



ARDS...

*...It's only the "Tip of the
Iceberg"...*

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Followers: Drs. Giovannini A, Mancosu A, Metelli M, Volontè F.

SUMMARY

- **Definition**
- **Therapeutic approaches**
- **Special guests:**

...ECMO...

...extracorporeal CO2 removal...

HISTORY

“Acute Respiratory Distress in Adults”. Ashbaugh DB, Petty TL, Levine BE. *Lancet* 1967; 2:319 – 323.

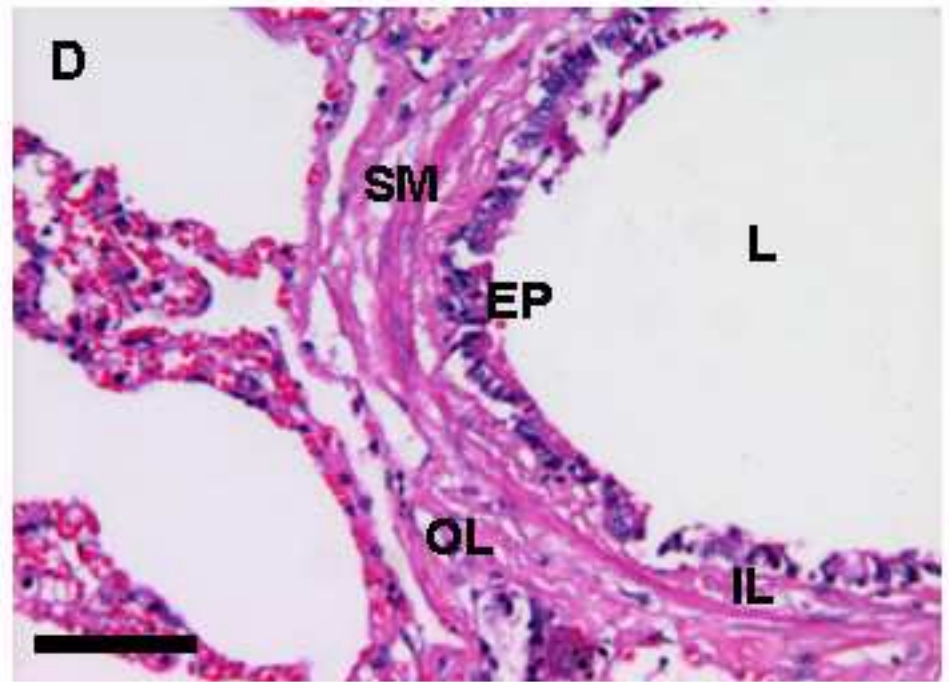
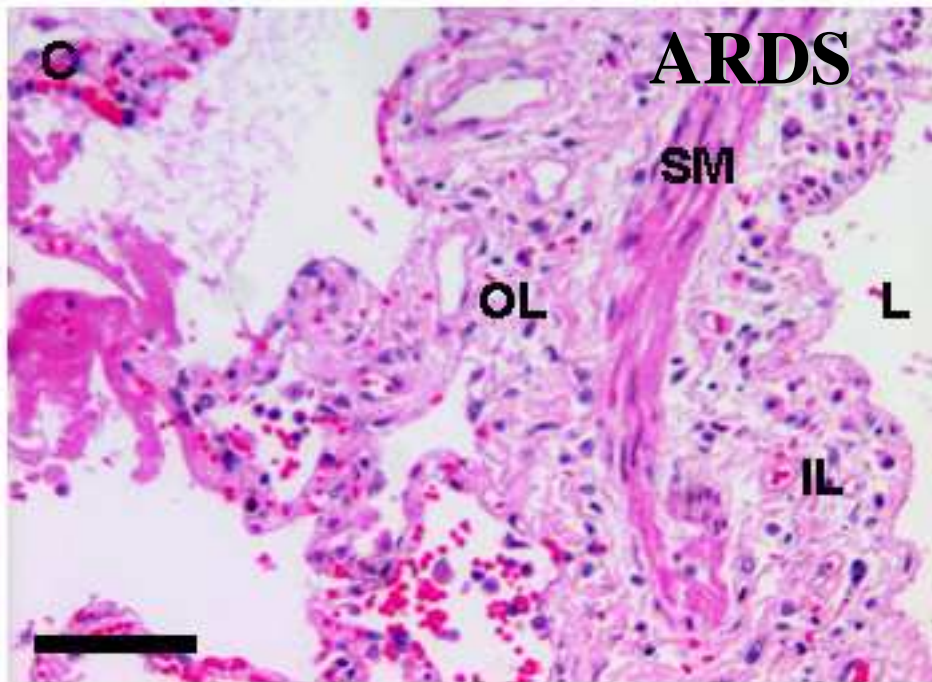
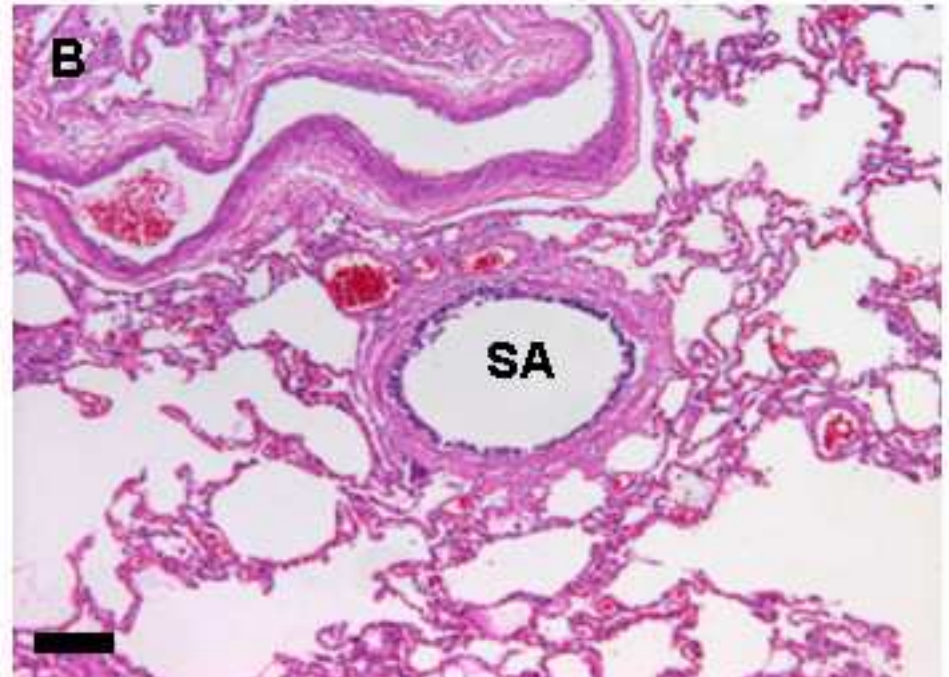
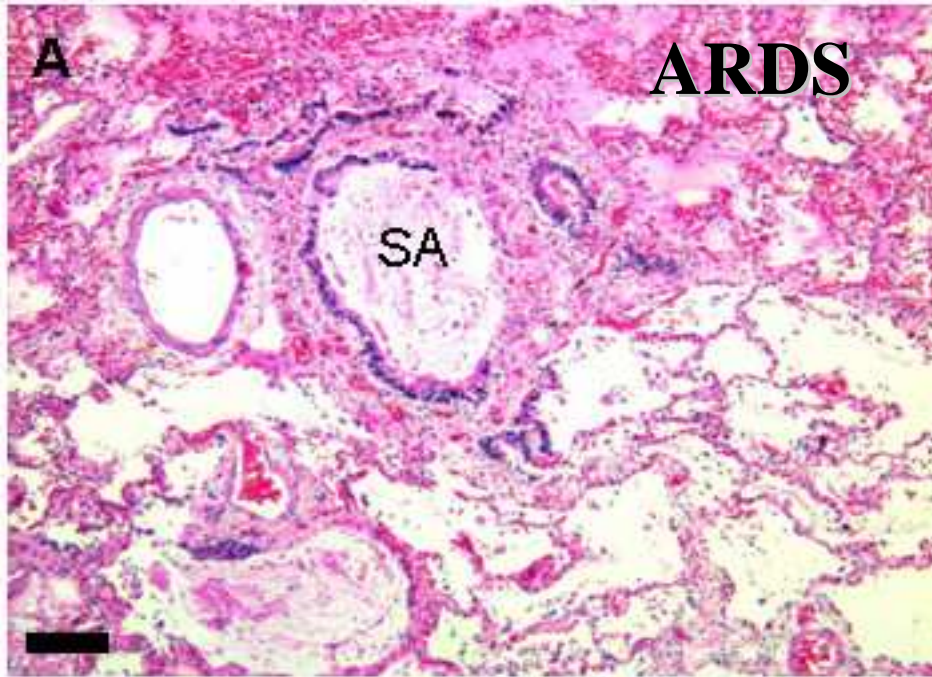
- 272 patients under mechanical ventilation
- 12 patients → *“severe acute respiratory failure”*
 - severe dyspnea, tachipnea
 - severe hypoxemia, cyanosis refractory to supplemental oxygen
 - decreased lung compliance
 - diffuse chest X-ray infiltrates

Histopathological changes:

- **widespread pulmonary inflammation**
- **interstitial, alveolar edema and hemorrhage**
- **alveolar macrophages**
- ***“hyaline membranes”***

In some cases...

*...responsive to the application of Positive
End-Expiratory Pressure (PEEP)*



*“An expanded definition of the **Adult** Respiratory Distress Syndrome”*. Murray JF, Matthay MA, Luce JM, Flick MR. *Am Rev Respir Dis* 1988; 138:720 – 723.

Table 1. Lung Injury Score

MURRAY SCORE

| | Score | | | | |
|---|-------|---------|---------|---------|------|
| | 0 | 1 | 2 | 3 | 4 |
| Chest X-ray, number of quadrants | None | 1 | 2 | 3 | 4 |
| Oxygenation, P/F ratio | ≥300 | 225–299 | 175–224 | 100–174 | <100 |
| PEEP, cm H ₂ O | ≤5 | 6–8 | 9–11 | 12–14 | ≥15 |
| Lung compliance, ml/cm H ₂ O | ≥80 | 60–79 | 40–59 | 20–39 | ≤19 |

Risk factor

- Pneumonia
- Non-pulmonary sepsis
- Aspiration of gastric contents
- Major trauma
- Pulmonary contusion
- Pancreatitis
- Inhalational injury
- Severe burns
- Non-cardiogenic shock
- Drug overdose
- Multiple transfusions or transfusion-associated acute lung injury (TRALI)
- Pulmonary vasculitis
- Drowning

“The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes and clinical trial coordination”. Bernard GR, Artigas A, Brigham KL et al. Am J Resp Crit Care Med **1994**; 149(3Pt1): 818 – 824.

ARDS:

- *acute hypoxemia*
- *$PaO_2/FiO_2 \leq 200\text{mmHg}$*
- *bilateral infiltrates on chest X-Ray*
- *absence of left atrial hypertension*

ALI:

- *the same variables but... $200\text{mmHg} < PaO_2/FiO_2 \leq 300\text{mmHg}$*

Table 2. Criteria for acute lung injury (ALI) and acute respiratory distress syndrome (ARDS)

| | Timing | Oxygenation, P/F ratio | Frontal chest X-ray | Pulmonary artery wedge pressure |
|------|-----------------|------------------------|-----------------------|--|
| ALI | Acute onset | ≤ 300 mmHg | Bilateral infiltrates | ≤ 18 mmHg or no clinical evidence of left atrial hypertension |
| ARDS | ≤ 200 mmHg | | | |

BUT...

- *P/F ratio cut off value (?)*
- *lack of standard ventilatory settings at the time of arterial blood gases*
- *poor “reliability” of chest radiograph criterion*
- *lack of a clear definition of “acute”*
- *difficulties distinguishing hydrostatic edema*

Table 1. The AECC Definition³—Limitations and Methods

| | AECC Definition | AECC Limitations |
|------------------|--|--|
| Timing | Acute onset | No definition of acute ⁴ |
| ALI category | All patients with $P_{aO_2}/F_{iO_2} < 300$ mm Hg | Misinterpreted as $P_{aO_2}/F_{iO_2} = 201-300$, leading to confusing ALI/ARDS term |
| Oxygenation | $P_{aO_2}/F_{iO_2} \leq 300$ mm Hg (regardless of PEEP) | Inconsistency of P_{aO_2}/F_{iO_2} ratio due to the effect of PEEP and/or F_{iO_2} ⁵⁻⁷ |
| Chest radiograph | Bilateral infiltrates observed on frontal chest radiograph | Poor interobserver reliability of chest radiograph interpretation ^{8,9} |
| PAWP | PAWP ≤ 18 mm Hg when measured or no clinical evidence of left atrial hypertension | High PAWP and ARDS may coexist ^{10,11} Poor interobserver reliability of PAWP and clinical assessments of left atrial hypertension ¹² |
| Risk factor | None | Not formally included in definition ⁴ |

ONLINE FIRST

Acute Respiratory Distress Syndrome

The Berlin Definition

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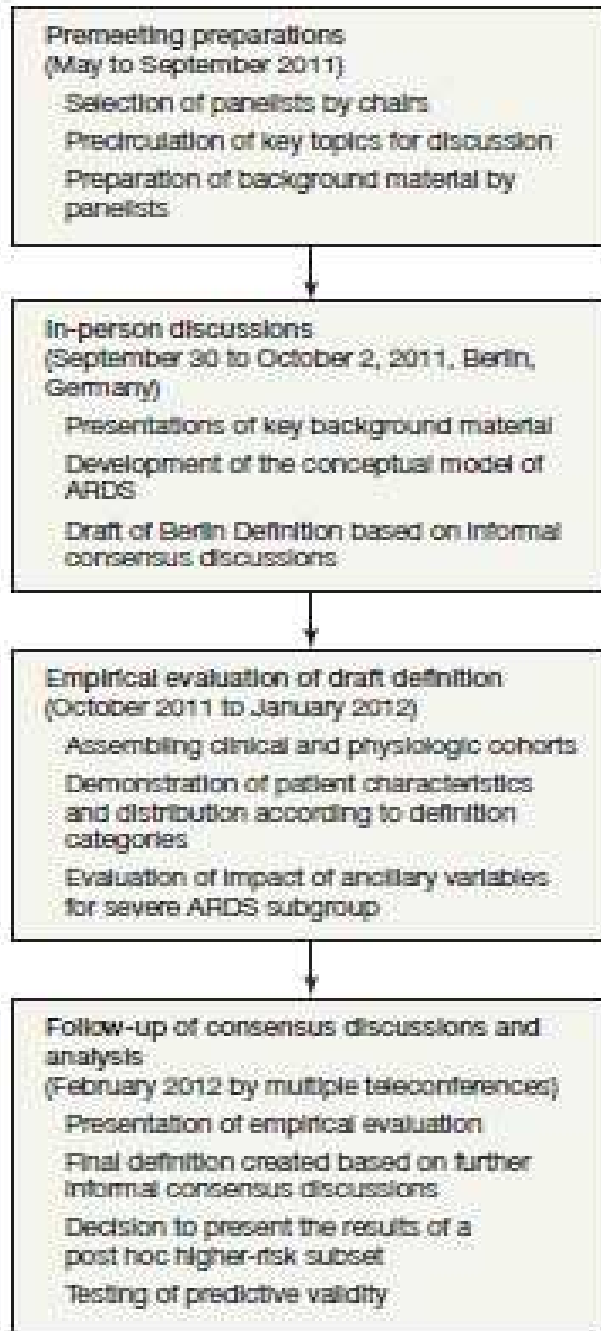
Table 1 Glossary of terms and their application in the Berlin definition

| | Definition | Addressed in the Berlin definition With |
|---------------------|---|--|
| Feasibility | Definition can be applied widely in actual practice | Maintenance of similar feasible criteria as AECC Removal of pulmonary artery catheter criteria |
| Reliability | Observers agree on case identification | Chest radiograph examples Inclusion of minimal PEEP levels Case vignettes to assess hydrostatic edema exclusion |
| Criterion validity | Definition agrees with reference standard | N/A |
| Predictive validity | Definition is able to stratify patients by prognosis or response to therapy | Creation of categories of ARDS severity |
| Face validity | Definition identifies patients who look like patients with the syndrome | Development of conceptual model of ARDS Chest radiograph examples Removal of clinical evidence of left atrial hypertension exclusion |
| Content validity | Definition captures all relevant aspects of the syndrome | Concordance with previous AECC definition Expert consensus |

AECC American-European Consensus Conference, ARDS acute respiratory distress syndrome, CT computed tomography, FiO_2 fraction of inspired oxygen, SpO_2 oxyhemoglobin saturation by pulse oximetry

***Fattibilità, Attendibilità,
Validità, Valore Predittivo...***

Figure. Outline of Consensus Process



ARDS Conceptual Model :

- ***acute, diffuse inflammatory injury***
- ***increased polmunary vascular permeability***
- ***increased lung weight***
- ***loss of areated lung tissue***
- ***clinical landmark: hypoxemia, bilateral radiographic opacities, increased venous admixture and phisiological dead space, decreased lung compliance***
- ***morphological hallmark: diffuse alveolar damage (edema, inflammation, hyaline membrane, hemorrhage)***

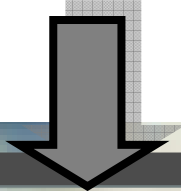
...DRAFT definition...

Table 3 The Berlin definition of ARDS

| Acute respiratory distress syndrome | | | |
|-------------------------------------|--|---|---|
| | Mild | Moderate | Severe |
| Oxygenation ^b | $200 < PaO_2/FiO_2 \leq 300$ with PEEP or CPAP ≥ 5 cmH ₂ O ^c | $100 < PaO_2/FiO_2 \leq 200$ with PEEP ≥ 5 cmH ₂ O | $PaO_2/FiO_2 \leq 100$ with PEEP ≥ 5 cmH ₂ O |

4 Ancillary variables for severe ARDS:

- 1. Radiographic severity***
- 2. Respiratory system compliance ≤ 40 ml/cmH₂O***
- 3. Positive End-Expiratory Pressure ≥ 10 cmH₂O***
- 4. Corrected Expired Volume per Minute ≥ 10 L/min***



Did not contribute to the predictive validity of severe ARDS for MORTALITY...were removed from definition...

| Acute respiratory distress syndrome | | | |
|-------------------------------------|--|---|--|
| Timing | Within 1 week of a known clinical insult or new/worsening respiratory symptoms | | |
| Chest imaging ^a | Bilateral opacities—not fully explained by effusions, lobar/lung collapse, or nodules | | |
| Origin of Edema | Respiratory failure not fully explained by cardiac failure or fluid overload; Need objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present | | |
| | Mild | Moderate | Severe |
| Oxygenation ^b | 200 < PaO ₂ /FiO ₂ ≤ 300 with PEEP or CPAP ≥5 cmH ₂ O ^c | 100 < PaO ₂ /FiO ₂ ≤ 200 with PEEP ≥5 cmH ₂ O | PaO ₂ /FiO ₂ ≤100 with PEEP ≥5 cmH ₂ O |

tion. Using the Berlin Definition, stages of mild, moderate, and severe ARDS were associated with increased mortality (27%; 95% CI, 24%-30%; 32%; 95% CI, 29%-34%; and 45%; 95% CI, 42%-48%, respectively; $P < .001$) and increased median duration of mechanical ventilation in survivors (5 days; inter-

ber of the limitations of the AECC definition. The approach of combining consensus discussions with empirical evaluation may serve as a model to create more accurate, evidence-based, critical illness syndrome definitions and to better inform clinical care, research, and health services planning.

Table 1. The AECC Definition¹—Limitations and Methods to Address These in the Berlin Definition

| | AECC Definition | AECC Limitations | Addressed in Berlin Definition |
|------------------|--|--|---|
| Timing | Acute onset | No definition of acute ^d | Acute time frame specified |
| ALI category | All patients with $PaO_2/FiO_2 < 300$ mm Hg | Misinterpreted as $PaO_2/FiO_2 = 201-300$, leading to confusing ALI/ARDS term | 3 Mutually exclusive subgroups of ARDS by severity ALI term removed |
| Oxygenation | $PaO_2/FiO_2 \leq 300$ mm Hg (regardless of PEEP) | Inconsistency of PaO_2/FiO_2 ratio due to the effect of PEEP and/or FiO_2 ^{2,7} | Minimal PEEP level added across subgroups FiO_2 effect less relevant in severe ARDS group |
| Chest radiograph | Bilateral infiltrates observed on frontal chest radiograph | Poor interobserver reliability of chest radiograph interpretation ^{8,9} | Chest radiograph criteria clarified Example radiographs created ⁸ |
| PAWP | PAWP ≤ 18 mm Hg when measured or no clinical evidence of left atrial hypertension | High PAWP and ARDS may coexist ^{10,11} Poor interobserver reliability of PAWP and clinical assessments of left atrial hypertension ¹² | PAWP requirement removed Hydrostatic edema not the primary cause of respiratory failure Clinical vignettes created ⁸ to help exclude hydrostatic edema |
| Risk factor | None | Not formally included in definition ^d | Included When none identified, need to objectively rule out hydrostatic edema |

Abbreviations: AECC, American-European Consensus Conference; ALI, acute lung injury; ARDS, acute respiratory distress syndrome; FiO_2 , fraction of inspired oxygen; PaO_2 , arterial partial pressure of oxygen; PAWP, pulmonary artery wedge pressure; PEEP, positive end-expiratory pressure.

^dAvailable on request.

