

Improvements in the definition of acute respiratory distress syndrome

Editorial

Acute respiratory distress syndrome (ARDS) is a life-threatening organ failure with impairment of pulmonary gas exchange due to several pulmonary and extra-pulmonary injuries. Patients with ARDS have refractory hypoxemia, dyspnea and non-cardiogenic pulmonary edema, generally requiring invasive mechanical ventilation, and acute rescue and supportive therapies. Acute respiratory distress syndrome (ARDS) was first described in 1967.¹ ARDS was described as “Respiratory distress syndrome” in the past, and it was clinically characterized by the acute onset of severe dyspnea, tachypnea, cyanosis refractory to oxygen, loss of compliance, and infiltration on the chest radiographs.

In 1994, The American-European Consensus Conference (AECC) definition of ARDS defined ARDS by the presence of the following four criteria: 1-acute onset; 2- hypoxemia, as indicated by the ratio of partial pressure of arterial oxygen to fraction of inspired oxygen [$\text{PaO}_2/\text{FiO}_2$] ≤ 200 mmHg; 3-bilateral infiltrates on frontal chest radiograph; 4-absence of left atrial hypertension. ARDS was considered the more severe form of Acute Lung Injury (ALI), defined by the same criteria, but with less severe hypoxemia ($\text{PaO}_2/\text{FiO}_2 \leq 300$ mmHg).²

After that, the Berlin definition of ARDS was declared in 2012. According to the Berlin definition, ARDS is a form of acute diffuse lung injury occurring in patients with a pre-disposing risk factor, meeting the following criteria: 1-onset within 1 week of a known clinical insult or new/worsening respiratory symptoms; 2-presence of bilateral opacities on the chest radiographs, not fully explained by effusions, lobar/lung collapse, or nodules; 3-diagnosis of respiratory failure not fully explained by cardiac failure or fluid overload, with the need for objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor is present; 4-presence of hypoxemia, defined by $\text{PaO}_2/\text{FiO}_2$ measured with a minimum requirement for PEEP of ≥ 5 cmH₂O (or non-invasive continuous positive airway pressure ≥ 5 cmH₂O for mild ARDS) and identifying three mutually exclusive categories of severity: mild with $200 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 \leq 300$ mmHg, moderate with $100 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 \leq 200$ mmHg, severe with $\text{PaO}_2/\text{FiO}_2 \leq 100$ mmHg.^{3,4}

Lorenzo Del Sorbo et al.,⁵ reported that several important issues were addressed in the Berlin definition of ARDS in an editorial. The often misused term ALI was removed. A specific timing of onset was defined. The need for a predisposing risk factor was incorporated. The exclusion criterion based on the presence of hydrostatic edema was redefined. The radiological criteria were reformulated. The requirement of a minimum PEEP to establish the severity of hypoxemia according to $\text{PaO}_2/\text{FiO}_2$ was introduced. Moreover, the three mutually exclusive categories of mild, moderate, and severe ARDS were validated, as they were associated with increasingly severe disease using mortality, ventilator-free days, and the duration of mechanical ventilation as outcomes in survivors.

Biomarkers in the acute respiratory distress syndrome have been investigated in many studies. But, there are no biomarkers of ARDS

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in use in clinical practice. In the future, considering technologic advances, pulmonary and extra-pulmonary causes of ARDS a specific biomarker related to ARDS may be established. Furthermore an ARDS Severity Score (ASS) may be described by an international ARDS council (Table 1).

Table 1 Improvements in the definition of ARDS

Year	Definition	What is New?
1967	First described	Respiratory distress syndrome
1994	AECC	ARDS was considered the more severe form of ALI, ARDS was $\text{PaO}_2/\text{FiO}_2 \leq 200$ mmHg ALI was removed, identifying three categories of severity: mild with $200 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 \leq 300$ mmHg, moderate with $100 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 \leq 200$ mmHg, severe with $\text{PaO}_2/\text{FiO}_2 \leq 100$ mmHg
2012	Berlin	
In the future	International ARDS Consul?	ARDS specific marker? (ASM) ARDS Severity Score? (ASS)

Ventilator setting is very controversial topic in the management of ARDS patients. Low tidal volume (VT) ventilation (6 ml/kg predicted body weight, PBW) reduces 28-day and total hospital mortality, but PBW-based VT ignores the lung volume actually available for ventilation. Whether pressure-controlled ventilation (PCV) can reduce ventilator-associated lung injury compared to volume-controlled (VCV) ventilation is a matter of debate. Airway pressure release ventilation provides a potential recruitment by increased airway pressure and allows spontaneous breathing, with some potential benefits (decreased sedation, shorter mechanical ventilation, and improvement in cardiac performance). High frequency oscillatory ventilation delivers very small tidal volumes, to prevent volutrauma, at a constant (relatively high) mean airway pressure. Despite their theoretical benefits, the clinical evidence of both techniques remains unproven and controversial for ARDS patients.⁶

The management of ARDS includes treatment of underlying causes, standard protective ventilation strategies, rescue and supportive therapies. Protective ventilation strategies are controlled oxygenation (aiming to avoid both hypoxia and hyperoxia), low tidal volumes (6 mL/kg of PBW), tolerance of higher PaCO_2 than has been

traditionally accepted (aggressive hypocapnia (PaCO₂ 25–30 mmHg) may lead to secondary cerebral ischemia), moderate PEEP (use PEEP >10 mmHg only if clinical required). Administration of rescue and supportive therapies such prone positioning, neuromuscular blockade (severe ARDS), adequate sedation strategy (score guided), infection control, extracorporeal CO₂ removal, ECMO, conservative fluid management (negative fluid balance), continuous high-volume hemofiltration may be decided in some specific cases.

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Conflicts of interest

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