

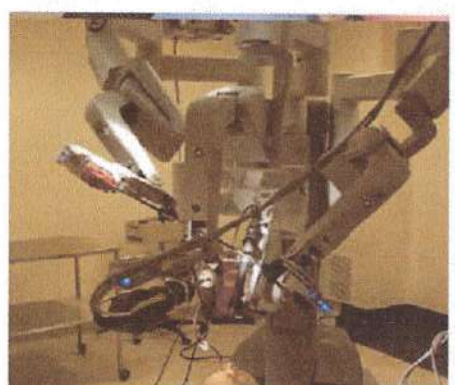
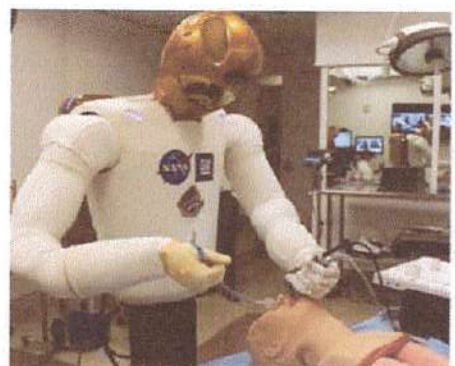
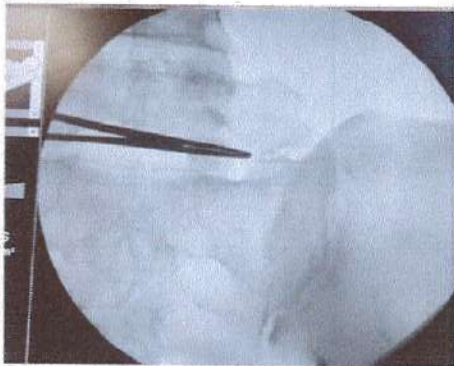
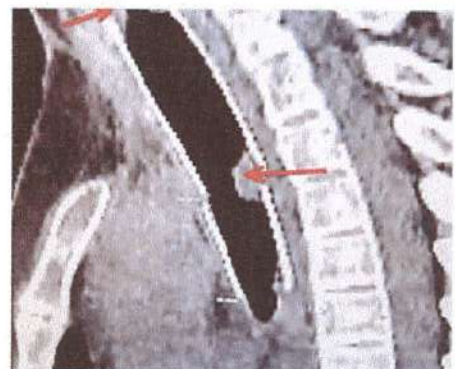
ISSN 1607-8322

ISSN 2220-5799 (Online)



# ANAESTHESIA, PAIN & INTENSIVE CARE

A Bimonthly, International Journal of Anesthesiology,  
Pain Management, Intensive Care & Resuscitation



Vol. 25, No. 3

[www.apicareonline.com](http://www.apicareonline.com)

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May 13, 2021

Dear Bambang Pujo Semedi, Prananda Surya Airlangga, Hanik Badriyah Hidayati, Nancy Margarita Rehatta, Mahmud,

I am pleased to inform you that your manuscript titled as "Lung Recruitment Maneuver: is it really safe?" (Manuscript Number: APIC-2021-04-053 was accepted for publication in the Anaesthesia, Pain & Intensive Care. You could check your possible publication date at your author page. You may login to your author account page, and visit accepted articles section in order to get official/formal acceptance letter as PDF.

I would like to remind that you could send your future manuscripts to Anaesthesia, Pain & Intensive Care.



*My best wishes and kind regards to your family and friends,  
Sincerely yours,  
Tariq H. Khan  
Editor-in-Chief*

## Lung recruitment maneuver: is it really safe?

Bambang Pujo Semedi <sup>1</sup> ✉, Prananda Surya Airlangga <sup>1</sup> ✉, Hanik Badriyah Hidayati <sup>2</sup>,  
Nancy Margarita Rehatta <sup>1,3</sup> ✉, Mahmud <sup>4</sup> ✉

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## Abstract

Mechanical ventilation is an important part of the management of severe respiratory failure. Several methods have been introduced to improve oxygenation, including the lung recruitment maneuvers (LRMs). In patients with acute respiratory distress syndrome (ARDS), LRMs may prevent ventilator-induced lung injury (VILI), improve survival and the benefits of implementing this method on ARDS also have been supported by several studies. Lung recruitment maneuvers (LRMs) is a method to recruit collapsed alveoli by temporarily or gradually increasing the transpulmonary pressure. Although LRM is believed to improve oxygenation, some recent studies have consistently shown that it does not produce benefits as expected. Especially in ARDS, LRMs does not show any real benefit, it may even cause unfavorable effects. Until now, it also was not clear how to differentiate LRM responders from non-responders. Based on available evidence, LRM is not recommended as a routine procedure for ARDS patients.

**Key words:** Mechanical ventilation, ARDS, lung recruitment maneuvers

**Citation:** Semedi BP, Airlangga PS, Hidayati HB, Rehatta NM, Mahmud. Anaesth. pain intensive care 2021;25(3):255–261. DOI: [10.35975/apic.v25i3.1511](https://doi.org/10.35975/apic.v25i3.1511)

**Received:** April 13, 2021; **Reviewed:** April 16, 19, 2021; **Accepted:** May 12, 2021

## 1. Introduction

In the effort to minimize the damage that mechanical ventilation may cause, lung protection strategies have been applied for ARDS patients.<sup>1</sup> LRM is part of an open lung approach (OLA), and adjunct to mechanical ventilation. LRM are a transient, sustained method to reopen collapsed alveoli, through increasing transpulmonary pressure. The main objectives of the LRM as part of lung-protective ventilation is to increase oxygenation.<sup>2</sup> However, their role in routine practice and how they should be performed remain

controversial.<sup>1,3,4</sup> This discussion will focus on the safety aspects of the LRM.

## 2. Lung Recruitment Maneuver

Lung Recruitment Maneuver (LRM) is an intended method of increasing transpulmonary pressure. The main goal is to reopen the alveoli that had previously collapsed. When the alveoli can be opened (recruited), there is an increased surface area for gas exchange, thereby promoting the ventilation's homogenous



distribution.<sup>2</sup> In the end, this mechanism will improve oxygenation.

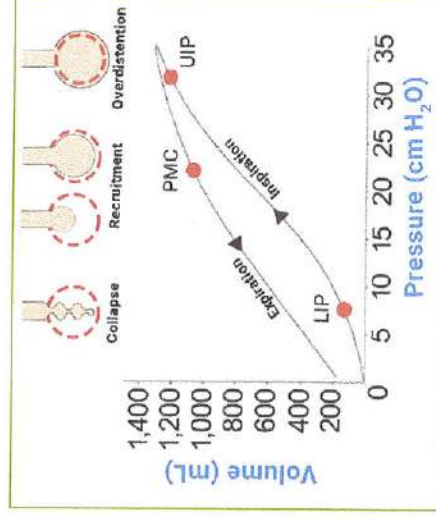
### 2.1. Rationalization of application LRM in mechanically ventilated patients

The main reason for using LRM is de-recruitment in mechanically ventilated patients. De-recruitment may occur because of: low tidal volume (VT); insufficient positive end-expiratory pressure (PEEP); and high  $\text{FiO}_2$  administration (which causes absorption atelectasis). This maneuver aims to open the collapsed alveoli, combined with the use of PEEP to prevent cyclic collapse as part of OLA ventilation. This combination also aims to increase the volume of the final expiratory lung; improve oxygenation, and reduce the risk of Ventilator-Induced Lung Injury (VILI).<sup>2</sup>

During the expiratory process, de-recruitment occurs along the rest of the expiration curve after the point of maximum curvature (PMC). There is no de-recruitment process if the airway pressure level decreases to the expiratory PMC.<sup>2</sup> Therefore, to keep the alveoli from collapsing, PEEP should be adjusted accordingly. It is also necessary to determine what the ideal pressure is, to make the lungs expand (recruitment), which does not harm the patient.

### 2.2. Technical variations in LRM

The development of the variation LRM technique including: using the pressure of 40  $\text{cmH}_2\text{O}$  for 30 seconds, mode of pressure-controlled ventilation (PCV), increase PEEP level to 40  $\text{cmH}_2\text{O}$  for 40 seconds, and set respiratory rate to zero with turn off apnea alarm. During the lung recruitment maneuver process, strict hemodynamic monitoring must be carried out.<sup>5</sup> Another technique is using three consecutive sighs/min with 45  $\text{cmH}_2\text{O}$  plateau pressure; 50  $\text{cmH}_2\text{O}$  peak pressure for 2 minutes, and given PEEP above UIP (in obese or trauma patients may require more than 60–70  $\text{cmH}_2\text{O}$ ). On trauma cases generally occur intra-abdominal compartment syndrome which reduces chest flow compliance. Staircase Recruitment Maneuver (SRM) via the stepped increase in pressure also can be used. Another alternative is a long slow increase until 40  $\text{cmH}_2\text{O}$  (RAMP) in inspiratory pressure.<sup>5</sup> Ventilator mode of Airway Pressure Release Ventilation (APRV) can be considered for recruitment. In comparison, VC-CMV has lower I:E ratio. Conventional ventilation would require a higher PEEP to achieve the same mean lung



**Figure 1:** The lung recruitment maneuver begins when the airway pressure > the lower inflection point (LIP), then continues until it reaches the maximum pressure; in some conditions it may go above the upper inflection point (UIP). After reaching UIP, airway pressure did not significantly increase the lung volume.<sup>2</sup>

(in certain conditions, it gives an unfavourable effect). Conventional ventilation produces a higher end-inspiratory volume to deliver the same tidal volume. Some of these characteristics make APRV have the potential to decrease the risk of injury-related to overdistension.<sup>6</sup>

### 2.3. Procedure after LRM

After the LRM was carried out, the first thing to do was to seek an optimal PEEP. There are several methods to determine the optimal PEEP (the lowest PEEP that produces the best compliance and oxygenation), for example by setting the PEEP at 25  $\text{cmH}_2\text{O}$ , reducing it by 2  $\text{cmH}_2\text{O}$  increments, then checking for compliance and  $\text{SpO}_2$  at each setting. Adverse effects following LRM such as haemodynamic instability and barotrauma, may occur during LRM, so its a need to monitor the patient. Repeat LRM can be performed for subsequent derecruitment. In general, if there is decreased compliance and decreased oxygenation, so that the goal of intervention can also be achieved without repeating LRM, for example by removing the mucus plug through suction or bronchoscopy; proning (changing the position of the patient); and chest physiotherapy.<sup>7</sup> These options are preferable instead of performing a repeat lung recruitment maneuver.



### 3. Point of Concern regarding ventilatory strategies in ARDS

Mechanical ventilation somehow increases the risk of VILI. In comparison, spontaneous breathing results in a larger diaphragm excursion on the dorsal parts. While in patients with mechanical ventilation, excursions are more dominant in the ventral parts. The difference in the vertical pressure gradient during mechanical ventilation has a greater variation, both during inspiration and expiration. At the time of expiration, patients who are mechanically ventilated shows very high transpulmonary pressure, which increases the incidence of VILI. This high pressure also results in a more positive pleural pressure at the lower parts, which promotes the collapse of alveoli.<sup>7</sup>

There is a depiction of the mechanical stress occurring in the lung tissue units during the respiratory cycle. The pulmonary matrix fibers are maintained in distention by local tensile stresses, which further increase with lung expansion during spontaneous inspiration in normal lungs. The parenchyma may be compressed (compressive stress), in mechanically ventilated patients. Compressive stress is an abnormal mechanical condition that triggers macromolecular breakdown and disorganization of the fibrous matrix scaffold, thus leading to VILI. Stress is defined as the force/unit area, which force can be generated by a volume or a pressure. Strain is the change in length in relation to being initial length. If the strain is too large, exceeding the fibre matrix network capacity, it will cause damage that gives rise to VILI. Avoid applying excessive pressure that causes the lung critical volume limit to be exceeded.<sup>8</sup>

Improper use of a ventilator will create new problems. The detrimental effects of mechanical ventilation are grouped into two categories, namely those associated with excessive or non-physiological changes in transpulmonary pressure ( $\Delta P_L$ ); and those associated with excessive or non-physiological variation in pleural pressure changes ( $\Delta P_{pl}$ ). Respiration with too negative pressure ventilation or too positive pressure ventilation is neither good. For example, in a patient with a very high Work of Breathing (WOB) (there are retractions and other signs), it actually creates a very high negative pressure, so that the transpulmonary

pressure is also high which causes damage (patient self-inflicted lung injury). In positive pressure ventilation, for example in patients with mechanical ventilation, if Peak pressure or Plateau pressure is high, it will also increase transpulmonary pressure; both of these mechanisms will cause adverse effects.<sup>8</sup>

#### 3.1. Pathways to ventilator-induced lung injury (VILI)

In mechanically ventilated patients, if there is extreme stress (transpulmonary pressure and microvascular pressure are too high, or the volume is too large), the rupture will occur. The rupture will cause cellular infiltration and inflammation. However, moderate stress also may cause mechano signaling (via integrins, cytoskeleton, ion channel) which triggers the inflammatory cascade and ultimately causes cellular infiltration and inflammation.<sup>9</sup>

The degree of expansion of the pulmonary alveoli affects alveolar and extra-alveolar vessels. Inflation of the alveoli results in capillary compression that is embedded in the wall but will dilate the extra-alveolar microvessels. When the lung volume exceeds the FRC, the pulmonary vascular resistance (PVR) will increase linearly as a function of lung volume.<sup>9</sup>

Tidal volume also has an effect on lung strain. Xie et al stated that the presence of hazardous areas, (such as driving pressure  $>15$  cmH<sub>2</sub>O, low compliance), actually reflects the patient's condition. The higher driving pressure is applied, related to higher lung strain. Worse conditions may occur in patients with lower respiratory system compliance.<sup>10</sup>

Tidal volumes should be adjusted based on individual respiratory strain and compliance. In ARDS patients, respiratory system compliance is closely related to tidal volume, pulmonary strain, and driving pressure. ARDS Lung is small not stiff; the condition is likened to "baby lung". In patients with low respiratory system compliance, increased tidal volume is more at risk of causing lung injury. Thus, it is more rational to target tidal volume based on decreased driving pressure. Using respiratory system compliance can help identify at-risk subjects, and provide assurance of safety at certain levels of pulmonary strain.<sup>10</sup>

The pathophysiology of VILI has initial mechanisms, which subsequently through mechano-transduction lead to a molecular damage response. The physical mechanisms of injury include two main phenomena

which may be overlapping. The overdistension in case of an unnecessarily high PEEP (volutrauma). Atelectrauma caused by the cyclic alveolar collapse and reopening in patients with excessive VT reduction.<sup>11</sup>

Three lung zones are at risk of VILI during tidal ventilation, namely: dependent; intermediate; and least dependent. In a dependent zone, even the PEEP level is high, there is a risk of collapse during tidal ventilation, and high risk for chronic collapse injury. In the intermediate zone there is re-expansion within each respiration and cyclic collapse risk, with high risk for atelectrauma due to shear-induced injury. In the least dependent zone, regions that remain inflated throughout tidal ventilation can be overinflated by VT of >6 mL/kg and Pplat exceeding >30–35 cmH<sub>2</sub>O, then lead to high risk for volutrauma and barotrauma. The use of mechanical ventilation eventually triggers different risk, then induces biotrauma (increases release of cytokine), and contributes to multiorgan failure and mortality risk.<sup>11</sup>

### 3.2. Effectiveness of LRM for ARDS patients

In ARDS patients, there are various lung conditions including: inflated, small airway collapse, alveolar collapse, and consolidation. If there is already a consolidation, it cannot be inflated, regardless of the pressure applied. Meanwhile, the part that experiences alveolar collapse requires high pressure (20–60 cmH<sub>2</sub>O), which is what the lung recruitment maneuver will do. Rationally, the small airway collapse can still be maintained with PEEP during expiration. Whereas in the inflated condition, attention must be taken because of the risk of volutrauma or barotrauma. These conditions make LRM difficult in ARDS patients. Consider chest wall compliance when performing LRM. In ARDS patients, where the problem is in the lungs not on the chest wall, then LRM is at risk of injuring the lung tissue.<sup>8</sup>

A study evaluating the response of Acute Lung Injury (ALI) and ARDS to LRM (by 40 cmH<sub>2</sub>O × 40 seconds), showed an association with the severity of pulmonary edema. Extravascular lung water index (EVLWI) >10 mL/kg indicates a less effective LRM, and is considered contraindicated.<sup>12</sup>

LRM response of ARDS patients can be predicted lung morphology. LRM-induced hyperinflation can be a

serious problem in ARDS characterized by focal pulmonary morphology, and as evidence of a dangerous warning against the use of high intrathoracic pressure in any ARDS patient. LRM can be performed in patients with non-focal ARDS, but should be prevented in patients with loss of focal aeration. Chest radiographs, chest CT scans or pulmonary echography should be considered to assess lung morphology.<sup>13</sup>

A randomized controlled trial study analyze recruitment maneuvers complication in acute lung Injury (ALI), found most common complications are desaturation and hypotension. Most complications occurred within 7 day of study initiation. This study found a significant correlation between the numbers of LRM and the complications or risk of mortality.<sup>14</sup>

A meta-analysis of randomized controlled trials (RCTs) states LRM does not provide a mortality benefit over other lung-protective ventilation (LPV) strategies in adult patients with ARDS. After controlling for illness severity and duration, it shows a significant correlation between the number of LRM and complications. This study does not recommend the routine use of LRM, due to its complications rate (especially in repeated LRM application), and uncertain benefit.<sup>3</sup>

The Alveolar Recruitment for Acute Respiratory Disorder Syndrome trial (ART Trial) found a significant discontinuation rate of LRM (nearly 16%). This phenomenon is mostly due to a decrease in SpO<sub>2</sub> or hypotension during the intervention. This study also found more pneumothorax and barotrauma in the intervention group. Subgroup analysis did not show a benefit in favor of LRM.<sup>4</sup>

A multicenter RCT Phase II, PHARLAP Trial in ARDS patients, analyzed maximal Open Pulmonary Ventilation Recruitment. In patients with moderate-to-severe ARDS, this study concluded that an open lung strategy (maximal RMs and PEEP titration vs conventional pulmonary protective ventilation) did not improve ventilator-free days or mortality rates. The only beneficial effect of this intervention was the reduced success of using rescue therapy for hypoxemia, but it was accompanied by some findings of cardiovascular events.<sup>1</sup>

Nowadays, in COVID-19 pandemic era, a study on lung recruitment of COVID-19 related ARDS, in a

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single center showed the lung condition of patients with SARSCoV-2 related ARDS, could not be properly recruited. The severity and management of COVID-19 patients also vary among regions.<sup>15</sup> LRM may have long been operated mostly to increase oxygenation, which is a good thing. Somehow, possible effects (reduction in VILI), improvement in oxygenation) and negative effect (increase in VILI, hemodynamics impairment) are balanced in LRM's general effect.<sup>16</sup>

#### 4. Conclusion

The evidence related to LRM is still remained conflicting. No studies were showing consistent patient-orientated outcome benefits. It is difficult to determine which patients will benefit from the recruitment maneuvers and which will experience overdistention. Oxygenation benefits found to be only short term significance. Controversies relies on who, when, how often and for how long to perform LRM. Eventually, we dont recommend LRM as a routine procedure. Although in certain case LRM can be useful because it increases oxygenation, and open atelectasis. Further research on the effect of LRM is needed to define the true benefit and to know with certainty under which circumstances LRM should be performed.

#### 5. Conflict of interest

Declared none. No funding was involved.

#### 6. Acknowledgement

The author would like to thank all professors and senior colleagues who have provided input and views on related topic and helped in preparation of this manuscript.

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