

# Study on improvement of recruitment maneuvers and extravascular lung water in oxygenation of high altitude acute respiratory distress syndrome

Lijun Lin,<sup>1</sup> Siqing Ma,<sup>2</sup> Yongli Yao,<sup>1</sup>  
Junming Luo,<sup>3</sup> Qingjun Shi,<sup>2</sup>  
Qiang Chen<sup>2</sup>

<sup>1</sup>Department of Endocrinology;

<sup>2</sup>Department of Intensive Care Unit;

<sup>3</sup>Department of Pathology, Qinghai Provincial People's Hospital, Xining, Qinghai, China

## Abstract

To understand the improvement of recruitment maneuvers and extravascular lung water in oxygenation of high altitude acute respiratory distress syndrome, 30 high altitude acute respiratory distress syndrome (HARDS) patients were enrolled in the study from May 2012 to October 2013 from Qinghai Provincial People's Hospital. All the patients received recruitment maneuvers and Pulse Contour Cardiac Output, hemodynamics monitoring including intrathoracic Blood Volume Index; Global End-diastolic Volume Index; Global ejection fraction; Pulmonary Vascular Permeability Index; Extravascular Lung Water Index; Pulse indicates cardiac Index; Stroke Volume Variation; Pulse pressure variation; Maximum pressure to increase speed; Systemic Venous Resistance Index, oxygenation and hemodynamics were determined before and after 72 hours of recruitment maneuvers. The results showed that after treatment with recruitment maneuvers and capacity limitation, PaO<sub>2</sub>/FiO<sub>2</sub> was increased significantly compared with those before treatment [PaO<sub>2</sub>/FiO<sub>2</sub> (mmHg): 124.70±43.37 vs 186.87±41.20, *t*=9.43, *P*<0.001], Intrathoracic Blood Volume Index (ITBVI), Global End-diastolic Volume Index (GEDVI), Pulmonary Vascular Permeability Index (PVPI), Extravascular Lung Water Index (EVLWI), Stroke Volume Variation (SVV) were reduced significantly compared with those before treatment [ITBVI (ml/m<sup>2</sup>): 1031.00±275.88 vs 907.13±242.56, *t*=1.26, *P*=0.041; GEDVI (ml/m<sup>2</sup>): 822.40±143.30 vs 722.83±169.65, *t*=1.75, *P*=0.016; PVPI (ml/kg): 2.71±1.21 vs 1.98±0.65, *t*=2.86, *P*=0.001; EVLWI (ml/kg): 12.30±4.19 vs

8.12±2.94, *t*=8.27, *P*<0.001; SVV (%): 17.30±5.65 vs 10.33±3.47, *t*=9.17, *P*<0.001]. Our results indicated that recruitment maneuvers and capacity limitation have been improved oxygenation in HARDS, extravascular lung water reduced, and lung capillary permeability also improved.

## Introduction

Acute respiratory distress syndrome (ARDS) is a most common life-threatening severe disease, which is a complication of severe trauma, infection, shock, poisoning etc. and caused by a respiratory failure syndrome.<sup>1</sup> The fatality rate is as high as 36% ~ 45%. Lung is a most common target organ.<sup>2</sup> Pathological features are various reasons lead to the capillary endothelial cells and alveolar epithelial cell injury caused by diffuse pulmonary interstitial and alveolar edema. The clinical characterizations are respiratory distress and progressive hypoxemia. The typical histopathological changes are diffuse alveolar damage.<sup>3</sup>

Plateau area as unfavorable factors which increased the difficulty of ARDS in treatment and rescue due to the lack of oxygen.<sup>4</sup> Plateau hypoxia itself involved in the pathogenesis of plateau ARDS, further aggravating the high altitude acute respiratory distress syndrome (HARDS) process as a primary/secondary cause.<sup>5</sup> Increasing Lung water, high permeability and pulmonary edema are the pathophysiological features of HARDS. The degree of pulmonary edema was positively correlated with the prognosis of HARDS.<sup>6</sup> When the pulmonary blood capillary permeability increasing, large amounts of fluid would be leaked into the alveolar space and lead to increased shunt and alveolar collapse which it leads serious air/blood flow ratio and stubborn hypoxemia, therefore, it would be great significance for gas exchange to effectively remove tissue fluid and maintain in alveolar cavity, to keep it the clearance of relatively dry.<sup>7</sup>

In this study, we investigated 30 plateau ARDS patients by using Pulse Contour Cardiac Output (PiCCO) monitor to measure the recruitment maneuvers, the blood vessels outside the lung water guiding fluid management, and dynamic observation of the patient's blood flow and blood oxygenation index. The purpose to understand the relationship between the recruitment maneuvers of liquid management and the clinical value of ARDS on the plateau.

Correspondence: Siqing Ma, Department of Intensive Care Unit, Qinghai Provincial People's Hospital, Xining 810007, Qinghai, China.

E-mail: siqing177@sina.com

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## Materials and Methods

The object of study: We chose HARDS patients admitted in Intensive Medicine of Qinghai Provincial people's Hospital from May 2012 to October 2013. This research is the single-center, prospective study.

The inclusion criteria: i) the age 18 to 80 years old, gender not limited; ii) acute onset; iii) oxygenation index (PaO<sub>2</sub> / FiO<sub>2</sub>) 150 MMHG or less; iv) a chest X-ray shows both lungs were patchy shadow; v) the pulmonary artery pressure, 18 MMHG or less, or no clinical evidence of left atrial pressure increased; vi) family members signed the agreement related to treatment.

The exclusion criteria: i) with chronic heart disease of plateau, congenital heart disease, high blood pressure, chronic emphysema, chronic cor pulmonale, patients with chronic pulmonary hypertension, age greater than 80 adult patients; ii) the cardiac pulmonary edema, large tracts of atelectasis, spontaneous pneumothorax, upper airway obstruction, acute pulmonary embolism; ii) died within 24 hours after

admission patients.

This study has been approved by the Qinghai Provincial People's Hospital Ethics Committee, and selected patients signed informed consent in this study.

The high altitudes HAPE complicated with ARDS diagnosis standard:<sup>8</sup> the ARDS usually occurs in HAPE 24 ~ 48 h after acute onset; the chest X-ray showed well-aerated shadow on both sides; without increased left atrial pressure, pulmonary wedge pressure 18 mmHg or less (1 mmHg = 133.332 kPa); PaO<sub>2</sub> < 60 mmHg, PaCO<sub>2</sub> < 50 mmHg, suggest hypoxic respiratory failure have occurred; the arterial oxygen partial pressure and oxygen fraction (PaO<sub>2</sub> / FiO<sub>2</sub>) is 100 ~ 150 mmHg.

## Methods

The monitoring methods: Using Seldinger indwelling central venous catheter (Arrow company, USA) and PiCCO catheter (Pulsion company, Germany), the blood vessels outside the lung water (EVLW) has been measured. The PiCCO technology is the joint application of pulse contour analysis and thermodilution. On the one hand, the pulse contour analysis continuous cardiac output (CCO), the determination of each stroke volume (SV) and so on need hot dilution method of cardiac output was measured by correction, on the other hand, intrathoracic blood volume (ITBV), extravascular lung water (EVLW) parameters, such as thermodilution method. 15 ml with 0 ~ 4 °C ice saline or 20 ml quickly from inside the central venous catheter injection, PiCCO monitor automatically calculate output monitoring data, measured three times in a row, parameter errors are within 15%, take the average. Continuous observation 0 h, 12 h, 24 h and 36 h, 72 h. And at the same time point line of arterial blood gas analysis to observe the oxygen partial pressure (PO<sub>2</sub>), CO<sub>2</sub> partial pressure (PaCO<sub>2</sub>), blood oxygen saturation (SaO<sub>2</sub>) of calculating oxygenation index

(PaO<sub>2</sub> / FiO<sub>2</sub>). The treatment: Recruitment maneuvers is commonly used method at present including controlling atelectasis (SI), PEEP incremental method (IP) and pressure control (PCV).<sup>3</sup> In the patients with ARDS, it can prevent to produce high pressure control ventilation airway pressure and secondary lung injury. Its advantage is that the pressure is adjustable and can be used for the treatment of patients with windage, timer switch backup. So this research adopts the pressure control (PCV) implementation of recruitment maneuvers.

Using PCV implementation of the recruitment maneuvers: start based ventilation 2 h after the recruitment maneuvers treatment, every time the recruitment maneuvers fully calm; Recruitment maneuvers before dispatch FiO<sub>2</sub> to 1.0, lasts for 5 min, adjust breathing machine to pressure mode (PCV), improve the level of suction pressure and PEEP at the same time, the general high voltage 40 ~ 45 cm H<sub>2</sub>O, PEEP 15 ~ 20 cm H<sub>2</sub>O, lasts 1 ~ 2 min, and then adjust to the regular ventilation mode.<sup>9</sup>

The evaluation of recruitment maneuvers: When oxygen concentration was 100%, PaO<sub>2</sub> higher than 350 ~ 400 MMHG or lung oxygenation index change < 5% after repeated recruitment maneuvers would believe to achieve full of alveoli recruitment maneuvers, and take a line the artery blood gas analysis and calculation of PaO<sub>2</sub> / FiO<sub>2</sub>. If the recruitment maneuvers is invalid at first time, we can through the chest taps, postural drainage, airway in attracting, sputum suction fiberoptic bronchoscope, raising the treatment to improve oxygenation and pulmonary compliance.

Repeat recruitment maneuvers once per 12 hours, continuous 3 days. When the inhaled oxygen concentration was 60%, SpO<sub>2</sub> > 96%, the lung was almost completely open within 3 days, and stop recruitment maneuvers. If patients undergoing recruitment maneuvers occur windage evidence (mainly refer to the X-ray), systolic blood

pressure < 90 MMHG or down 30 MMHG, compared with the original basis of blood pressure and SpO<sub>2</sub> down more than 5%, compared with recruitment maneuvers before and below 0.85, the adjustment of recruitment maneuvers, strict observation.

PEEP after recruitment maneuvers: Initially set PEEP to 20 cm H<sub>2</sub>O, then FiO<sub>2</sub> to reduce to a minimum, maintain SpO<sub>2</sub> 90% ~ 95%, reduce 2 cm H<sub>2</sub>O PEEP every 20 ~ 30 minutes, until the patient SpO<sub>2</sub> fell, the oxygenation of PEEP level before falling is the best PEEP.<sup>2</sup>

Restrictive liquid management: Maintain 3 ml/kg < EVLW < 7 ml/kg, if EVLW ≥ 7 ml/kg, restricting liquid and improve colloid osmotic pressure, diuresis, CRRT treatment, etc.

## Statistical methods

To count all information to (±s), using the SPSS 17.1 software for data analysis, comparison between the two groups using paired sample t test, multiple sets of sample comparison between using single factor analysis of variance, P<0.05 was statistical significant.

## Results

The oxygenation index and PICCO monitor results of 30 cases of H-ARDS patients before and after the recruitment maneuvers (Table 1).

Each time point index before and after treatment of the following characteristics: i) PaO<sub>2</sub>/FiO<sub>2</sub> significantly improved within 12 hours after treatment, There was significant difference compared with before treatment (139.47±57.66 vs 124.70±43.37, P<0.01), in the subsequent treatment, PaO<sub>2</sub> / FiO<sub>2</sub> are improved obviously, respectively: 24 hours (158.23±36.85 vs 124.70±43.37, P<0.01), 48 hours (168.2±33.43 vs 124.70±43.37, P<0.01), at 72 h (186.87±41.20 vs 124.70±43.37, P<0.01), and there is signif-

**Table 1. Schedule recruitment maneuvers Pulse Contour Cardiac Output indexes and oxygenation index before and after contrast (plus or minus, n=30).**

Index	0h	12h	Time 24h	48h	72h	F Value	P Value
PaO <sub>2</sub> /FiO <sub>2</sub> (mmHg)	124.70±43.37	139.47±57.66**	158.23±36.85**	168.2±33.43**	186.87±41.20**	9.43	<0.001
Extravascular Lung Water Index (ml/kg)	12.30±4.19	10.69±2.30*	11.41±2.83	10.06±2.37**	8.12±2.94**	8.27	<0.001
Global End-diastolic Volume Index (ml/m <sup>2</sup> )	822.40±143.30	766.70±162.49	761.70±153.66	736.33±163.01*	722.83±169.65*	1.75	0.016
Intrathoracic Blood Volume Index (ml/m <sup>2</sup> )	1031.00±275.88	974.13±224.98	979.20±199.75	932.13±210.19	907.13±242.56*	1.26	0.041
MAP (mmHg)	94.27±13.38	94.33±15.90	96.37±13.92	98.27±14.07	96.33±14.08	0.61	0.26
CI (L/min.m <sup>2</sup> )	3.99±1.17	4.24±1.21	4.19±1.11	4.08±.88	4.33±.97	0.46	0.223
Pulmonary Vascular Permeability Index (ml/kg)	2.71±1.21	2.31±.73	2.34±.68	2.30±.76	1.98±.65**	2.86	0.001
Stroke Volume Variation (%)	17.30±5.65	15.10±5.74	14.17±5.05*	11.90±4.34**	10.33±3.473**	9.17	<0.001

Note: \*compared with before treatment (P < 0.05), \*\*compared with before treatment (P<0.01).

icant difference before treatment; ii) The PVPI decreased significantly after 72 hours treatment, there was a significant difference compared with before treatment ( $1.98 \pm 0.65$  vs  $2.71 \pm 1.21$ ,  $P < 0.01$ ); iii) The EVLWI reduced gradually after 12 hours treatment, in the after 12 hours, compared with before treatment was  $10.69 \pm 2.30$  vs  $12.30 \pm 4.19$ ,  $P < 0.05$ , 48 hours after treatment compared with before treatment was  $10.06 \pm 2.37$  vs  $12.30 \pm 4.19$ ,  $P < 0.01$ , 72 hours after treatment compared with before treatment was  $8.12 \pm 2.94$  vs  $12.30 \pm 4.19$ ,  $P < 0.01$ , there were significant differences; iv) The GEDVI gradually decreased during the treatment, there is an obvious difference at 48 hours and 72 hours, respectively, at 48 hours group were  $736.33 \pm 163.01$  vs  $822.40 \pm 143.30$ ,  $P < 0.05$ , at 72 hours group were  $722.83 \pm 169.65$  vs  $822.40 \pm 143.30$ ,  $P < 0.05$ ; v) The ITBVI gradually reduced, in 72 hours appear significantly decreased, compared with before treatment was statistically difference ( $907.13 \pm 242.56$  vs  $1031.00 \pm 275.88$ ,  $P < 0.05$ ); vi) The SVV gradually reduced during the treatment, in 24 hours, 48 hours, 72 hours, there is an obvious difference compared with before treatment, respectively were  $14.17 \pm 5.05$  vs  $17.30 \pm 5.65$ ,  $P < 0.05$ ,  $11.90 \pm 4.34$  vs  $17.30 \pm 5.65$ ,  $P < 0.01$ ,  $10.33 \pm 3.473$  vs  $17.30 \pm 5.65$ ,  $P < 0.01$ ; vii) The CI has increased trend during the treatment, significantly increased in 72 hours, but no statistical difference compared with before treatment.

## Discussion and Conclusions

This study confirmed that the  $\text{PaO}_2$  /  $\text{FiO}_2$  obviously increased during the treatment, the possible mechanism is: i) the foundation of ARDS pathophysiological change was alveolar collapse, recruitment maneuvers is within an acceptable airway peak pressure, intermittent give higher pressure, to encourage collapse of alveolir-cruitment maneuvers, improve oxygenation, correct hypoxemia;<sup>10</sup> ii) Recruitment maneuvers can reduce pulmonary capillary pressure, reduce pulmonary interstitial fluid content, promote the absorption of interstitial fluid, thereby reducing blood vessels outside the lung water content, reduce the oxygen diffusion distance, helps improve ARDS lung compliance, correct hypoxemia, improve lung tissue oxygenation state through the capacity management.<sup>11</sup>

Our study confirms that the AECC standard for diagnosis of ARDS, EVLWI can predict the occurrence of ALI ahead of 2 days clinical symptoms.<sup>12</sup> Some scholars proposed to PVPI join the ARDS diagnosis

standard, in order to early diagnosis and guide treatment.<sup>13</sup> Our study, using  $\text{EVLW} \geq 7$  ml/kg as a guidance for or restricting liquid and improve colloid osmotic pressure, dieresis to assess the degree of lung edema, liquid management. CRRT methods such as reducing blood vessels lung water, EVLW had a significant difference within 24 hours and had an obviously significant difference in 48 hours compared before and after treatments;<sup>14</sup> PVPI gradually reduced as there is significant difference in the 72 hours compared before and after treatments. These results indicated that in maintaining the circulation stability, guarantee under the premise of organ perfusion, restrictive fluid management strategy is beneficial in patients with ARDS.<sup>15</sup> Intensive Medical Branch of Chinese Medical Association also recommended that on the premise of guarantee organization organ perfusion restrictive fluid management can help to improve oxygenation and lung injury in patients with ARDS.<sup>16</sup> Our research also got the same result.

ARDS often with severe dysfunction of circulation and respiration at the same time, therefore, to determine reasonable capacity level has important clinical significance. GEDVI and ITBVI is heart volume load index, which can accurately reflect the heart load capacity.<sup>17</sup> In this study, EVLWI provide a measure of the guide liquid treatment which lasts  $3 \text{ ml/kg} < \text{EVLW} < 7 \text{ ml/kg}$ . If  $\text{EVLW} \geq 7 \text{ ml/kg}$  capacity limits, we should do capacity limits. GEDVI has obvious difference before treatment with controlled in 48 hours, ITBVI also has obvious difference before treatment with controlled in 72 hours. This result indicated that actively liquid management had obviously decreased cardiac preload.<sup>18</sup>

SVV can be used to predict liquid treatment, can predict whether through liquid treatment increased cardiac output, studies have shown that SVV 10% or less, treatment capacity is invalid, liquid reactive is poor.<sup>19</sup>

Recruitment maneuvers can increase intrathoracic pressure oppression of the heart, result in higher right atrial pressure, reduce venous return, with the decrease in cardiac output. In this study, CI was no statistical difference before and after therapy, consideration a short time about recruitment maneuvers, implement the pathophysiology changes of the lung quickly disappear, no obvious adverse clinical consequences.<sup>20</sup>

Although this study recruitment maneuvers and protective lung ventilation strategy in HARDS patients with restrictive fluid management can significantly improve the patient's oxygenation function, but for refractory ARDS, can also through the

prone position ventilation,<sup>21</sup> high frequency oscillatory ventilation<sup>22</sup> and inhaled  $\text{NO}$ ,<sup>22</sup> glucocorticoid,<sup>23</sup> extracorporeal life support (extracorporeal membrane oxygenation,  $\text{CO}_2$  removal) in vitro, and other measures to improve the gas exchange, reduce lung injury.<sup>24</sup>

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