Acute Respiratory Distress Syndrome New Guidelines

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Acute Respiratory Distress Syndrome (ARDS)

An acute, diffuse, inflammatory lung injury leading to increased pulmonary vascular permeability, bilateral alveolar infiltrates, loss of aerated tissue, hypoxemia and respiratory failure.

Epidemiology

Globally

- 10% of ICU admissions
- Twenty four percent of patients receiving MV in the ICU.
- More than 3 million patients annually.

- 26 to 58% mortality

The Berlin Definition - Diagnosis (2012)

- Respiratory symptoms beginning within one week of a known clinical insult, or new or worsening symptoms during the past week.

- Bilateral opacities consistent with pulmonary edema on a chest X-Ray or CT.
  - Not fully explained by pleural effusions, lobar/lung collapse, or pulmonary nodules.

- Respiratory failure not fully explained by cardiac failure or fluid overload.
  - An objective assessment (eg, echocardiography) to exclude hydrostatic pulmonary edema is required if no risk factors for ARDS are present.

- A moderate to severe impairment of oxygenation as defined by the ratio of arterial oxygen pressure to fraction of inspired oxygen (PaO2/FiO2).

Ferguson ND, Fan E, Camporota L, et al. The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material. Intensive Care Med. 2012;38(10):1573-82.

The Berlin Definition
Severity of the ARDS

(!) Severity of hypoxemia

- Mild ARDS
  - 200 mmHg < PaO2/FiO2 ≤300 mmHg, on ventilator settings with PEEP or CPAP ≥5 cm H2O.
- Moderate ARDS
  - 100 mmHg < PaO2/FiO2 ≤200 mmHg on ventilator settings with PEEP ≥5 cm H2O.
- Severe ARDS
  - PaO2/FiO2 ≤100 mmHg on ventilator settings with PEEP ≥5 cm H2O.

Am J Respir Crit Care Med. 2016 Jan 1;193(1):52-9. doi: 10.1164/rccm.201503-0584OC.

Hospital Incidence and Outcomes of the Acute Respiratory Distress Syndrome Using the Kigali Modification of the Berlin Definition.

Riviello ED[1,2], Kiviri W[3], Twagirumugabe T[3], Mueller A[4], Banner-Goodspeed VM[4], Officer L[4], Novack V[5], Mutumwinka M[6], Talmor DS[4], Fowler RA[7].

- Riviello, et al. proposed a modification of the Berlin Definition for use in resource-constrained settings.

- Aim: to increase the ARDS diagnosis rates in resource-constrained centers where ABGs, MV and CT scan are not available.

Kigali modification of the Berlin Definition of ARDS (2016)

It was suggested that

- SpO2 can be used instead of PaO2
  - SpO2/FiO2 ratio of 315 equals to PaO2/FiO2 ratio of 300 mmHg
- Chest ultrasound can be used instead of chest CT.
- There is no PEEP requirement.

Riviello ED, Kiviri W, Twagirumugabe T, et al. Hospital Incidence and Outcomes of the Acute Respiratory Distress Syndrome Using the Kigali Modification of the Berlin Definition. Am J Respir Crit Care Med. 2016 Jan 1;193(1):52-9.

Etiologic Factors

Various insults, leading to the development of

non-hydrostatic pulmonary edema

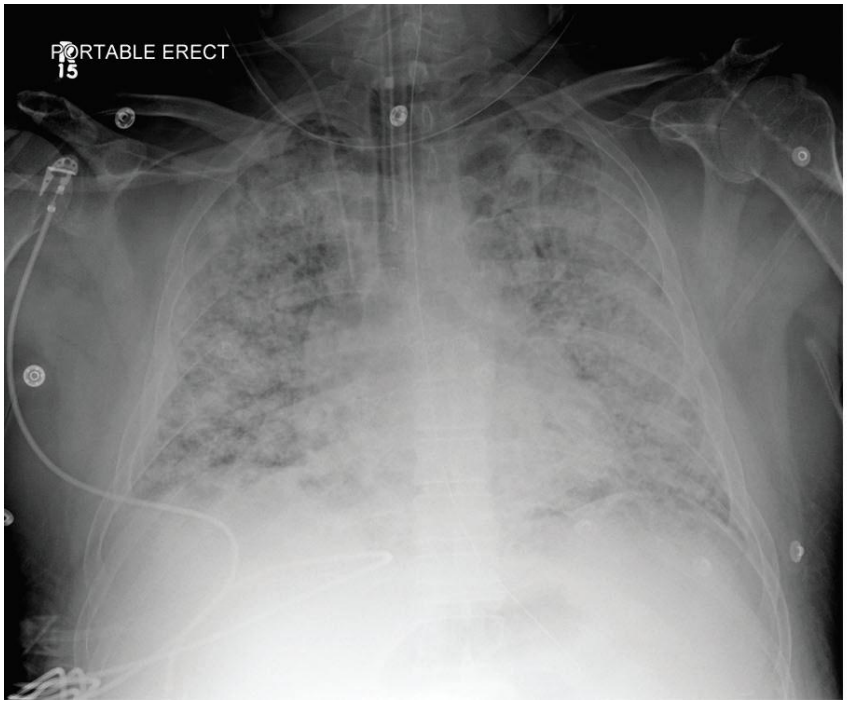
- Pulmonary
  - Pneumonia, aspiration etc.
- Non-pulmonary
  - Sepsis, pancreatitis, trauma etc.

Clinical Presentation

- The clinical features
  - usually appear within 6-72 hours of an inciting event
  - worsen rapidly.
- Typical presentation
  - dyspnea, cyanosis (ie, hypoxemia), and diffuse crackles.
- Respiratory distress is usually evident.
  - Tachypnea, tachycardia, diaphoresis, use of accessory muscles.

Labs and Imaging

- ABGs
  - hypoxemia
    - often accompanied by acute respiratory alkalosis
- The chest radiograph
  - bilateral alveolar infiltrates
- CT scan
  - widespread patchy or coalescent airspace opacities



Diffuse bilateral pulmonary infiltrates.

The distribution of the infiltrates predominantly in the dependent regions

Fan E, Brodie D, Slutsky AS. Acute Respiratory Distress Syndrome: Advances in Diagnosis and Treatment. JAMA. 2018;319(7):698-710.

Diagnostic Evaluation

- Identify specific cause of the ARDS
- Exclude other conditions that also have the same presentation
- Diagnosis of exclusion.

Differential Diagnosis

- Cardiogenic pulmonary edema
- Diffuse alveolar hemorrhage
- Cryptogenic organizing pneumonia
- Rapidly disseminating cancer
- Idiopathic acute eosinophilic pneumonia
- Acute exacerbation of chronic interstitial lung diseases
- Acute interstitial pneumonia (Hamman-Rich syndrome)
- …

Management

- Treat the underlying cause (!)

- Mechanical ventilation (MV) - **The cornerstone of management**
  - Begin with optimization of lung protective ventilation
    - = Low tidal volume ventilation (LTVV)
    - Minimizing ventilator-induced lung injury (VILI) (!)

- VILI is a form of iatrogenic, secondary lung injury
  - Contribute to the development of multi-organ failure and death.

LTVV

- V_T: 4–8 ml/kg PBW

Goals	
Plateau pressure (Pplat)	≤30 cm H2O
Oxygenation	PaO2 55 - 80 mmHg
	SpO2 88 - 95 %

UpToDate. Mark D Siegel, Robert C Hyzy. Mechanical ventilation of adults in acute respiratory distress syndrome.

LTVV

LTVV in patients with ARDS - Initial ventilator settings	
Calculate predicted body weight (PBW)	
Male =	50 + 0.91 [height (cm) - 152.4]
Female =	45.5 + 0.91 [height (cm) - 152.4]
Set mode to volume assist-control	
• Set initial V_T to 6 mL/kg PBW	
Set initial ventilator rate ≤35 breaths/min	

UpToDate. Mark D Siegel, Robert C Hyzy. Mechanical ventilation of adults in acute respiratory distress syndrome.

LTVV

LTVV in patients with ARDS - Initial ventilator settings								
Arterial oxygenation and PEEP								
Use these FiO2/PEEP combinations to achieve oxygenation goal								
FiO_2	0.3	0.4	**0.5**	**0.6**	0.7	0.8	**0.9**	**1.0**
PEEP	5	5 to 8	**8 to 10**	10	10 to 14	14	14 to 18	18 to 24

PEEP should be applied starting with the **minimum value** for a given FiO2.

UpToDate. Mark D Siegel, Robert C Hyzy. Mechanical ventilation of adults in acute respiratory distress syndrome.

Three Considerations

- High PEEP
- Recruitment maneuvers (RMs)
- Open Lung Ventilation (OLV)

High Peep

- Higher levels of PEEP
  - may open up collapsed alveoli
  - the volume of each tidal breath is shared by more open alveoli.
  - alveolar over-distension decreases

RMs

- A recruitment maneuver is **the brief application of a high level of continuous positive airway pressure** (e.g. 35 to 40 cm H2O) for 40 seconds **to open up (recruit) collapsed alveoli**.

OLV

- A strategy combining LTVV with a RM and subsequent titration of applied PEEP to maximize alveolar recruitment.

The routine use of high PEEP, OLV, and RMs should be avoided.

Other Considerations

- Whether a trial of NIMV should be performed?
- The preferred mode of MV?
- Prevention of VILI
  - Extracorporeal carbon dioxide removal (ECCO2R)
  - Prone positioning
- Pharmacologic therapies
- High Frequency Oscillatory Ventilation (HFOV)

Invasive vs Noninvasive MV

- Most need invasive MV support.
- NIMV may be considered if the patient
  - is hemodynamically stable
  - is easily oxygenated
  - does not need immediate intubation
  - has no contraindications

Mode

- Volume limited ≈ Pressure limited.
- A volume limited approach may be easier to use to adhere to LTVV strategy.
- Fully supported modes (e.g, assist control) are generally favored over partially supported ones (e.g, SIMV).

Prevention of VILI - ECCO2R

ECCO2R

- Takes CO2 out of blood through an extracorporeal gas exchanger.
- May help in patients with a **PaO2/FiO2 ratio of ≤150 mm Hg**
- **Remains an experimental therapy.**

Prevention of VILI - Prone positioning

- **Provides a significant mortality benefit** by in patients with a PaO2/FiO2 ratio <150 mm Hg

https://image.slidesharecdn.com/themanagementofacuterespiratorydistresssyndrome-100415230025-phpapp02/95/the-management-of-acute-respiratory-distress-syndrome-28-728.jpg?cb=1271372528

Pharmacologic Therapies

- **β2 agonists** can increase sodium transport by activating β2 receptors on alveolar type I and type II cells, accelerating resolution of pulmonary edema.
  - A multicenter RCT of 7 days of intravenous salbutamol **was stopped early due to increased 28-day mortality in the salbutamol group**.

- **Keratinocyte growth factor (KGF)** is important in alveolar epithelial repair.
  - (X) There is **evidence of harm from KGF**
    - fewer VFDs, longer duration of MV, and higher 28-day mortality.

- **Statins** can reduce inflammation and progression of lung injury and were shown to reduce non-pulmonary organ dysfunction.
  - SAILS, HARP-2: **No benefit**

Pharmacologic Therapies

- They are not surely beneficial.
- Demonstrate possible harm.
- Currently no role for none of them in the routine management.

HFOV

- Delivers very small tidal volumes* around a relatively high mean airway pressure^{o}.
  - * limiting volutrauma
  - ^{o} limiting atelectrauma

- Theoretically, an ideal lung protective strategy

- Two large, multicenter RCTs[1,2] do not support the routine use.

[1]Lall R, Hamilton P, Young D, et al. A randomised controlled trial and cost-effectiveness analysis of high-frequency oscillatory ventilation against conventional artificial ventilation for adults with acute respiratory distress syndrome. The **OSCAR** (OSCillation in ARDS) study. Health Technol Assess. 2015 Mar;19(23):1-177, vii.

[2]Ferguson ND1, Cook DJ, Guyatt GH, et al; **OSCILLATE** Trial Investigators; Canadian Critical Care Trials Group.High-frequency oscillation in early acute respiratory distress syndrome. N Engl J Med. 2013 Feb 28;368(9):795-805.

Supportive care

- Patients with ARDS require meticulous supportive care
  - intelligent use of sedatives and neuromuscular blockade
  - hemodynamic management
  - nutritional support
  - control of blood glucose levels
  - expeditious evaluation and treatment of nosocomial pneumonia
  - prophylaxis against DVT and GI bleeding.

Supportive care - Sedation and Analgesia

They can be useful to the extent they improve tolerance of MV and decrease oxygen consumption

Supportive care - Neuromuscular Blockade

- Neuromuscular blockade up to 48 hours is probably safe and potentially beneficial in patients with a PaO2/FiO2 ≤120 mmHg.

Supportive care
- Nutritional support

- The optimal approach - uncertain.

- Low-volume initial enteral feeding is preferable.

  (If the GI tract is available for nutritional intake)

Supportive care - Nosocomial pneumonia

- Treat according to clinical guidelines designed for ventilator-associated pneumonia in the general ICU population.

Supportive care - DVT prophylaxis

- The risk of DVT and PE is high.
- All patients require some form of thromboprophylaxis

Supportive care - Glucocorticoids

- Methylprednisolone **1 mg/kg/day** may be administered to the patients with **early moderate-severe ARDS**
  - **Early: <14 days**

Supportive care - Fluid management

- Conservative fluid management may help patients by reducing edema formation.
  - Reasonable targets:
    - CVP: <4 mmHg
    - PAOP: <8 mmHg

X

- Hypotension and organ hypo-perfusion should be avoided.

ATS/ESICM/SCCM Clinical Practice Guideline Recommendations for MV in Adults With ARDS

Intervention	ARDS Severity	Strength of Recommendation	Comments
MV with low V_T and inspiratory pressures	All ARDS	Strong	Initial tidal volume should be set at 6 mL/kg PBW and can be increased up to 8 mL/kg PBW if the patient is double triggering or if inspiratory pressure decreases below PEEP
Prone positioning >12 h/d	Severe	Strong	Lack of consensus for recommendation in moderate ARDS
HFOV	Moderate or severe	Strong (-)	Strong recommendation **against the routine use of** HFOV in patients with moderate or severe ARDS, but may be considered in patients with refractory hypoxemia (ie, PaO2/FiO2 <64 mm Hg)
Higher PEEP	Moderate or severe	Conditional	Can implement a higher PEEP strategy that was used in the large randomized clinical trials included in the evidence synthesis
Recruitment Maneuvers	Moderate or severe	Conditional	Caution in patients with preexisting hypovolemia or shock
VV ECMO	Severe	Not applicable	No recommendation for or against use due to insufficient evidence

Fan E, Del Sorbo L, Goligher EC, et al; American Thoracic Society, European Society of Intensive Care Medicine, and Society of Critical Care Medicine. An official American Thoracic Society/European Society of Intensive Care Medicine/Society of Critical Care Medicine clinical practice guideline: mechanical ventilation in adult patients with acute respiratory distress syndrome. Am J Respir Crit Care Med. **2017**;195(9):1253-1263.

JAMA. 2017 Oct 10;318(14):1335-1345. doi: 10.1001/jama.2017.14171.

Effect of Lung Recruitment and Titrated Positive End-Expiratory Pressure (PEEP) vs Low PEEP on Mortality in Patients With Acute Respiratory Distress Syndrome: A Randomized Clinical Trial.

Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART) Investigators, Cavalcanti AB[1], Suzumura ÉA[1], Laranjeira LN[1], Paisani DM[1], Damiani LP[1], Guimarães HP[1], Romano ER[1], Regenga MM[1], Taniguchi LNT[1], Teixeira C[2], Pinheiro de Oliveira R[3], Machado FR[4], Diaz-Quijano FA[5], Filho MSA[6], Maia IS[7], Caser EB[8], Filho WO[9], Borges MC[10], Martins PA[11], Matsui M[12], Ospina-Tascón GA[13], Giancursi TS[14], Giraldo-Ramirez ND[15], Vieira SRR[16], Assef MDGPL[17], Hasan MS[18], Szczeklik W[19], Rios F[20], Amato MBP[21], Berwanger O[1], Ribeiro de Carvalho CR[21].

- A multicenter, randomized trial conducted at 120 ICUs from 9 countries
- 1010 patients with moderate to severe ARDS were enrolled.

CONCLUSIONS AND RELEVANCE: In patients with moderate to severe ARDS, a strategy with lung recruitment and titrated PEEP compared with low PEEP increased 28-day all-cause mortality. These findings do not support the routine use of lung recruitment maneuver and PEEP titration in these patients.

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Contributions?

Questions?