

## The Current Care for Acute Respiratory Distress Syndrome

**Kaneyuki Kawamae, Ken Iseki \***

*Department of Emergency Medicine, Yamagata University  
School of Medicine, Yamagata 990-9585, Japan*

*\*Fukushima Medical University, 1 Hikariga-oka, Fukushima City,  
Fukushima Prefecture 960-1295, Japan*

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### **ABSTRACT**

The mortality rate of acute respiratory distress syndrome (ARDS) has been still high. A many kinds of strategies for ARDS are being tried in the world. The important factors which influence for pathological-physiology of ARDS during the mechanical ventilation are gravity consolidation, atelectasis, and ventilator induced lung injury (VILI). VILI is caused by shear stress that is induced by the repeated collapse and recruit of alveolus. Alveolar over-distention caused by large tidal volume also induces VILI. To prevent the VILI, the open lung strategy (The lung protective strategies for ARDS) is recommended. The high positive end expiratory pressure (PEEP) that prevents the shear stress and a small tidal volume are necessary for ARDS treatment.

The concept of the open lung strategy is re-open of alveolus and keeping the recruited alveolus. Recruitment maneuver, preventive therapy by PEEP, and prone positioning are lately proposed in the world. Recruitment maneuver is likely to inspire the gas at the level of vital capacity. Preventive PEEP is useful for the secondary lung injury of sepsis, burn and trauma. Prone position in Intensive Care Unit that is recognized to increase the oxygenation for lung injury patients may improve the mortality of severe ARDS patients.

**Key words :** Acute Respiratory Distress Syndrome, acute lung injury,  
recruitment maneuver, pressure volume curve, prone position

## INTRODUCTION

Diagnosis and treatment of acute respiratory distress syndrome (ARDS) has been an issue for many years<sup>1,3,3)</sup>, and yet it presents new aspects as well. This article will cover the definition of the disease, as well as a description of its causative factors, pathological-physiology, and treatment options. In particular, as an open lung strategy for ARDS has already become known worldwide, other promising strategies such as recruitment maneuver, protective positive end expiratory pressure (PEEP), and prone position methods were mentioned here.

### Definition of ARDS

The American-European Consensus conference for ARDS proposed and improved the definition of ARDS in 1994<sup>4)</sup> and 1998, respectively. ARDS is characterized by: 1) development of acute symptoms, 2) diffuse abnormal shadows on both sides of the lungs in the chest X-ray, 3)  $\text{PaO}_2/\text{FIO}_2$  (P/F ratio) of 200 or less, if P/F ratio is less than 300, it is called acute lung injury (ALI) and 4) no signs of left heart failure. These criteria are recommended for a standard diagnosis.

### Etiology and Epidemiology of ARDS

The definition of ARDS included the P/F ratio 150 or 200 or less, by more than PEEP 5  $\text{cmH}_2\text{O}$ , infiltration on chest X-ray, the mortality rate were ranging from 50 to 65% in 1983 and decreased 37% in 1993<sup>5)</sup>.

However, the mortality rate of ARDS by the new definition is 40 to 60%<sup>6-10)</sup>. The survival rates of ALI and ARDS at 90 days later were 42.2% and 41.1%<sup>11)</sup>, respectively. There is no difference in the prognosis between ARDS and ALI in those rates<sup>11)</sup>. The direct cause of death

was associated deeply with sepsis or the multiple organ failure, rather than lungs itself<sup>7-10)</sup>.

### Causative disease of ARDS

There are various diseases that may lead to the development of ARDS. Sepsis, massive blood transfusion, pneumonia (aspiration, bacterial, viral, pneumocystis carini, etc.), chest trauma, post-cardio-pulmonary resuscitation, external circulation and poison gas inhalation are some of the known causes. However, it is not clear what actually leads to induction of ARDS, because the symptoms of ARDS do not always develop in association with any of these underlying conditions. It is reported that the frequency of the ARDS ranges from 1.5 to 5.6 ARDS patients per 100,000 people per year in Europe and America<sup>10)</sup>. 1.8% of all patients who were treated in ICU had ARDS, according to the Japanese Respiratory Care Association<sup>11)</sup>. Although the mortality rate of ARDS ranges from 50 to 60%, recovery rates have improved recently.

### Patho-physiology of ARDS

#### 1. Pathology of ARDS

After stimulus to the lung originating either from the inside or the outside of lung, inflammatory cells (macrophages, neutrophils, etc.) induce chemical mediators such as cytokines, leukotriens, platelet activating factor, and adhesion molecules. These mediators lead to further inflammatory reactions and increase the permeability of lung capillaries. Therefore, water contents and inflammatory cells migrate from blood vessels to the tissue<sup>12)</sup>. On the other hand, mechanical ventilation as a treatment for ARDS has a bad influence on the lungs (ventilator-induced lung injury)<sup>13)</sup>. Furthermore, gravity consolidation

and atelectasis may occur along with the development of ARDS.

## 2. Gravity consolidation

If a patient in bed continues keeping a fixed posture, the lung compression by superimposed pressure and small airway secretions in the dependent region of the lungs cause a respiratory insufficiency. If the patient is immobilized with muscle relaxants or sedatives, spontaneous breathing will be controlled and the gravity consolidation will continue.

Diffuse change is formed in the dependent lung region when the ARDS patient remains in one position during mechanical ventilation for a long period of time. The extra vascular lung water contents that are produced by increased permeability accumulate in the backside of the lung under the influence of gravity. Unlike

atelectasis of one lung lobe, the abnormal changes associated with gravity consolidation appear to be slight on a chest X-ray. However, the changes are much more notable on a chest X-CT or in chest echography. Consolidation on the chest X-CT (Fig.1) is characterized by a diffuse abnormal shadow in the dependent region, and diagnosis is not difficult. A weakness or rales of the respiratory sound detected at the side of the back by auscultation can yield clues as to the proper diagnosis. Although the bronchus that exists in consolidation is usually not obstructed or kept open, it is frequently influenced by atelectasis, edema, congestion, etc. Without any treatment, infection and organ change will result, and the prognosis will be worsened further.

## 3. Atelectasis



Fig. 1 . Gravity Consolidation (chest X-CT)

The high-density area is seen in the dependent region of lung. There is an intra-alveolar edema without collapse of alveolus, in the high-density area. When the supine position is kept for long period continuously without any movement on the bed, the lung consolidation will be performed on the dorsal region of lung. It is possible to cause lung infection, pulmonary injury, and respiratory failure. It should be prevented by respiratory physical therapy such as the body position change.

Atelectasis has an important influence on the pathological changes associated with ARDS. Two mechanisms for development of atelectasis are involved. One is compression atelectasis (loose atelectasis), which is caused by the physical compression from the outside to the alveolus in the dependent region. The other mechanism is known as absorption atelectasis (sticky atelectasis). These are developed in the small V/Q compartment, primarily in Zone 3, because gas in the alveolus is absorbed by blood continuously. The loose atelectasis can be re-opened by 12-20 cmH<sub>2</sub>O of transmural pressure. The sticky atelectasis that means perfect collapsed, so a pressure higher than 30 cmH<sub>2</sub>O will be needed. Atelectasis phenomena may generate shear stress on the surrounding terminal bronchiolar walls and alveolus resulting in compensatory distension of the remaining normal area, thus amplifying the ventilation-induced lung injury. A primary motivation for developing novel strategies for respiratory care is to devise new ways to prevent atelectasis.

#### 4. Pressure-Volume curve

In order to evaluate morbid lungs, there are methods<sup>14)-17)</sup> to measure the pressure-volume curve. It consists of an inspiration curve and an expiration curve (Fig.2). The inclination of lines will become small if lung compliance falls. In an inspiration curve, if it becomes the unusual lungs of low compliance, two crooked points can be found out. They consist of a lower part and an upper part. The former is called the lower inflection point (LIP), and the later is the upper inflection point (UIP). In terms of the curve by the lung volume and an airway pressure, we can estimate how the lung injured is. In order to perform less stressful ventilation, the level of PEEP should be

selected more than LIP, and the peak inspiratory pressure (PIP) below UIP. If the end of expiration becomes below LIP, opening and closing of alveolus or a peripheral respiratory tract will be repeated resulted in lung tissue injury by shear stress. Moreover, if the PIP exceeds UIP, the over-distension of alveolus will arise and inflammatory substances, such as cytokines, will be induced. It is named bio-trauma that causes baro-trauma.

### The lung protective strategies for ARDS

#### 1. Strategies for ARDS

The lung injury that is induced by mechanical ventilation itself is called "ventilator induced lung injury (VILI)", and it has a bad influence on the prognosis for ARDS. One approach to relieve VILI is the lung protection strategy. VILI is caused by too much extension of the alveolus and by shear stress that is induced by repetitive opening and closing of the alveolus as above. The lung protective strategy attempts to avoid shear stress and over-distention. It involves use of optimal PEEP and small tidal volume.

A recent study<sup>18)</sup> showed a significant difference in mortality (30% vs. 40%) between a lung protective ventilation (LPV) group receiving 6 ml/kg tidal volume and a more conventionally ventilated group of patients receiving 12 ml/kg tidal volume. This study included a large number of patients (n=850). As a result of this study, some recommendations are now suggested for the ventilation of ARDS patients: low tidal volume (5-7ml), relatively high level PEEPe which is the pressure just before closure of the peripheral bronchus or collapse of the alveolus during the expiration from vital capacity, (ideally according to LIP to keep the lungs open), and limitation of the plateau pressure to 35

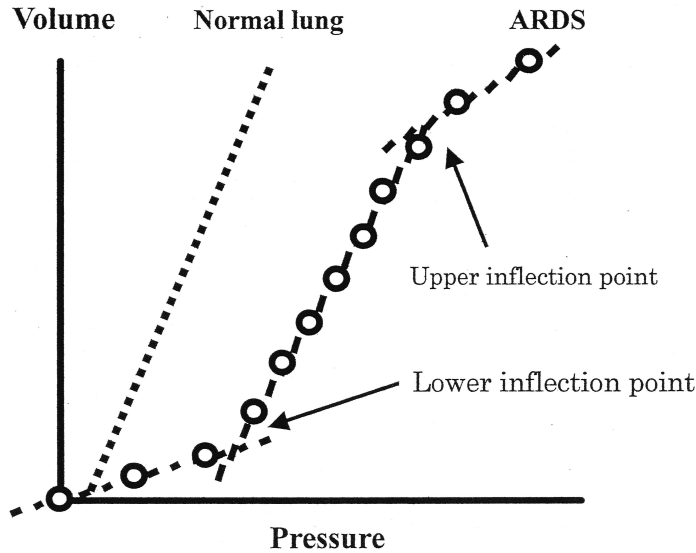


Fig. 2 . Pressure-volume (PV) curve

PV curve shows the static lung compliance. The inclination of lines will become small if lung compliance falls. In an inspiration curve of the unusual lungs with low compliance, two crooked points can be found out. There are a lower part and an upper part, the former is called the lower inflection point (LIP), the latter the upper inflection point (UIP).

mmH<sub>2</sub>O.

## 2. Other strategies for ARDS

### 1) Recruitment maneuver and PEEP<sub>e</sub>

Inflating the lung slowly and keeping the lung volume close to vital capacity (sustained inflation, or SI) can re-open the collapsed alveolus in the lung. PEEP<sub>e</sub> is determined by the LIP at the expiration loop of PV curve. The end expiratory volume at the level of PEEP<sub>e</sub> is higher than that of the LIP of the inspiration loop (Fig.3). To perform SI requires adequate airway pressure and a fixed amount of time to inflate with a deep breath to about the total lung capacity during the ventilation. In clinical studies, inflating pressures of 30-45 cmH<sub>2</sub>O for 20 seconds<sup>19</sup>, 60 cmH<sub>2</sub>O for 30 seconds<sup>20</sup>, or pressure controlled ventilation (PCV) of 20 cmH<sub>2</sub>O peak inspiratory pressure (PIP) for 2 minutes with 40 cmH<sub>2</sub>O PEEP have

been tried<sup>21</sup>. However, these particular procedures are not yet established as treatment methods.

Even if the lung extends to total lung capacity (TLC), the alveolus is still collapsed in ARDS patients. The opening pressure is quite high in patients with severe pneumonia, when it extends to TLC temporarily. The normal compartment of the lung expands to overdistention in this case. Blood flow is redistributed to the low compliance compartment from the normal site, and oxygenation is decreased by serious V/Q mismatches. However, this approach is effective for the lung pathological changes that are seen in early stages of ARDS, such as edema and compression atelectasis. Considering how effective SI is at any stage of ARDS, it is clearly desirable to determine the optimal level of PEEP. This

can be done by decreasing PEEP gradually while checking on oxygen saturation by sensor at finger tip (SpO<sub>2</sub>) after SI.

## 2) Preventive therapy by PEEP

A lung edema having increased permeability was made in mongrel dogs, 0, 5, or 10 cmH<sub>2</sub>O of PEEP was added 1 hour after acid injection, and the extra vascular lung water volume (EVLWV) did not change before and after treatment by PEEP<sup>22)</sup>.

In another similar experiment, Ruiz et al.<sup>23)</sup> made the permeability-increased lung edema models and allocated them to three groups. Animals were ventilated without PEEP (Group A), PEEP of 10 cmH<sub>2</sub>O administered immediately (Group B), or 2 hours (Group C) after oleic acid administration. PaO<sub>2</sub> and the lung water volume 6 hours later showed 467, 180, 39 mmHg and 11, 19 or 25ml/kg,

respectively.

Furthermore, using the same animal model system, Coalminer et al.<sup>24)</sup> also created three groups having tidal volumes of 12, 12 or 6 ml/kg, and PEEP of 0, 10, and 10 cmH<sub>2</sub>O, immediately after injection of an oleic acid, respectively. The amounts of EVLW were 23 and 16 or 10 ml/kg. Adjusting 6 ml/kg of low tidal volume and 10 cmH<sub>2</sub>O of PEEP at an early stage of lung edema decreased the EVLWV. It is concluded that when a lung edema can be predicted following hemorrhagic shock, sepsis, burn, aspiration pneumonia, and so on, respiratory failure may be prevented by an early adjustment to low tidal volume and PEEP, before the oxygenation saturation gets worse.

## 3) Non invasive positive pressure ventilation (NIPPV)

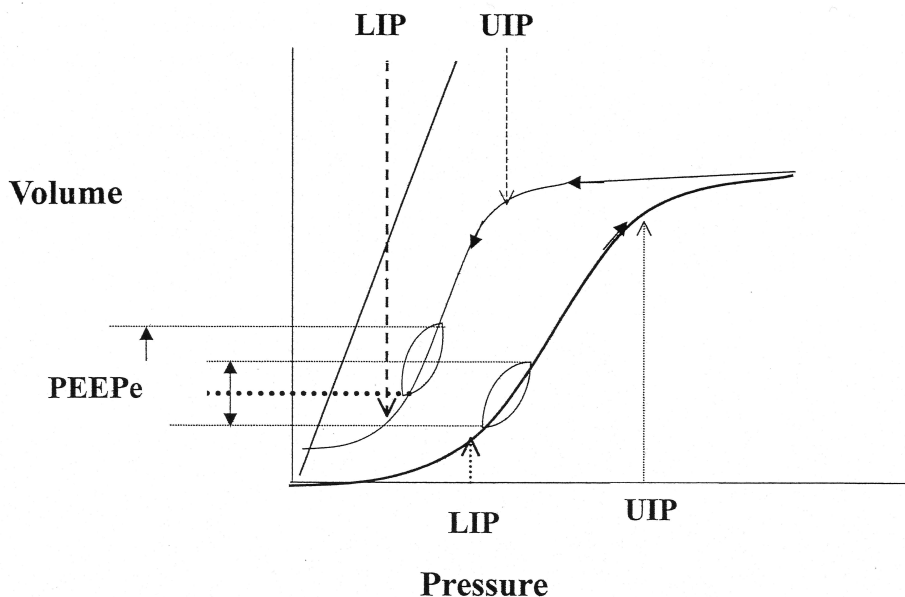


Fig. 3 . PEEPe and PV curve

Keeping the lung volume close to vital capacity can re-open the collapsed alveolus in the lung. The pressure just before closure of the peripheral bronchus or collapse of the alveolus during the expiration from vital capacity is called PEEPe. The end expiratory volume at the level of PEEPe is higher than of the LIP of the inspiration loop.

Non-invasive artificial respiration (non-invasive positive pressure ventilation: NIPPV) is one of the artificial ventilation involved with facemask as interface and pressure support without tracheal intubation. NIPPV was succeeded as a medical treatment for ARDS in recent years<sup>25</sup>. There were less frequently used sedates and few complications, such as pneumonia, ventilator associated pneumonia (VAP), sinusitis, and sepsis. The period of artificial respiration and the days of hospitalization were also short. The severity of respiratory insufficiency of those patients was not serious, since PaO<sub>2</sub> improves within 1 hour after start of an artificial respiration that cause hypercapnea<sup>28</sup> and hypoxia, not few cases who cannot bear the mask ventilation are obliged to intubate the endotracheal tube<sup>29</sup>. It should be investigated further.

#### 4) The prone position

Adjustment to a prone position from a supine position during artificial respiration improves oxygenation in the case of ALI caused by pneumonia, atelectasis, consolidation in the dependent lung and pulmonary edema. In the early stages of lung injury, local edema or atelectasis exists to a limited extent in the dependent lung, and gas contents still remain normal in the non-dependent region. Gas enters into the dependent lung and blood flow is redistributed into the non-dependent region by changing body posture to a prone position. Consequently, the ratio of ventilation / blood-perfusion improves as does oxygenation. On the other hand, the heart presses the left lung when the body is in a supine position<sup>30</sup>. However, the heart is located in the lowest region attached to the sternum in the prone position. The compression by the heart upon the lung is reduced, and compressive

atelectasis can be alleviated. Moreover, improvements result from support of the movable region around the diaphragm. Furthermore, in the prone position, the distance from anterior to posterior of the thorax shortens, and differences in intra-alveolus pressure between anterior and posterior regions are also decreased. This means that the uneven gas distribution in the lung should be improved uniformly. In the supine position, VILI is severer in the dependent region<sup>31</sup>. Switching to a prone position should reduce VILI in the dependent lung and also contribute to prevention of VILI.

Switching to a prone position is effective in the early stage of ARDS. However, it is not so effective in the late stage, when fibrosis is progressing<sup>32</sup>. There is no evidence as to the possible effectiveness of the prone position at this stage, e.g. how long the prone position should be kept, how often it should be performed, and so on.

#### The method and notes

Clinically, the severity of the patient's disease, the effectiveness of prone positioning, the reaction of the circulation to treatment, the period of improvement, the cooperation of the patient, and so on are taken into consideration in determining how frequently the shifts to prone position should be carried out, and how long the patient should be kept in the prone position. Moreover, in order to reduce complications in the circulation, moving the patient to the lateral position once, by a gradual shift from the lateral position rather than moving him or her to the prone position suddenly, is recommended.

#### Complications

Problems that may accompany prone positioning during mechanical ventilation include

hypotension, arrhythmia, accidental extubation, and pulling out of catheters and tubes<sup>33</sup>. The most frequent complication is decubitus. When a patient is conscious, or has a joint contraction, the prone position can induce pain. Therefore pain management is necessary in these circumstances.

Randomized Controlled Trial of the prone position

Gattinoni and his group in Europe reported on "Effect of prone positioning on the survival of patients with acute respiratory failure" in 2001<sup>33</sup>. When patients satisfied the criteria for ARDS, they were allocated to either the prone group (for six hours in a day, and for ten days at most) or to the supine group. No significant differences were noted between the two groups. However, in the subgroup of patients who received a "severe" score, the mortality in the prone group was lower than that in the supine group. Complication rates for the two groups were comparable. Therefore, they suggest that the prone position should be tried for respiratory failure patients.

## CONCLUSION

Significant progress is being made in the development of new strategies to treat ARDS patients.

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## The Current Care for ARDS

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