extubation must be done.

Results

The results showed demographic and baseline data of the patients and the mean age was (48.93 ± 9.91 years for the PC group) with female predominance (53.3%), while the mean age was (46.11 ± 7.94 for the VC group) with male predominance (53.3%), as shown in Table 1.

Follow up of baseline laboratory data in both groups showed no significant differences between both groups regarding complete blood picture, erythrocyte sedimentation rate, and kidney function tests as in Table 2.

Regarding vital signs (RR, HR, and SpO_2). there were no significant differences between both groups as in Figs. 1–3.

Table 1 Demographic and baseline data of patients

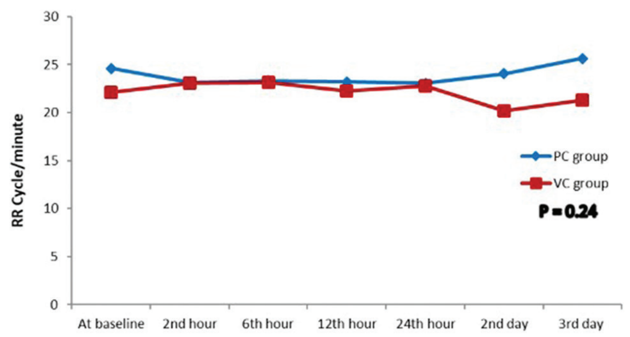
Variables	PC group (*n*=15)	VC group (*n*=15)	*P*
Age (years)	48.93±9.91	46.11±7.94	0.40
Sex			
Male	7 (46.7)	8 (53.3)	0.50
Female	8 (53.3)	7 (46.7)	
Smoking status			
Smoker	5 (33.3)	5 (33.3)	0.05
Smoking index	350 (300-600	400 (400-600)	0.72

Data were expressed in the form of mean (SD) and *n* (%). *P* value was significant if less than 0.05. PC, pressure control; VC, volume control.

Follow up of ABG demonstrated a statistically significant higher pH and lower $PaCO_2$ in the VC group as shown in Figs. 4 and 5.

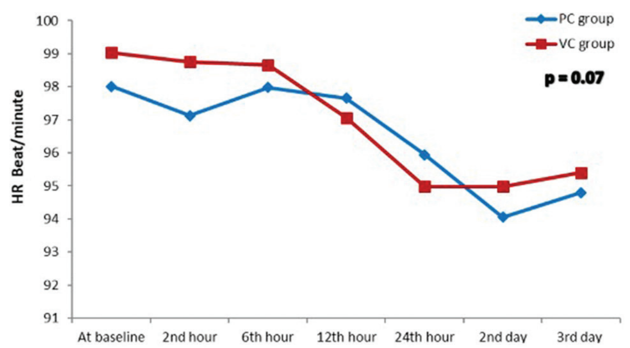
Ventilatory setting parameters that were comparable in the two groups showed statistically significant higher V_T and V_E in the VC group as recorded in Figs. 6 and 7.

Figure 1



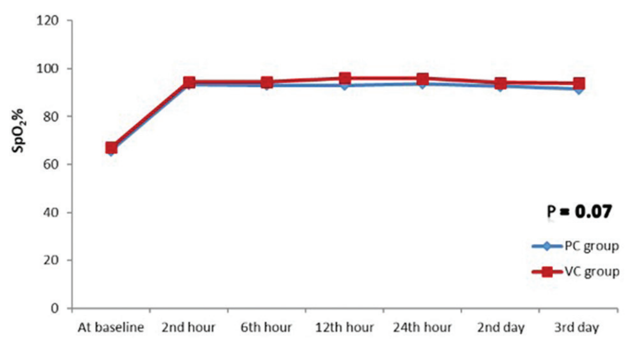
Changes in respiratory rate in both studied groups. Data was expressed in form of mean (SD). *P* value was significant if less than 0.05. PC, pressure control; VC, volume control; RR, respiratory rate.

Figure 2



Changes in HR in both groups. Data was expressed in form of mean (SD). *P* value was significant if less than 0.05. PC, pressure control; VC, volume control; HR, heart rate.

Figure 3



Changes in SpO_2 in both groups. Data was expressed in form of mean (SD). *P* value was significant if less than 0.05. PC, pressure control; VC, volume control; SpO_2, peripheral capillary oxygen saturation.

Table 2 Baseline laboratory data in both groups

	PC group (*n*=15)	VC group (*n*=15)	*P*
CBC			
Leukocytes count (×10³/ml)	12.42±6.64	13.90±3.67	0.45
Polymorphs (×10³/ml)	9.06±3.99	10.77±4.01	0.13
Red blood cells (×10³/ml)	4.94±0.76	4.53±0.67	0.13
Hemoglobin (mg/dl)	13.34±1.84	13.54±1.36	0.68
Hematocrit value (%)	41.26±5.76	40.86±5.87	0.85
Platelet count (×10³/ml)	216.53±46.83	235.53±62.67	0.35
Thrombocytopenia	1 (6.7%)	0	0.50
ESR (ml/h)			
First hour	26.09±9.11	30.11±13.11	0.11
Second hour	33.13±19.34	41.01±8.76	0.98
KFTs			
Serum creatinine (mg/dl)	0.86±0.21	0.81±0.23	0.45
Blood urea (mg/dl)	4.46±1.45	4.43±1.21	0.91
Cr Cl (ml/min)	90.76±13.76	91.22±12.98	0.09

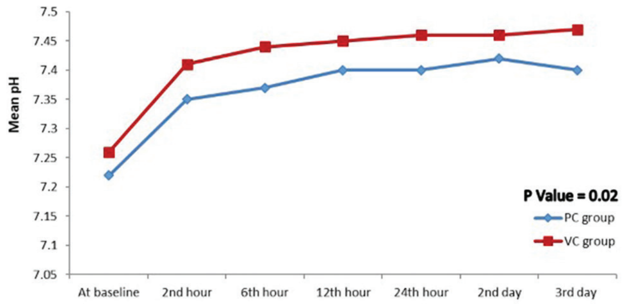
Data were expressed in the form of mean (SD). *P* value was significant if less than 0.05. CBC, complete blood picture; Cr Cl, creatinine clearance; ESR, erythrocyte sedimentation rate; KFTs, kidney function test; PC, pressure control; VC, volume control.

Follow up of P_{IP} in both groups showed that there was no significant difference between both groups ($P > 0.05$) (Fig. 8).

Weaning of patients and outcome in both groups in Fig. 9 demonstrated that weaning was successful while seven (46.7%) patients of the PC group and four (26.7%) patients of the VC group showed failed extubation and died.

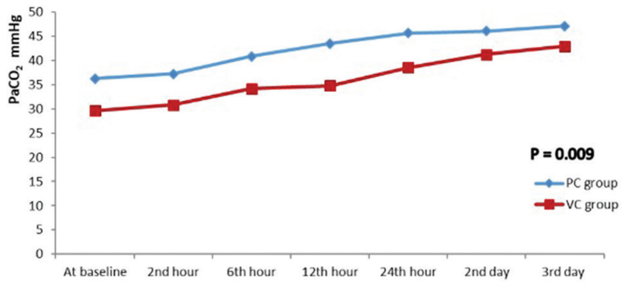
Ventilatory parameters during weaning in successful groups (Table 3) showed that there were no significant differences ($P > 0.05$) with the exception of higher V_E and V_T in the VC group.

Figure 4



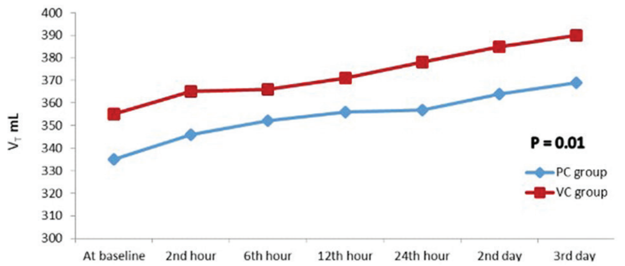
Changes in pH in both groups. Data was expressed in form of mean (SD). *P* value was significant if less than 0.05. PC, pressure control; VC, volume control; pH, hydrogen ion concentration.

Figure 5



Changes in $PaCO_2$ in both groups. Data was expressed in form of mean (SD). *P* value was significant if less than 0.05. PC, pressure control; VC, volume control; $PaCO_2$, partial pressure of carbon dioxide.

Figure 6



Changes in V_T in both groups. Data was expressed in form of mean (SD). *P* value was significant if less than 0.05. PC, pressure control; VC, volume control; V_T, tidal volume.

Discussion

ARDS constitutes a major phenotype of acute hypoxemic respiratory failure. PC and VC modes are used for the management of moderate and severe ARDS. Each mode has its benefits and drawbacks [13].

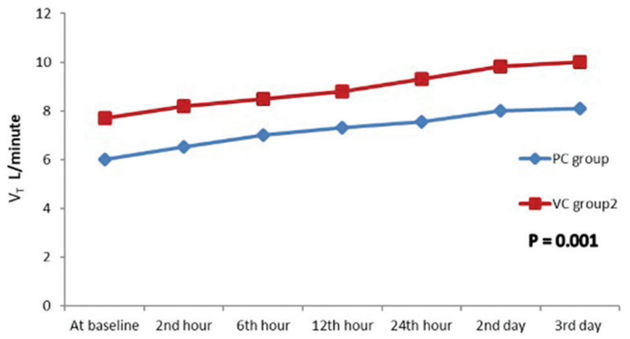
In this study, we aimed to compare between two modes using the LPS. In PC, LPS was achieved, while drawback was hypoventilation. On the other hand, adequate ventilation was achieved with VC but lung protection cannot be assured.

Regarding the demographic and baseline data of the patients it has been noticed that the mean age was (48.93 ± 9.91 years for the PC group with female predominance (53.3%), while the mean age was (46.11 ± 7.94 for the VC group) with male predominance (53.3%). This was in agreement with Esteban *et al.* [14], Meade *et al.* [10], and Waleky *et al.* [15].

Regarding HR, RR, and SpO_2 there was no significant difference between both groups in our study. This denotes that the parameters of respiratory distress are not different between both groups and both modes equally relieve the patient distress. Many studies as those of Sachdev *et al.* [16], and Samantaray *et al.* [17] reported a significant improvement in vital signs in VC. On other hand, Gupta *et al.* [18] found that there was significant improvement in vital signs in the PC group.

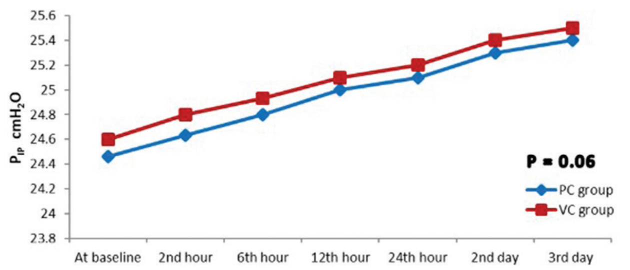
ABG revealed a significant higher pH and lower $PaCO_2$ in the VC group. These results are consistent

Figure 7



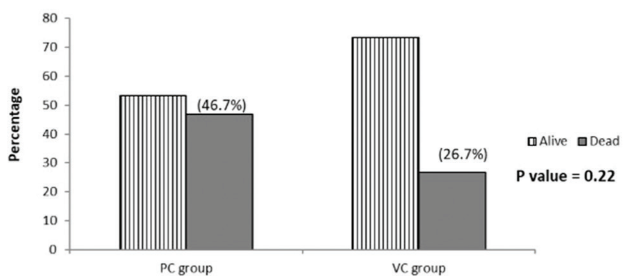
Changes in Minute ventilation in both groups. Data was expressed in form of mean (SD). *P* value was significant if less than 0.05. PC, pressure control; VC, volume control; V_E, minute ventilation.

Figure 8



Changes in P_{IP} in both groups. Data was expressed in form of mean (SD). *P* value was significant if less than 0.05. PC, pressure control; VC, volume control; P_{IP}: peak inspiratory pressure.

Figure 9



Outcome of patients in both groups. Data was expressed in form of frequency (percentage), mean (SD), median (range). *P* value was significant if less than 0.05. PC, pressure control; VC, volume control.

with Bouachour *et al.* [19], Tiruvoipati *et al.* [20], and Abou Shehata *et al.* [21] Their results provided ABG after 1 h, 2 h, second day, and 3rd day of using VC with gradual reduction of the used FiO2 in the same period; pH and PCO_2 were 7.14 ± 0.12, 7.28 ± 0.25, 7.33 ± 0.10, 7.38 ± 0.10, and 7.37 ± 0.07 and PCO2 were 83.71 ± 28.11, 62.66 ± 19, 56.18 ± 15, 49.37 ± 14, and 54.82 ± 13 showing a significant improvement of higher pH and lower PCO_2 during VC. Gupta *et al.* [18], during their study found less increase in PCO_2, better partial pressure of oxygen and better oxygenation in PC. Ambrosino *et al.* [22] found that

Table 3 Ventilatory parameters during weaning.

Variables	PC group (*n*=8)	VC group (*n*=11)	*P*
HR (beats/min)			
At time of weaning	93.25±13.19	86.90±9.64	0.24
30 min later	97.50±13.19	88.36±10.07	0.10
60 min later	99.12±12.84	90.36±9.65	0.19
RR (cycle/min)			
At time of weaning	25.01±2.86	22.37±3.50	0.09
30 min later	26.54±3.76	24.57±2.12	0.23
60 min later	27.72±3.52	25.11±3.42	0.11
VE (l/min)			
At time of weaning	7.44±1.85	9.01±1.71	0.07
30 min later	8.26±1.45	10.13±2.11	**0.03**
60 min later	8.53±0.95	9.94±1.58	**0.02**
VT (l)			
At time of weaning	335.73±32.90	367.87±31.34	**0.04**
30 min later	344.01±49.47	381.50 ±39.15	0.10
60 min later	373.67±37.05	391.25±51.20	0.42
RSBI (breaths/min/l)			
At time of weaning	75.75±16.32	82.18±20.26	0.47
30 min later	66.25±11.84	78.27±21.78	0.17
60 min later	64.37±7.32	74.73±17.51	0.13

Data were expressed in the form of frequency (percentage), mean (SD), median (range). *P* value was significant if less than 0.05. HR, heart rate; PC, pressure control; RR, respiratory rate; RSBI, rapid shallow breathing index; VC, volume control; VE, minute ventilation; V_T, tidal volume.

lower baseline $PaCO_2$ value and higher pH values correlated with the success of ventilation. Both increase in $PaCO_2$ and decrease in pH may represent signs of respiratory pump insufficiency and reduced alveolar ventilation and major causes of weaning failure.

We monitored patients on low tidal volume within 6–4 ml/kg; it was noticed that V_T and V_E were higher in the VC group. During PC, the inspiratory pressure was set to achieve the same V_T. This agrees with many studies who included target tidal volumes of 6 ml/kg of predicted body weight, plateau airway pressures not exceeding 30 cm H_2O, and PEEP at LIP as in the studies by Petrucci and Feo, [23] Kallet *et al.* [24], and Amato *et al.* [25]. The Acute Respiratory Distress Syndrome Network—ARDS Net and the ARMA trial [26]. The ARMA trial [26] reported that the mean V_T was significantly different between both modes and showed reduced incidence of barotrauma and a significantly higher proportion of patients weaned from ventilation were seen in the low tidal volume group. The results showed that 28-day mortality was significantly reduced by the application of a LPS. Hager *et al.* [27] and Dellinger *et al.* [28] postulated that an ultraprotective ventilation strategy based on reduction in VT from 6 to 4 ml/kg and plateau pressure from 30 to 25 cmH_2O may minimize tidal hyperinflation and attenuate pulmonary inflammation and improve the patient outcome. However, mechanical ventilation with ultralow tidal volume and lower plateau pressure may enhance atelectasis in some lung regions that may require PEEP increase to maintain oxygenation.

Regarding P_{Peak} there were no significant differences between both groups. This denotes that both modes should be equally effective and safe. On the other hand, Gupta *et al*. [18] concluded less increase in peak inspiratory pressure in PC. Their results reported that 60 patients of intubated patients on mechanical ventilation were divided into group V, where patients put on VC and group P, where patients put on PC and baseline ventilation parameters were compared between the groups at every 8 hours. During the study they found that there was less increase in peak inspiratory pressure in PC than VC.

Regarding weaning of patients and outcome in both groups, there were no significant differences between the two groups. Seven (46.7%) patients of PC and four (26.7%) patients of VC group failed extubation and died. This was in contrast to the two studies by Gupta *et al*. [18], Meade *et al*. [10], and Esteban *et al*. [14] which reported better outcome and lower mortality in the PC (38%) than in the CV (32%).

Ventilatory -parameters during weaning in successful groups had no significant differences with the exception of higher V_E and V_T in the VC group. These consequences were with Bouachour *et al*. [19] and Hilbert *et al*. [29]; these indices were good predictors of success of weaning in the VC group.

Conclusion

We conclude that both modes are equally effective in improvement of oxygenation in patients of ARDS who were ventilated with LPS, while VC achieved better ventilation, higher pH, and lower PCO_2 than PC. However, it needs strict monitoring of plateau pressure to maintain safety.

Limitations

There is potential limitation in this study. Larger prospective controlled studies are necessary to ensure definite conclusion about the value of VC in patients of ARDS who were ventilated with LPS. We recommend increasing the sample size in next studies that may provide better and reliable evidence on VC mode in ARDS.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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