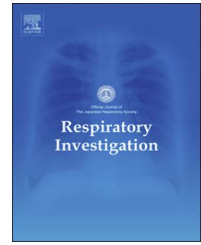




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## Review

# How to approach the acute respiratory distress syndrome: Prevention, plan, and prudence

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## ABSTRACT

The acute respiratory distress syndrome (ARDS) is typically manifested by refractory hypoxemia with high mortality. A correct diagnosis is the first step to achieve better outcomes. An early intervention to manage modifiable risk factors of ARDS development and the avoidance of aggravating factors that increase disease severity and progression should be carefully addressed. A management plan is necessary at an early stage of ARDS to determine the level of intensive care. It should be carefully decided which therapeutic measures should be performed depending on the patient's underlying clinical condition. The clinician's considerate prudence is required in decisions of when to apply intensive measures for an ARDS treatment. Mechanical ventilator support should be carefully used depending on the patient's severity and pathological phase. Decreasing inappropriate alveolar strain through a low tidal volume under optimal positive end-expiratory pressure is key for ventilator support in ARDS. The extracorporeal membrane oxygenation applied in the experienced centers seems to improve the survival of patients with severe ARDS. A constellation of physical and psychological problems can develop or persist for up to 5 years in patients with ARDS. Therefore, an early mobilization with rehabilitation, even during an intensive care unit stay, should be seriously considered whenever feasible. Lastly, prevention of aspiration, stress ulcers, deep vein thrombosis, catheter-related infection, overhydration, and heavy sedation is essential to achieve better outcomes in ARDS.

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## 1. Introduction

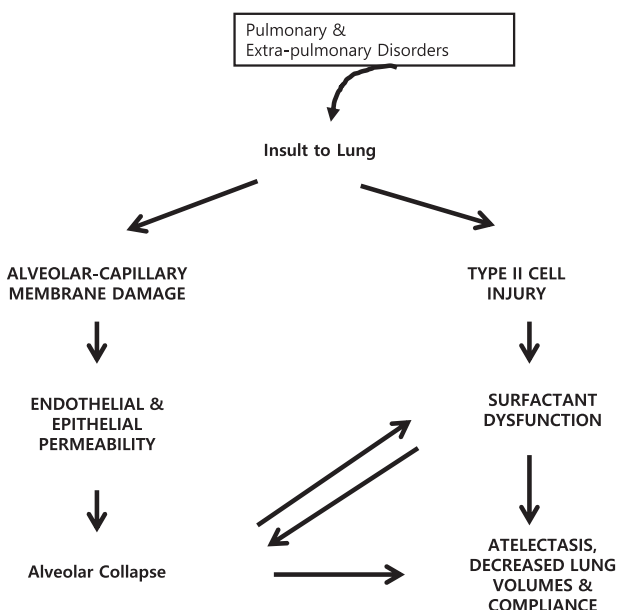
Acute respiratory distress syndrome (ARDS), a form of increased-permeability pulmonary edema, is characterized by refractory hypoxemia together with a severely decreased compliance of the respiratory system caused by diffuse alveolar collapse and flooding (Fig. 1). ARDS is a syndrome and is therefore shaped by various clusters of relevant clinical manifestations. The first report on ARDS in 1967 described its clinical manifestations in a cohort of 272 patients, with 12 patients exhibiting refractory hypoxemia [1]. Recently, a new consensus definition of ARDS, the Berlin definition, has been published [2]. The Berlin definition of ARDS maintains some features of the 1994 definition [3] including diagnostic criteria of timing, chest imaging, origin of edema, and hypoxemia. According to the Berlin definition of ARDS, a minimum level of positive end-expiratory pressure (PEEP) and mutually exclusive  $\text{PaO}_2/\text{FiO}_2$  thresholds can be used to differentiate between the three levels of severity (mild, moderate, severe) of ARDS.

The clinical burden of ARDS in intensive care units (ICUs) has not been lowered since a half century ago. In a large observational study focused on understanding the global impact of severe acute respiratory failure [4] in 29,144 patients admitted to ICUs, 3022 patients (10.4%) fulfilled ARDS criteria, and the mortality rate was higher than 45% in severe ARDS [4]. The high mortality of ARDS is associated with limited efficient therapeutic measures. Although our understanding of ARDS pathophysiology and pathogenesis has improved, the proven beneficial measures are still focused on management with ventilators. To improve the outcome of

ARDS under limited efficient therapeutic measures, preventive strategies for at-risk patients, proper management plans set in advance, and prudence in performing known efficient measures in ICUs are crucial.

## 2. Prevention

Identification of at-risk patients is the first step to avoid secondary hits, which refers to any triggers that potentiate the pathogenesis of ARDS. The primary attacks are a result of a direct lung injury, such as pneumonia, or extra-pulmonary conditions, such as sepsis. Potential secondary hits include injurious mechanical ventilation [5], multiple blood product transfusions [6], too much positive fluid balance, hospital-acquired infections (ventilator-associated pneumonia), shock, and gastric aspiration. Careful selection of patients with acute hypoxemia to receive high-flow nasal oxygen therapy [7] or non-invasive positive pressure ventilation [8] is one way to avoid intubation-related complications. Thus, a correct diagnosis of ARDS is important to initiate proper management earlier. Many cases were not diagnosed as ARDS, although there was diffuse alveolar damage in the autopsied lungs [9]. Clinical manifestations mimicking ARDS, such as diffuse alveolar hemorrhage, bilateral severe pneumonia without combined permeability edema, or immunologic lung disorders, should be discriminated from ARDS. It is well known that there is a latent period that may last up to 7 days, during which a primary attack may cause ARDS. In the LUNG SAFE study, 79% of patients with ARDS developed it in the first 48 h [8]. Major predisposing factors to develop ARDS were more frequently observed when admitted to the ICU compared to when admitted to a hospital [10]. These findings suggest that there is a window of time to prevent the development of ARDS by preventing second hits or predisposing factors in at-risk patients. To enhance the identification of at-risk patients, a clinical prediction tool, such as the lung injury prediction score (LIPS) [11,12] can be used. The LIPS was formulated using routinely available clinical data and identifies patients at high risk for ARDS early in the course of their illness (Table 1). A LIPS greater  $\geq 4$  was associated with the development of ARDS (odds ratio, 4.17; 95% confidence interval, 2.26–7.72) in a retrospective study [12].



**Fig. 1 – Pathophysiology of acute respiratory distress syndrome.**

## 3. Plan

With recent advancements in intensive care, many patients with ARDS do not die due to oxygenation failure but due to multi-organ failures. The underlying causes of ARDS and combined comorbidities are quite diverse in determining the outcomes of patients with ARDS. The attending physician should prepare a management plan after multiple discussions with relevant caregivers and the patient regarding the major therapeutic options available at earlier stages of ARDS. The plan should include the extent of treatment measures

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