

Atelectasis and alveolar recruitment maneuvers in acute lung injury.

Khaled M Abo El eneen, Ayman A Radi, Ahmed A Abd El Aziz and Wael s Abd elwadood

Department of Anesthesia, Faculty of Medicine, Menofya University, Egypt.
waelss@live.com

Abstract: Objective: Review alveolar recruitment maneuvers in acute lung injury. **Study selection:** Systematic reviews that addressed alveolar recruitment maneuvers in acute lung injury. **Data Extraction:** Special search was done at midline with key words (recruitment maneuvers) in the title of papers; extraction was made, including assessment of quality and validity of papers that met with the prior criteria that describe review. **Data synthesis:** The main result of the review. Each study was reviewed independently; obtained data is rebuilt in new language according to the need of the researcher and arranged in topics through the article. **Recent Findings:** If the future of ARDS treatment lies in improvements in the management of multiorgan failure, then the pharmacological approach to treating lung injury may change. For example, reducing pathological fibrosis may be possible when more is understood about the regulation of collagen turnover in the normal and injured lung. This may enhance the repair of the alveolar epithelial cell barrier, the clearance of intra-alveolar exudate, and the normal turnover and function of surfactant. **Conclusions:** Assessing the efficacy of RM on oxygenation only is largely insufficient and the complete evaluation, as for any ventilatory strategy in ARDS, must consider the effects on hemodynamics, lung recruitment, over distension, stress and strain, and biotrauma associated with RM are both at the lung level (VILI) and at the systemic level.

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1. Introduction;

Acute lung injury (ALI) and the acute respiratory distress syndrome (ARDS) describe clinical syndromes of acute respiratory failure with substantial morbidity and mortality. ARDS mortality rate has declined over the last 2 decades. In the 1980s, mortality rates were approximately 64–70%. In the 2002, mortality rates were 29–42 %.(1)

It may be possible to open up or 'recruit' at least some of the collapsed areas by the use of continuous or repetitive application of increased levels of distending alveolar pressure, much higher than that recommended for the ventilation of patients with Acute Lung Injury (ALI). (1)

2. Material and Methods

The guidance published by the Centre for Reviews and Dissemination was used to assess the methodology and outcomes of the studies. This review was reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses statement. An institutional review board and ethics committee approved this study.

Search Strategy

A systematic search was performed of several bibliographical databases to identify relevant reports in any language. These included MEDLINE, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, TRIP database, Clinical

Trials Registry, ISI Web of Knowledge, and Web of Science. Articles electronically published ahead of print were included. The search was performed in the electronic databases from the start of the database up to 2013.

Study Selection

All the studies were independently assessed for inclusion. They were included if they fulfilled the following criteria:

Participants: Patients with acute lung injury

Interventions: Therapeutic modalities including ventilatory and non ventilatory methods of treating patients with ARDs.

Outcomes: Improvement prognosis in patients with ARDs.

If the studies did not fulfill the above criteria, they were excluded. Articles in non-English languages were translated. The article title and abstracts were initially screened and then, the selected articles were read in full and further assessed for eligibility. All references from the eligible articles were reviewed in order to identify additional studies.

Data Extraction

Study quality assessment included whether ethical approval was gained, prospective design, eligibility criteria specified, appropriate controls used, adequate follow-up achieved, and defined outcome measures such as regression of liver cirrhosis and changes in gastric hemodynamics.

Quality Assessment; the quality of all the studies was assessed. Important factors included, prospective study design, attainment of ethical approval, evidence of a power calculation, specified eligibility criteria, appropriate controls, specified outcome measures and adequate follow-up. It was expected that confounding factors would be reported and controlled for and appropriate data analysis made in addition to an explanation of missing data.

Data Synthesis

Because of heterogeneity in postoperative follow-up periods and outcome measures reported, it was not possible to pool the data and perform meta-analysis. Comparisons were made by structured review.

3. Results (Finding)

Improved pharmacological therapies against multiorgan system failure with new methods in lung recruitment are excellent procedures. Over the next decade, the management of patients with acute lung injury may improve with the availability of additional pharmacological agents that specifically target ventilation, gas diffusion, lung perfusion and improved lung recruitment methods.

4. Discussion

Pathophysiology of acute lung injury and atelectasis;

Causes of ALI/ARDS;

Direct causes;

1-Pneumonia.

2-Aspiration of gastric Contents.

3-Severe trauma with multiple transfusions.

4-Pulmonary contusions.

Indirect causes; 5- Sepsis

6-Fat or air emboli 7-Drug overdose or toxic ingestions

8-Near drowning9- Acute pancreatitis

10-Inhalational injury. (2)

A) Pathophysiology Of Increased Permeability Pulmonary Edema; Altered lung fluid balance leading to increased permeability pulmonary edema is a pathophysiological hallmark of ALI/ARDS. Increased permeability edema is caused by an increase in pulmonary capillary permeability resulting in an increase in trans vascular flux of fluid and protein into the lung interstitium. (3)

B) Cellular and Molecular Mechanisms Of Injury;

1-Endothelial Injury;

Widespread injury to and activation of both the lung and systemic endothelium with a resultant increase in permeability and expression of adhesion molecules is characteristic of ALI/ARDS. (4)

2-Epithelial Injury;

Epithelial lesions in the earliest ultra-structural studies of patients dying with ALI/ARDS include a spectrum from cytoplasm swelling, vacuolization, and bleb formation to necrosis and complete denuding of epithelial cells. (5)

3-Neutrophil-Mediated Injury;

Several lines of evidence suggest a critical role for the neutrophil in the pathogenesis of most cases of ALI/ARDS.

Histologic studies of early ALI/ARDS consistently show a marked accumulation of neutrophils in the lung. Pulmonary edema fluid and broncho alveolar lavage fluid from ALI/ARDS patients also have a predominance of neutrophils. Labeled autologous neutrophils when reinfused into patients with ALI/ARDS localize to the lung. (6)

4-Cytokine-Mediated Inflammation and Injury;

Tumor necrosis factor (TNF)-a and IL-1 are early response cytokines that are produced predominantly by monocytes and macrophages in response to a direct or indirect insult to the lung such as endotoxin or other microbial products. Anti-inflammatory cytokines such as IL-10 and IL-11 may also protect against lung injury. (7)

5-Oxidant-Mediated Injury;

Reactive oxygen species may be responsible for much of the cellular damage that occurs in ALI/ARDS. (8)

7-Coagulation Pathway;

A variety of markers of activation of coagulation have been measured in the plasma, bronchoalveolar lavage fluid, or pulmonary edema fluid. (9)

8-Fibrosing Alveolitis;

Following the acute or exudative phase of ALI/ARDS, some patients have an uncomplicated course with rapid resolution. Others progress to fibrotic lung injury. (10)

Basis of pharmacological treatment of acute lung injury.

Anti-Inflammatory Therapy

(I) General Anti-Inflammatory Therapy

1. Glucocorticoids; Steroids act throughout the inflammatory process a recent study using prolonged low dose methylprednisolone showed reduced durations of mechanical ventilation. (11)

2. Statins; In addition to their cholesterol lowering effects statins improve epithelial and endothelial function. (12)

3. Renin-Angiotensin System Modification; Losartan, an AT1R antagonist, may reduce the damage caused by ventilator induced lung injury. (13)

4. Matrix Metalloprotease Modification; The matrix metalloproteases (MMPs) are a group of structurally related enzymes which together are capable

of degrading all the components of the extracellular matrix (ECM). (14)

(II) Inflammatory Signaling Modification;

1. Ketoconazole; Ketoconazole is an imidazole antifungal agent with anti-inflammatory properties.

2. Ibuprofen; Ibuprofen is a non-steroidal anti-inflammatory agent which inhibits cyclo-oxygenase. (15)

3. Complement Inhibition; Complement causes cellular injury *via* the production of the membrane attack complex. (16)

4. Insulin; Insulin has anti-inflammatory effects *via* inhibition of the pro-inflammatory transcription factor NFkB. And by maintaining serum glucose levels between 80 and 110 mg/dL. (17)

5. Immunonutrition; Fish oils, which contain the omega 3 poly unsaturated fatty acids eicosapentaenoic acid (EPA), gamma-linolenic acid (GLA) and docosahexaenoic acid (DHA), can lessen the production of pro-inflammatory arachidonic acid metabolites. (18)

(III) Cellular Response Modification

1. Anti-Adhesion Molecule Therapy; Blockage of CD18, a neutrophil adhesion molecule necessary for diapedesis, reduces the severity of experimental lung injury. (19)

2. Immune Cell Blockade; Pentoxifylline and its derivative lisofylline have various inhibitory effects on immune cell function. (20)

4) Physiological Derangement

(I) Drugs improving Ventilation

1. Surfactant; although the infantile form of ALI/ARDS has been successfully treated with exogenous surfactant, adult studies have been disappointing. (21)

2. Bronchodilators; Inhaled beta-agonists (salbutamol) demonstrated beneficial effects on lung mechanics.

3. Mucolytics; Dornase alfa reduces sputum viscosity and improves sputum clearance. (22)

(II) Drugs improving Gas Diffusion;

1. Limitation of Generation of Alveolar Oedema; Hydrostatic pressure may be manipulated in a number of ways. Fluid intake can be restricted or fluid output increased.

2. Maximizing Clearance of Alveolar Oedema; Beta-agonists up regulate AFC *via* an effect on sodium ion movement.

3. Epithelial Repair; Stem cells have the capacity for limitless self-renewal and differentiation e.g. Hepatocyte growth factor and transforming growth factor (TGF). (23)

(III) Drugs improving Perfusion

1. Vasodilators; Nitric oxide (NO) inhalation and Intravenous prostacyclin in the form of PGE1 has also

been investigated in ARDS.2. Vasoconstrictors; Endothelin 1 is a potent vasoconstrictor. Almitrine is a pulmonary vasoconstrictor. 3. Coagulation; Tissue factor pathway inhibitor (TFPI), factor VIIa, heparin, have beneficial effects. (24)

Ventilatory management of ARDS (Lung recruitment methods)

1) Low Tidal Volume Ventilation;

Low tidal volume ventilation (LTVV) is also referred to as lung protective ventilation. The evidence suggests that LTVV improves mortality. LTVV caused hypercapnic respiratory acidosis in some patients. LTVV can be performed via reduction in tidal volume from 8 to 6 mL/kg IBW and the initial respiratory rate is set to meet the patient's minute. (25)

2) Permissive hypercapnia;

It is a ventilatory strategy that accepts alveolar hypoventilation in order to maintain a low alveolar pressure and minimize the complications of alveolar over distension (e.g., ventilator-associated lung injury). (26)

3) High Peep:

The high PEEP approach is a type of open lung ventilation. The trials found that high PEEP increased oxygenation. Increased applied PEEP cause pulmonary barotraumas or ventilator associated lung injury. (27)

Recent advances of lung recruitment.

1-The Open Lung Concept;

The open lung is one in which there is little or no atelectasis and an optimal gas exchange. Pressure-controlled ventilation is used with a peak pressure of 40– 60 cm H₂O and a ratio of the duration of inspiration to that of expiration of 1:1 to 2:1 (I: E ratio). The lowest pressure is realized when the tidal volume remains stable and the arterial blood gases are constant. Open lung units are more efficient and function at a lower pressure when alveolar radii are larger. The opening pressure is higher when surface tension is elevated. (28)

2-Prone positioning

Prone positioning is a passive means by which lung recruitment can be achieved. This improvement is directly related to the improved ventilation/ perfusion (V/Q) Index associated with prone positioning .demonstrated an improvement in oxygenation. (29)

3-Biological variable ventilation

BVV considers that each breath varies in tidal volume within a range of approximately 2—12 ml/kg. Software drives the ventilator to deliver a random tidal volume, breath to breath, from within prescribed range. This differs from chaotic ventilation as the range and degree of variability is programmed and predetermined. (30)

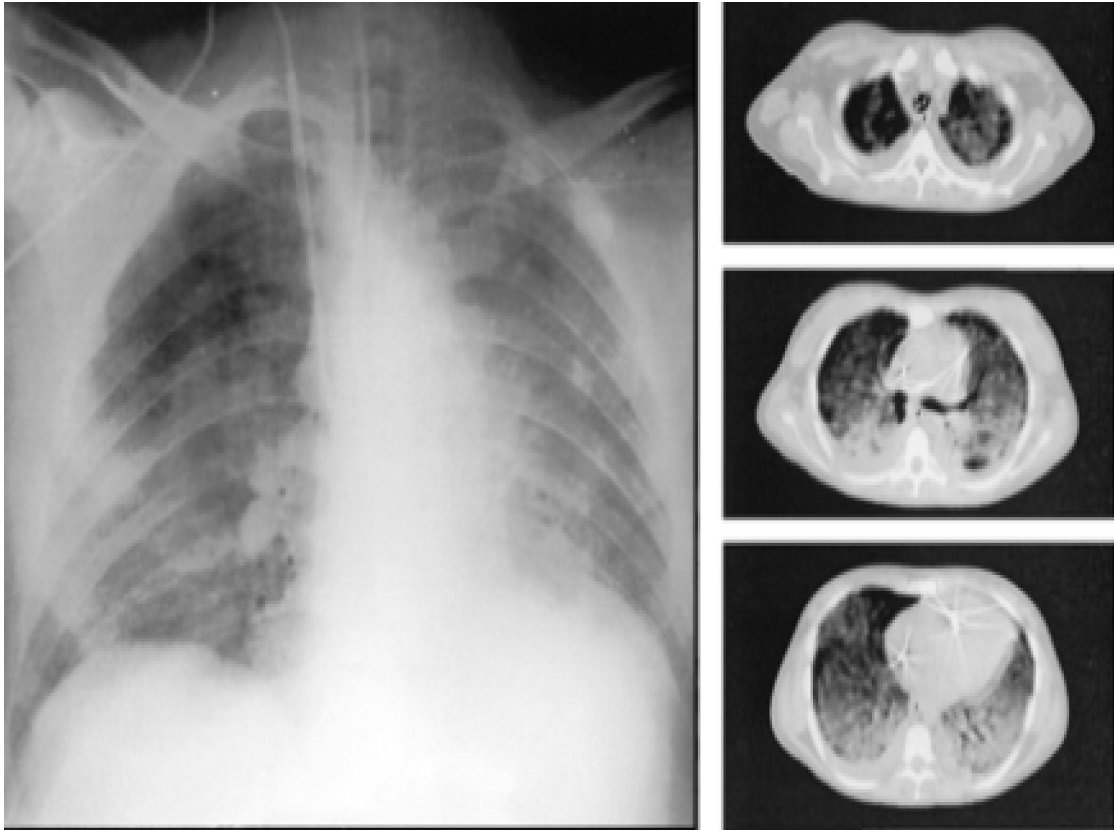


Fig (1) The ARDS ‘baby Lung’

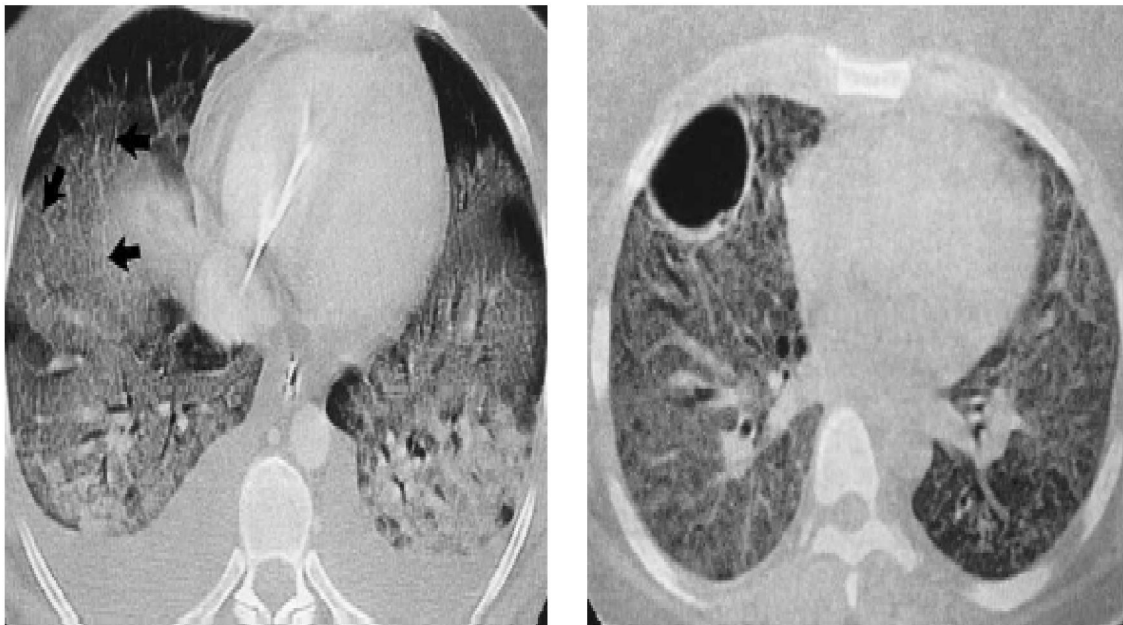


Fig (2) CT scan: ARDS exudative and fibrotic Phases.

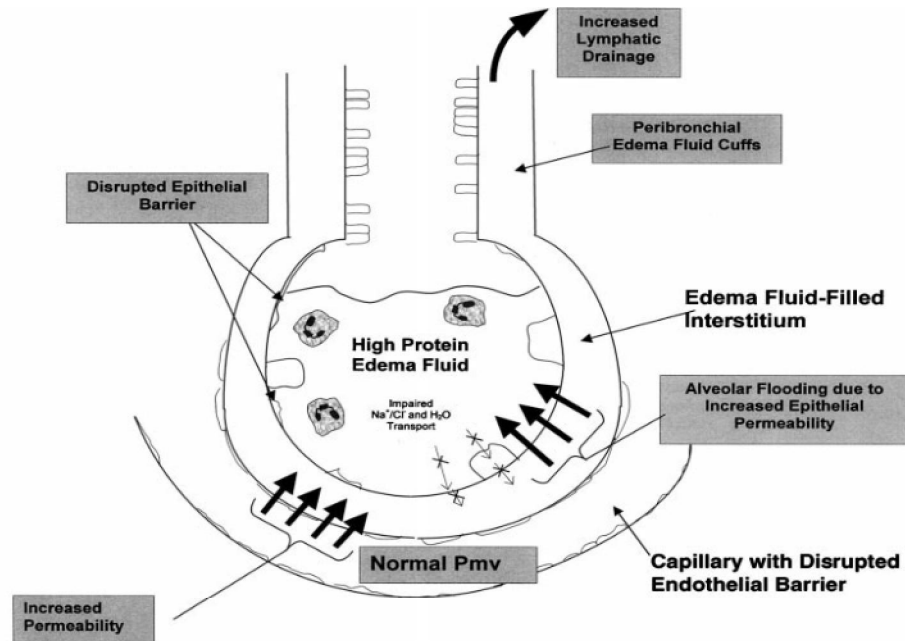


Figure (3) Physiological basis of pulmonary edema in acute lung injury and acute respiratory distress syndrome. Acute lung injury is characterized by an increase in the permeability of the micro vascular membrane resulting in a marked increase in the amount of fluid and protein leaving the vascular space.



Figure (4). Changes in chest x-ray appearance following a recruitment maneuvers.

Recommendations:

According to the evidence derived from this study, we recommend that early control of acute lung injury will lead to more control and less complications of ARDs.

Conclusions:

Despite promising scientific advances, non-ventilatory strategies for ALI/ARDS remain elusive. The best evidence is for minimizing pulmonary oedema *via* fluid restriction when appropriate.

RMs have probably long been used mostly to improve oxygenation, which is a good thing if this improvement results from or is associated with lung recruitment.

However, the global effect of RM is actually a balance between positive effects (reduction in ventilator induced lung injury VILI, improvement in oxygenation) and negative effects (increase in VILI, hemodynamic impairment). From this balance, one can expect favorable or poor outcome of the patient.

Correspondence author:

Name: Wael Saad Abd el wadood M.B.B.Ch*

Resident of Anesthesia El-Bagour Hospital, El Menofya,

Address: El-Bagour, El Menofya.

Email: waelss@live.com**References;**

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