Recent Advances in the Management of the Acute Respiratory Distress Syndrome

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KEYWORDS

• ARDS • ALI • Epidemiology • Advances • Management • PEEP • Driving pressure
• Mechanical ventilation

KEY POINTS

- Low tidal volume ventilation (6 mL/kg predicted body weight) with limits on plateau pressure is the standard of care for patients with acute respiratory distress syndrome.
- A fluid conservative strategy decreases ventilator days and intensive care unit length of stay.
- The best approach to the titration of positive end-expiratory pressure has not been determined, but a strategy that minimizes driving pressure is promising.
- Recent clinical trials strongly support the use of neuromuscular blockers and prone positioning for severe and refractory hypoxemia.
- A focus on acute respiratory distress syndrome risk factor reduction and the development of tools predicting progression to acute respiratory distress syndrome have the potential to further reduce the incidence, morbidity, and mortality of this syndrome.

INTRODUCTION

The acute respiratory distress syndrome (ARDS) has been the subject of intense research efforts since it was first described in 1967.[1] The understanding of ARDS benefitted greatly from the development of a consensus definition in 1994 that allowed investigators to more consistently identify the syndrome.[2] As a result of subsequent study, the understanding and management of ARDS has improved. Standard of care has changed, and outcomes are better. This review highlights the new definition and epidemiology of the syndrome, key advances in management, areas of continued uncertainty, and future directions.

DEFINITIONS AND EPIDEMIOLOGY

The American-European Consensus Conference (AECC) defined ARDS in 1994 as the acute onset of hypoxemia (partial pressure of oxygen, arterial [Pa_{O_2}]/fraction of inspired oxygen [F_{IO_2}] $\leq$200 mm Hg) with new bilateral infiltrates in the setting of either a normal pulmonary arterial wedge pressure (PAWP $\leq$18 mm Hg) or the absence of suspected of left atrial hypertension when PAWP was not available.[2] In the setting of less severe hypoxemia (Pa_{O_2}/F_{IO_2} $\leq$300 mm Hg), the term *acute lung injury* (ALI) was applied. Although these definitions have provided an important mechanism to identify patients with ALI and ARDS for both management and research purposes, several limitations have been appreciated. For example, "acute" was not well defined, although most clinical trials of patients with ALI and ARDS have limited enrollment to patients meeting the other criteria for less than 72 hours. Further, in some patients, the magnitude of the Pa_{O_2}/F_{IO_2} ratio (P/F ratio) changes with the application of positive end-expiratory pressure (PEEP).[3] In addition, the presence of new bilateral infiltrates on chest radiographs was not

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consistently appreciated by providers (poor inter-observer reliability). Lastly, the distinction of non-hydrostatic versus hydrostatic pulmonary edema was not well appreciated. As a result, the definition of ALI and ARDS was refined in 2012 (Table 1).[4]

The extent to which the new definition will improve the identification or study of patients with ARDS is not yet clear. However, it does provide a more precise definition of "acute," gives a more granular description of severity, and provides better guidance in assessing those patients with components of both hydrostatic and nonhydrostatic pulmonary edema. In the remainder of this review, the acronym *ARDS* will include patients with ALI and ARDS unless otherwise stated. This is consistent with the new definition.

Incidence and Outcomes

Because the Berlin Definition is new, there are few epidemiologic data based on its criteria. Estimates of incidence and outcomes are, therefore, predominantly limited to data from studies relying on the AECC criteria, some of which are now 10 years old. In one such study of 1113 ARDS patients undergoing mechanical ventilation in King County, Washington, the overall incidence was estimated at 79 cases per 100,000 person-years. Hospital mortality rate was 38.5% (42.2% among the subgroup of 828 patients with ARDS).[5] Of note, incidence and mortality increased with age. For patients 15 to 19 years old, incidence was 16 per 100,000 person-years, whereas the incidence for patients 75 to 84 years old 306 per 100,000 person-years. Mortality rates in these age groups increased from 24% to 60%, respectively. Based on these data, it was estimated that there were 190,600 new cases of ARDS in the United States each year with a case fatality rate of 39% (74,500 deaths), and 3.6 million associated hospital days.

In another population-based cohort, the incidence of ARDS based on the AECC definition decreased from 82 to 39 cases per 100,000 person-years between 2001 and 2008 (Fig. 1).[6] Of note, this decrease was attributed to ARDS acquired after hospitalization and may be the result of changes in clinical practice intended to decreased ARDS risk factors. These changes included the use of lung protective ventilatory strategies, efforts to limit blood product exposure, and improved protocols for the management of sepsis and pneumonia.

Two studies compared the performance of the AECC and Berlin Definition for ARDS.[7,8] In a 6-month observational study of patients admitted to 10 intensive care units (ICUs) in France undergoing noninvasive ventilation (NIV) or invasive mechanical ventilation, 278 of 3504 patients fulfilled the AECC criteria.[7] Of these, 18 would not have been identified by the Berlin Definition because PEEP was less than 5 cm H_2O, and another 20 would not have fit into a category because the P/F ratio was $\leq$200 while receiving support from NIV (Note: Berlin Definition does not categorize patients on NIV and P/F $\leq$200). Of the 240 patients meeting criteria for ARDS by the Berlin Definition,

Table 1
Limitations of AECC criteria for ARDS and solution proposed by the Berlin definition for ARDS

	AECC Limitations	Berlin Solution
Timing of onset	• Acute not defined	• $\leq$7 d of known risk factor or new or worsening symptoms
P/F ratio & pressure	• P/F $\leq$300 • Irrespective of PEEP[a]	• P/F $\leq$300 on PEEP or Continuous positive airway pressure[b] $\geq$of 5 cm H_2O
Severity	• ALI if P/F $\leq$300 • ARDS if P/F $\leq$200	• Mild ARDS: P/F $\leq$300[b] • Moderate ARDS: P/F $\leq$200 • Severe ARDS: P/F $\leq$100
Chest radiograph	• Inconsistent interpretation	• Specific chest radiograph criteria defined[c] • Example chest radiograph produced
PAWP	• PAWP $\leq$18 mm Hg *or* • No suspicion of left atrial hypertension	• PAWP requirement removed • Hydrostatic edema cannot be primary cause of respiratory failure
Risk factor	• None defined	• Risk factor needs to be present • If risk factor not clear, hydrostatic edema must be ruled out

[a] Intubation and mechanical ventilation not required.
[b] Continuous positive airway pressure may be delivered by noninvasive means, but limits severity to mild ARDS.
[c] Criteria may be met on computed tomography as well as chest radiograph.