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Anaesthesia & Critical Care Medicine Journal
ISSN: 2577-4301

Current Improvements to the Acute Respiratory Distress Syndrome Definition

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Mini Review

Volume 10 Issue 1

Received Date: December 23, 2024

Published Date: January 10, 2025

DOI: 10.23880/accmj-16000246

Abstract

ARDS was first described with cases in 1967 and it became a broad agenda with 4 basic criteria determined at the American-European Consensus conference in 1994, and then it reached its peak with the Berlin Definition in 2012, with effects that continue to this day. However, later on, the definition was moved to a better level with objections to the Berlin definition and remarkable new recommendations. However, remarkable new recommendations after Berlin brought its definition to a better level. An attempt was made to better define it with many biomarkers in blood and broncho alveolar lavage. It was recommended to define ARDS Specific Marker (ASM) and ARDS Severity Score (ASS), which could help determine its severity and mortality. Although there is no definitive treatment, many recommendations have been made for its management. Low tidal volume ventilation, prone position and High-Flow Nasal Oxygen (HFNO) application to non-intube patients have remained important in management over a long period of time. PEEP titration, negative fluid balance, non-invasive ventilation, use of muscle relaxants and Extracorporeal Membrane Oxygenation (ECMO) applications were also discussed on a patient-by-patient basis. Despite improvements in definition and management, the mortality rate of it still remains high. There continues to be a need for new studies and methods regarding the definition and management of ARDS.

Keywords: ARDS; Berlin Definition; Management

Abbreviations

ARDS: Acute Respiratory Distress Syndrome; ASM: ARDS Specific Marker; ASS: ARDS Severity Score; HFNO: High-Flow Nasal Oxygen; ECMO: Extracorporeal Membrane Oxygenation; TRALI: Transfusion-Related Acute Lung Injury.

Introduction

Acute Respiratory Distress Syndrome (ARDS) follows a process that is always updated, with its definition and treatment changing and evolving throughout history. Since 1967, when it was first described as a respiratory distress syndrome [1], there have been significant advances internationally regarding its name, diagnosis and treatment recommendations. ARDS, defined by 4 criteria determined at the American-European Consensus Conference in 1994 [2], and the Berlin definition, later declared in 2012 [3], constitute important milestones. As a result of these processes, it was understood that ARDS is accompanied by acute, diffuse inflammatory lung injury leading to increased pulmonary permeability, nonhydrostatic edema causing loss of aerated lung tissue, increased physiological dead distance, increased lung weight, and decreased lung compliance.

The causes of ARDS were divided into two groups: pulmonary and extra-pulmonary. Pulmonary causes include pneumonia, aspiration of gastric contents, toxic inhalational

injury, near drowning and pulmonary contusion. Extra pulmonary causes include sepsis from non-pulmonary source, trauma or burn injury, pancreatitis, drug overdose, transfusion of blood products (transfusion-related acute lung injury [TRALI]), cardiopulmonary bypass, reperfusion edema after lung transplantation or embolectomy [2,4].

Recommendations to Berlin Definition

A number of limitations were reported regarding the Berlin definition criteria of ARDS and some recommendations were made. We can list some of them as follows:

- It was requested to remove the PEEP requirement, which is involved in determining the degree of hypoxemia, and thus to pave the way for diagnosing patients without positive pressure ventilation.
- It was recommended to use the noninvasive SpO2/FiO2 ratio instead of PaO2/FiO2, which requires arterial blood gas testing, and to use SpO2/FiO2≤315 with SpO2≤97% to determine hypoxemia.
- It has been suggested to add lung ultrasound as an imaging modality to identify bilateral opacities in the lung.
- Especially during the COVID 19 pandemic, the use of high-flow nasal oxygen (HFNO) in hypoxemic respiratory failure has become very common. It was suggested to allow HFNO with a minimum flow rate of 30 L/min [5,6].

ARDS Specific Marker (ASM) and ARDS Severity Score (ASS)

Many biomarkers have been measured in different parts of the body, such as blood and bronchoalveolar lavage fluid, in defining ARDS and determining the risk. Soluble receptor for advanced glycation end products (sRAGE) is an intermediate in sepsis-induced ARDS and is a marker of lung epithelial injury. Surfactant protein-D (SP-D) is also a marker of lung epithelial injury and is synthesized in alveolar type 2 cells and non-ciliated bronchiolar epithelium, involved in lung inflammation. Soluble intercellular adhesion molecule-1(sICAM-1) is a marker of both lung epithelial and endothelial injury [7]. Biomarkers may help understand the histopathology of ARDS and may also provide insight into the course, severity and mortality of the disease. In an editorial article, Eroglu A [8] noted that an ARDS specific marker (ASM) and ARDS Severity Score (ASS) may be defined by the International ARDS council to be established in the future.

Recommendation of the Management of ARDS

Recommendations on intensive care management of ARDS show a significant change and progress over the historical process. Low tidal volume ventilation (LTV), i.e. 6 mL/kg and 30 cmH20≥ plateau pressure, has been recommended as protective ventilation in ARDS instead of traditional ventilation [9]. Higher PEEP application and lower PEEP application were compared and it was suggested that patients could be managed with higher or lower PEEP by titrating PEEP to FiO_2 [10]. Two fluid management strategies were investigated in ALI and, while no difference in mortality was found, it was suggested that negative fluid balance may be beneficial in patients after initial resuscitation [11]. The use of neuromuscular blockers in the early stages of ARDS is prioritized in the prone position and may also be beneficial in the early stages in severe ARDS cases [12]. In severe ARDS, if PaO_2/FiO_2 is <150, prone position for 16≥ h/day is recommended [13]. High-Flow Nasal Oxygen (HFNO) through nasal cannula is recommended for non-intubated ARDS patients with hypoxemic respiratory failure [14]. It has been reported in two separate studies that non-invasive mechanical ventilation and HFNO applications have no difference compared to standard oxygen therapy in immunocompromised patients in terms of 28-day mortality and clinical outcomes [15,16]. Extracorporeal Membrane Oxygenation (ECMO) remains a lifesaving option in very refractory ARDS cases [17]. High-flow nasal oxygen alone and HFNO additional non-invasive ventilation groups were compared in immunocompromised patients with acute respiratory failure, and it was stated that 28-day mortality and clinical outcomes were not different [18]. Today, the mortality rate of ARDS remains high. For this reason, there is still a need for new studies and methods to reduce mortality in the management of ARDS.

Year	Criteria	What is new?
1967-First described [1]		Respiratory distress syndrome in adult cases
1994-The American-European Consensus Conference (AECC) [2]	Four criteria. ARDS was considered the more severe form of Acute Lung Injury (ALI).	1. Acute onset 2. Hypoxemia, PaO2/FiO2≤200 3. Bilateral infiltrates on frontal chest radiograph 4. Absence of left atrial hypertension.

2012-Berlin Definition [3]	Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
	Chest imaging	Bilateral opacities that are not fully explained by effusions, lobar/ lung collapse, or nodules
	Origin of edema	Respiratory failure not fully explained by cardiac failure or fluid overload
	Hypoxemia Mild	200 mm Hg < PaO2/FiO2≥ 300 mm Hg with PEEP or CPAP≥ 5 cmH2O
	Hypoxemia Moderate	100 mm Hg < PaO2/FiO2≤ 200 mm Hg with PEEP≥5 cmH2O
	Hypoxemia Severe	PaO2/FiO2≤ 100 mm Hg with PEEP≥5 cmH2O
2016-Modification of the Berlin Definition (Kigali) [5]	1. Removal of a PEEP requirement, to allow patients to be diagnosed without positive pressure ventilation 2. Use SpO2/FiO2>315 instead of PaO2/FiO2, which requires AKG testing. 3. Use of lung ultrasound as an acceptable imaging modality to assess for bilateral opacities, in addition to plain radiograph and CT.	1. Removal of a PEEP requirement 2. Using SpO2/FiO2≤315 3- using lung ultrasound
2019-COVID 19 Pandemic		High flow nasal oxygen (HFNO)
2023-The Global Definition of ARDS [6]	1. Allowing HFNO with a minimum flow rate of 30 L/min, or NIV or CPAP with at least 5 cmH2O of end-expiratory pressure 2. Allowing either PaO2/FiO2≤300 or SpO2/FiO2≤315 withSpO2 97% to identify hypoxemia 3. Adding ultrasound as a modality of imaging to identify bilateral opacities 4. Not requiring PEEP, oxygen flow, or specific respiratory support devices to diagnose ARDS in resource variable settings.	
In the future-Eroglu A [8]	International ARDS Council	ARDS Specific Marker (ASM) ARDS Severity Score (ASS)

Table 1: ARDS definition development process.

Conclusion

Significant progress in the definition and management of ARDS has been made at the international level since its first description. Despite all these improvements, there is a need for new and more studies and methods on the definition and management of ARDS.

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