

ARDS & Ventilator Setting

Department of Intensive Care Medicine
Dong Hyun, LEE

CONFERENCE REPORTS AND EXPERT PANEL

ESICM **guidelines** on acute respiratory distress syndrome: **definition, phenotyping** and respiratory support **strategies**



AMERICAN THORACIC SOCIETY DOCUMENTS

An Update of
Distress Syndrome
An Official American Thoracic Society



WORKSHOP

A New Global Definition of Acute Respiratory Distress Syndrome

Michael A. Matthay^{1,2,3}, Yaseen Arabi⁵, Alejandro C. Arroliga⁶, Gordon Bernard⁷, Andrew D. Bersten⁹, Laurent J. Brochard¹⁰, Carolyn S. Calfee^{1,2,3}, Alain Combes¹¹, Brian M. Daniel⁴, Niall D. Ferguson^{12,13}, Michelle N. Gong¹⁴, Jeffrey E. Gotts¹⁵, Margaret S. Herridge¹⁶, John G. Laffey¹⁷, Kathleen D. Liu^{1,2}, Flavia R. Machado¹⁸, Thomas R. Martin¹⁹, Danny F. McAuley²⁰, Alain Mercat²¹, Marc Moss²², Richard A. Mularski²³, Antonio Pesenti^{24,25}, Haibo Qiu²⁶, Nagarajan Ramakrishnan²⁷, V. Marco Ranieri²⁸, Elisabeth D. Riviello²⁹, Eileen Rubin³⁰, Arthur S. Slutsky¹⁰, B. Taylor Thompson³¹, Theogene Twagirumugabe³², Lorraine B. Ware⁸, and Katherine D. Wick³³

ONLINE FIRST

Acute Respiratory Distress Syndrome

The Berlin Definition

The ARDS Definition Table

VALID AND RELIABLE
Definitions are essential



Table 3. The Berlin Definition of Acute Respiratory Distress Syndrome

Acute Respiratory Distress Syndrome	
Timing	Within 1 week of a known clinical insult or new or 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 (eg, echocardiography) to exclude hydrostatic edema if no risk factor present
Oxygenation ^b	
Mild	200 mm Hg < PaO ₂ /FIO ₂ ≤ 300 mm Hg with PEEP or CPAP ≥5 cm H ₂ O ^c
Moderate	100 mm Hg < PaO ₂ /FIO ₂ ≤ 200 mm Hg with PEEP ≥5 cm H ₂ O
Severe	PaO ₂ /FIO ₂ ≤ 100 mm Hg with PEEP ≥5 cm H ₂ O

Abbreviations: CPAP, continuous positive airway pressure; FIO₂, fraction of inspired oxygen; PaO₂, partial pressure of arterial oxygen; PEEP, positive end-expiratory pressure.

^aChest radiograph or computed tomography scan.

^bIf altitude is higher than 1000 m, the correction factor should be calculated as follows: [PaO₂/FIO₂ × (barometric pressure/760)].

^cThis may be delivered noninvasively in the mild acute respiratory distress syndrome group.

Limitations of Berlin Definition



Invasive or Non-Invasive Mechanical Ventilation

Invasive Blood Sampling for PaO₂

Widespread of High Flow Nasal Cannula

Berlin Definition in Resource Limited Area (CXR, ABGA, MV...)

Increase of Ultrasound Use in ARDS

ORIGIN

키갈리

르완다의 수도

Hospital I Syndrome



	Berlin Criteria	Challenges in Resource Poor Settings	Kigali Modification of the Berlin Criteria
Timing	Within 1 wk of a known clinical insult or new or worsening respiratory symptoms	None	Within 1 wk of a known clinical insult or new or worsening respiratory symptoms
Oxygenation	$Pa_{O_2}/F_{I_{O_2}} \leq 300$	Scarcity of arterial blood gas diagnostics	$Sp_{O_2}/F_{I_{O_2}} \leq 315$
PEEP requirement	Minimum 5 cm H ₂ O PEEP required by invasive mechanical ventilation (noninvasive acceptable for mild ARDS)	Scarcity of mechanical ventilators	No PEEP requirement, consistent with AECC definition
Chest imaging	Bilateral opacities not fully explained by effusions, lobar/lung collapse, or nodules by chest radiograph or CT	Scarcity of chest radiography resources	Bilateral opacities not fully explained by effusions, lobar/lung collapse, or nodules by chest radiograph or ultrasound
Origin of edema	Respiratory failure not fully explained by cardiac failure or fluid overload (need objective assessment, such as echocardiography, to exclude hydrostatic edema if no risk factor present)	None	Respiratory failure not fully explained by cardiac failure or fluid overload (need objective assessment, such as echocardiography, to exclude hydrostatic edema if no risk factor present)





Table 1. Diagnostic Criteria for the New Global Definition of ARDS

Conceptual model: ARDS is an acute, diffuse, inflammatory lung injury precipitated by a predisposing risk factor, such as pneumonia, nonpulmonary infection, trauma, transfusion, burn, aspiration, or shock. The resulting injury leads to increased pulmonary vascular and epithelial permeability, lung edema, and gravity-dependent atelectasis, all of which contribute to loss of aerated lung tissue. The clinical hallmarks are arterial hypoxemia and diffuse radiographic opacities associated with increased shunting, increased alveolar dead space, and decreased lung compliance. The clinical presentation is influenced by medical management (position, sedation, paralysis, positive end-expiratory airway pressure, and fluid balance). Histological findings vary and may include intraalveolar edema, inflammation, hyaline membrane formation, and alveolar hemorrhage.

Criteria That Apply to All ARDS Categories

Risk factors and origin of edema	Precipitated by an acute predisposing risk factor, such as pneumonia, nonpulmonary infection, trauma, transfusion, aspiration, or shock. Pulmonary edema is not <i>exclusively or primarily</i> attributable to cardiogenic pulmonary edema/fluid overload, and hypoxemia/gas exchange abnormalities are not primarily attributable to atelectasis. However, ARDS can be diagnosed in the presence of these conditions if a predisposing risk factor for ARDS is also present.
Timing	Acute onset or worsening of hypoxemic respiratory failure within 1 week of the estimated onset of the predisposing risk factor or new or worsening respiratory symptoms.
Chest imaging	Bilateral opacities on chest radiography and computed tomography or bilateral B lines and/or consolidations on ultrasound* not fully explained by effusions, atelectasis, or nodules/masses.

Criteria That Apply to Specific ARDS Categories

	Nonintubated ARDS [†]	Intubated ARDS	Modified Definition for Resource-Limited Settings [‡]
Oxygenation [§]	$Pa_{O_2}:F_{I_{O_2}} \leq 300$ mm Hg or $Sp_{O_2}:F_{I_{O_2}} \leq 315$ (if $Sp_{O_2} \leq 97\%$) on HFNO with flow of ≥ 30 L/min or NIV/CPAP with at least 5 cm H ₂ O end-expiratory pressure	Mild [¶] : $200 < Pa_{O_2}:F_{I_{O_2}} \leq 300$ mm Hg or $235 < Sp_{O_2}:F_{I_{O_2}} \leq 315$ (if $Sp_{O_2} \leq 97\%$) Moderate: $100 < Pa_{O_2}:F_{I_{O_2}} \leq 200$ mm Hg or $148 < Sp_{O_2}:F_{I_{O_2}} \leq 235$ (if $Sp_{O_2} \leq 97\%$) Severe: $Pa_{O_2}:F_{I_{O_2}} \leq 100$ mm Hg or $Sp_{O_2}:F_{I_{O_2}} \leq 148$ (if $Sp_{O_2} \leq 97\%$)	$Sp_{O_2}:F_{I_{O_2}} \leq 315$ (if $Sp_{O_2} \leq 97\%$) [†] . Neither positive end-expiratory pressure nor a minimum flow rate of oxygen is required for diagnosis in resource-limited settings.

Conceptual Model of New Global ARDS Definition



Acute, diffuse, inflammatory lung injury

Precipitated by... pneumonia, non-pulmonary infection, trauma, transfusion, burn, aspiration, shock...

Injury leads to... increased pulmonary vascular and epithelial **permeability**, lung edema, and gravity-dependent atelectasis,
→ loss of aerated lung tissue

Conceptual Model of New Global ARDS Definition



Clinical hallmark

Shunting \uparrow , Alveolar dead space \uparrow

Lung compliance \downarrow

→ **Arterial hypoxemia & diffuse radiographic opacities**

Clinical presentation is influenced by medical management. (position, sedation, paralysis, positive end-expiratory airway pressure, fluid balance).

Histological findings: intra-alveolar edema, inflammation, hyaline membrane formation, and alveolar hemorrhage.

All ARDS Category



Risk Factor & Edema Origin

- Precipitated by acute predisposing risk factor (pneumonia, infection, trauma, transfusion, aspiration, shock...)
- Not cardiogenic pulmonary edema/fluid overload
- Not atelectasis

Timing

- 1 week

Chest Imaging

- Bilateral opacities on CXR / CT
- Bilateral B lines / consolidations on ultrasound
- Not fully explained by effusions, atelectasis, or nodules/masses

A & B Lines in Lung Ultrasound



Specific ARDS Category



Criteria That Apply to Specific ARDS Categories

Nonintubated ARDS[†]

Intubated ARDS

Modified Definition for Resource-Limited Settings[‡]

Oxygenation^{\$||}

$Pa_{O_2}:Fi_{O_2} \leq 300$ mm Hg or
 $Sp_{O_2}:Fi_{O_2} \leq 315$ (if $Sp_{O_2} \leq 97\%$)
 on HFNO with flow of
 ≥ 30 L/min or NIV/CPAP
 with at least 5 cm H₂O
 end-expiratory pressure

Mild[¶]: $200 < Pa_{O_2}:Fi_{O_2} \leq 300$ mm Hg
 or $235 < Sp_{O_2}:Fi_{O_2} \leq 315$
 (if $Sp_{O_2} \leq 97\%$)
 Moderate: $100 < Pa_{O_2}:Fi_{O_2} \leq 200$ mm Hg
 or $148 < Sp_{O_2}:Fi_{O_2} \leq 235$
 (if $Sp_{O_2} \leq 97\%$)
 Severe: $Pa_{O_2}:Fi_{O_2} \leq 100$ mm Hg
 or $Sp_{O_2}:Fi_{O_2} \leq 148$
 (if $Sp_{O_2} \leq 97\%$)

$Sp_{O_2}:Fi_{O_2} \leq 315$
 (if $Sp_{O_2} \leq 97\%$)[†].
 Neither positive
 end-expiratory pressure
 nor a minimum flow rate
 of oxygen is required for
 diagnosis in resource-limited
 settings.

New Global ARDS Definition



Non-Intubated ARDS

- PF Ratio ≤ 300
- SF ratio < 315 (SpO₂ $< 97\%$)
(High Flow > 30 L/min / CPAP > 5 cmH₂O)


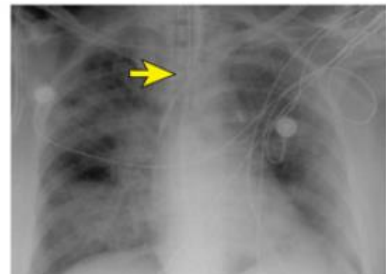

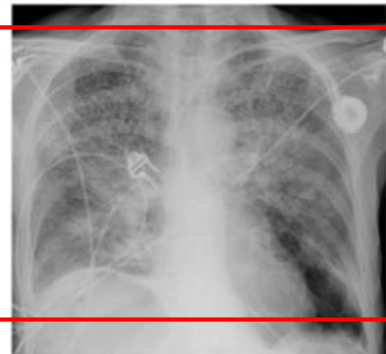

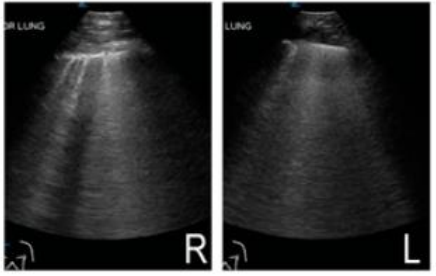
Intubated ARDS

- PF Ratio ≤ 300 / ≤ 200 / ≤ 100
- SF ratio ≤ 315 / ≤ 235 / ≤ 148 (SpO₂ $< 97\%$)

Resource Limited Setting

- SF ratio < 315 (SpO₂ $< 97\%$)



Patient Description	Imaging	Oxygenation	ARDS Categories
 <p data-bbox="522 228 1006 399">68-year-old M with abdominal sepsis, septic shock, and acute hypoxemic respiratory failure</p>		Mechanically ventilated FiO ₂ 0.5 PaO ₂ 75 P/F = 150 mm Hg	Intubated ARDS Severity: Moderate <i>Typical patient included in prior Berlin definition</i>
 <p data-bbox="522 564 1019 778">54-year-old F with history of breast cancer, COVID-19 pneumonia, and worsening shortness of breath for the past 6 days</p>		High-flow nasal oxygen HFNO 40L/min FiO ₂ 0.80 SpO ₂ 91% S/F = 114	Nonintubated ARDS <i>New category in Global definition</i>
 <p data-bbox="522 878 1006 1178">39-year-old F with abdominal sepsis and gram-negative bacteremia in a under-resourced hospital without blood gases, radiography, or mechanical ventilation</p>		Supplemental oxygen by face mask at 15L/min FiO ₂ 0.6 SpO ₂ 85% S/F = 142	ARDS in resource-limited settings <i>New category in global definition, consistent with the Kigali modification</i>



ESICM guidelines on acute respiratory distress syndrome: **definition**, phenotyping and respiratory support strategies



Domain 1: ARDS definition

- › Domain 2: ARDS phenotyping
- › Domain 3: High-flow nasal oxygenation
- › Domain 4: CPAP/NIV
- › Domain 5: Low tidal volume ventilation
- › Domain 6: PEEP and recruitment
- › Domain 7: Prone positioning
- › Domain 8: Neuromuscular blocking agents
- › Domain 9: Extracorporeal life support

whether predictive validity for mortality is the best measure of an ARDS definition. Diagnostic accuracy in ARDS is challenging without a universal reference standard. Future work in refining the ARDS definition should carefully consider other facets of validity as well as reliability [30]. At the same time, we need new prospective observational studies to better categorize patients with acute non-cardiogenic hypoxemic respiratory failure, including ARDS, across a broad range of characteristics, includ

Phenotype

eli
distress syndr
and respirato

Clin
ger

유전자형과 노출환경노출의 상호 작용으로 인해 임상적으로 관찰 가능한 일련의 형질

Subgroup

within the worl
established:

Subset of patients within a **phenotype**, which may be defined using

any
pat
sub

표현형 내의 하위 집단. 변수를 사용하여 정의할 수 있음.
(ex. ARDS의 PaO₂/FiO₂ 중증도 분류)

Sub-phenotype

Distinct subgroup discriminated from other subgroups based on a set

or
bas
trai

다른 Subgroup과 확실하게 구별되는 하위 그룹. 다차원적인 기준과 데이터 기반 평가를 기준으로 함. 다른 집단에서도 재현 가능해야 함.

Endotype

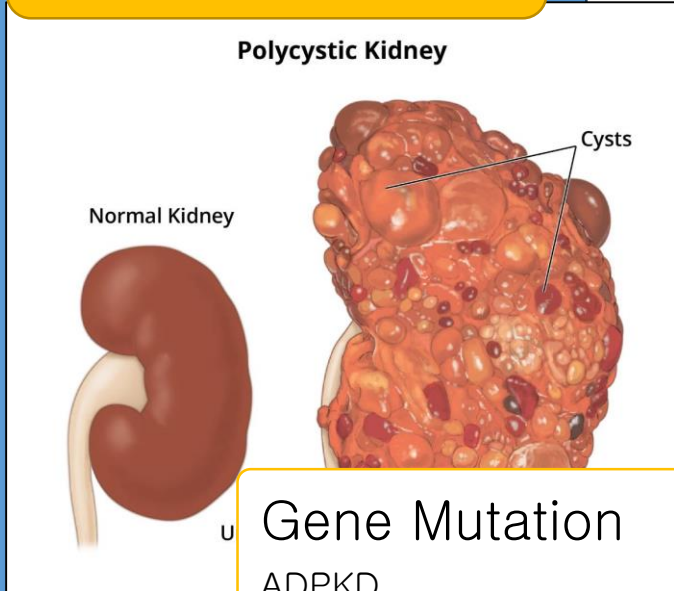
Sub
me

다른 Subgroup과 확실하게 구별되는 하위 그룹. 다차원적인 기준과 데이터 기반 평가를 기준으로 함. 다른 집단에서도 재현 가능해야 함.

CKD

Phenotype

Sub-phenotype



Gene Mutation

ADPKD
ARPKD

Endotype



Subgroup

Stage of CKD	eGFR result	What it means
Stage 1	90 or higher	- Mild kidney damage - Kidneys work as well as normal
Stage 2	60-89	- Mild kidney damage - Kidneys still work well
Stage 3a	45-59	- Mild to moderate kidney damage - Kidneys don't work as well as they should
Stage 3b	30-44	- Moderate to severe damage - Kidneys don't work as well as they should
Stage 4	15-29	- Severe kidney damage - Kidneys are close to not working at all
Stage 5	less than 15	- Most severe kidney damage - Kidneys are very close to not working or have stopped working (failed)

Failed Studies in ARDS



Aspirin

Vitamin D

Vitamin C?

Ketoconazole

Surfactant

PLT Activating Factor

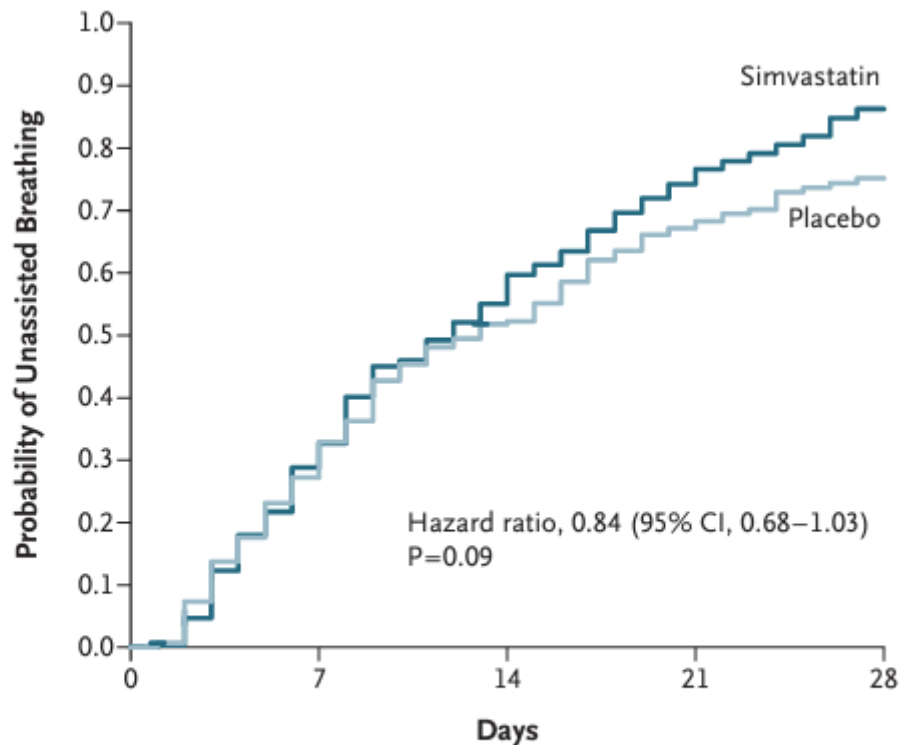
Lisofylline (Cytokine ↓)

Statins

Omega-3



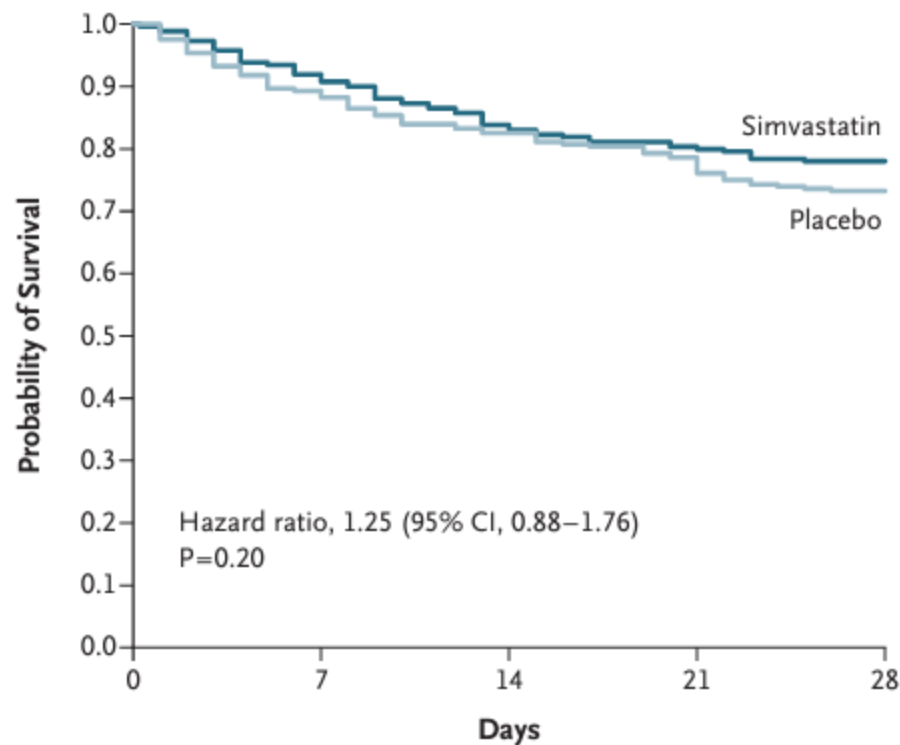
A Unassisted Breathing



No. at Risk

Simvastatin	258	166	87	43	19
Placebo	279	178	102	60	33

B Survival



No. at Risk

Simvastatin	259	238	217	208	202
Placebo	280	250	231	220	205



	Hypoinflammatory subphenotype (n=353)	Hyperinflammatory subphenotype (n=186)	p value
--	---------------------------------------	--	---------

Age (years)	51 (16)	60 (15)	<0.0001
-------------	---------	---------	---------

Female sex	158 (45%)	71 (40%)	0.22
------------	-----------	----------	------

Direct A

- Aspira
- Pneum
- Traum
- Other
- None

Indirect

- Sepsis
- Pancre
- Other
- None

Vasopre

- PaO₂ to
- Plateau
- Tidal vo

Platelet

Bilirubin

Creatini

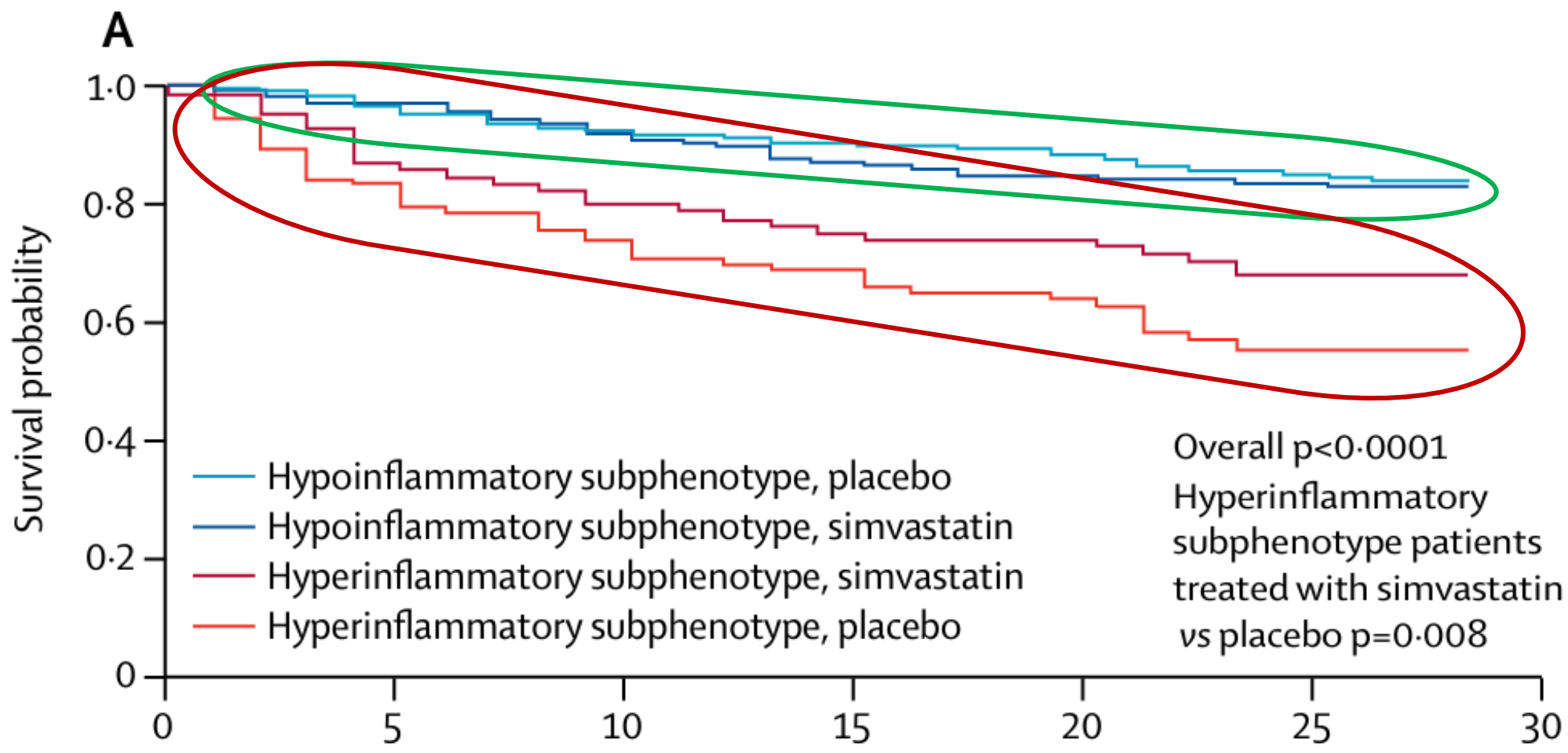
C-reactive protein, mg/L	174 (203)	200 (110)	0.0000
--------------------------	-----------	-----------	--------

Interleukin 6, pg/mL	79 (35-197)	348 (133-1355)	<0.0001
----------------------	-------------	----------------	---------

sTNFr1, pg/mL	3511 (2382-5008)	11202 (7810-16703)	<0.0001
---------------	------------------	--------------------	---------

Randomised to simvastatin	175 (50%)	84 (45%)	0.38
---------------------------	-----------	----------	------

otypes and





Acute Respiratory Distress Syndrome Subphenotypes Respond Differently to Randomized Fluid Management Strategy

Katie R. Famous¹, Kevin Delucchi², Lorraine B. Ware^{3,4}, Kirsten N. Kangelaris⁵, Kathleen D. Liu^{6,7}, B. Taylor Thompson⁸, and Carolyn S. Calfee^{1,7}; for the ARDS Network

¹Division of Pulmonary and Critical Care Medicine, Department of Medicine, ²Department of Psychiatry, ⁵Division of Hospital Medicine, Department of Medicine, ⁶Division of Nephrology, Department of Medicine, and ⁷Department of Anesthesia, University of California San Francisco, San Francisco, California; ³Department of Medicine, and ⁴Department of Pathology, Microbiology, and

Immun
Massa

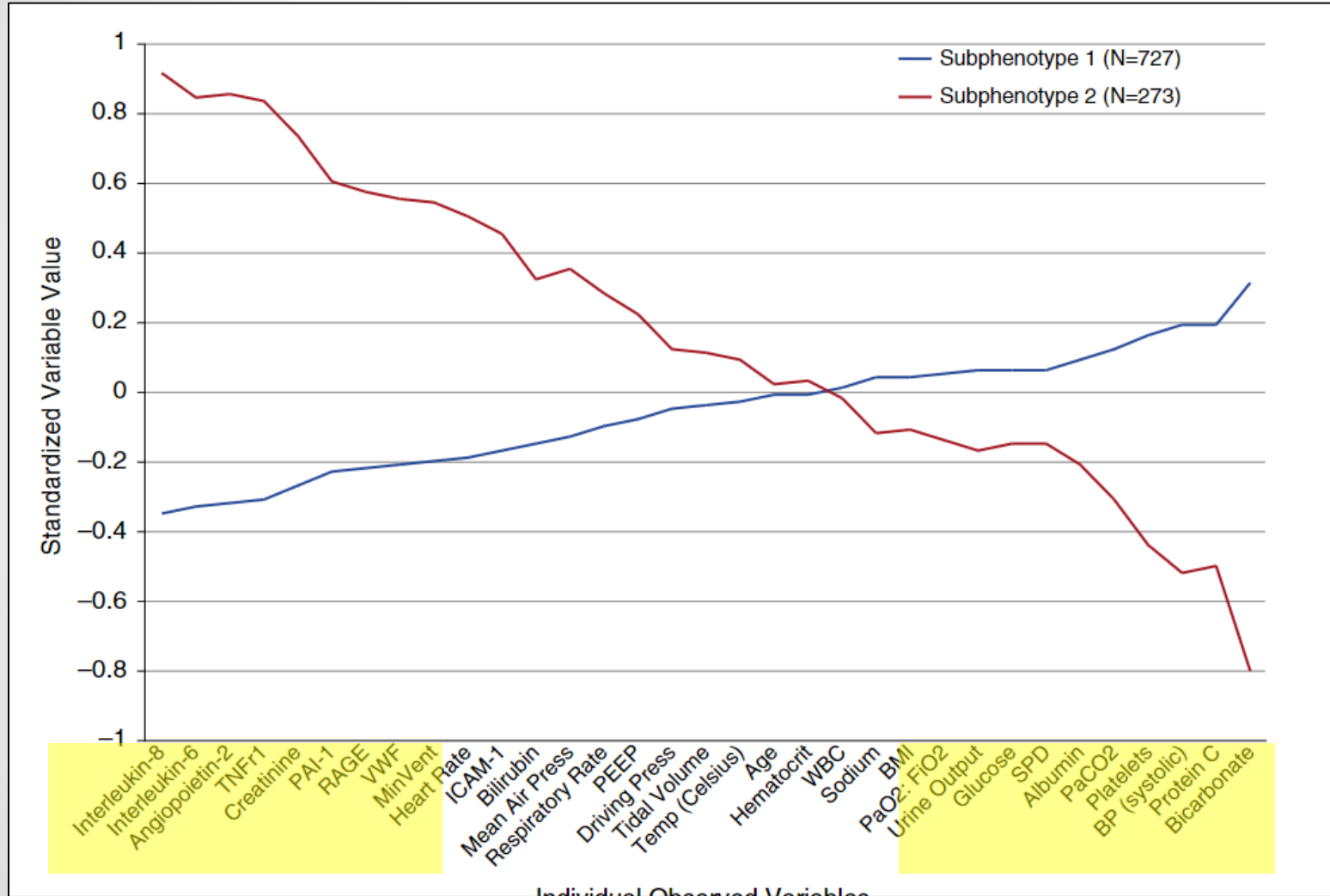
ORCID

Subphenotypes in acute respiratory distress syndrome: latent class analysis of data from two randomised controlled trials



Carolyn S Calfee, Kevin Delucchi, Polly E Parsons, B Taylor Thompson, Lorraine B Ware, Michael A Matthay, and the NHLBI ARDS Network

Hyper-Inflammatory vs Hypo-Inflammatory





The discovery of biological subphenotypes in ARDS: a new medicine?

Karin Wildi^{1,2,3*} , Samantha Livi

PHENOTYPE: ARDS



ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies



이제 Hyperinflammatory ARDS에서는 Simvastatin을 써야 하나요?

Steroid도 특정 subgroup에서는 써야 하는 거 아닌가요?

Hyper- vs Hypo- inflammatory ARDS 나누는 기준은 뭐죠?



Stability of sub-phenotypes (ARDS 초기 vs 후기 등에서 그대로 유지되는지?)

which patients must continue to meet criteria. Experts agree that ARDS is not a transient condition [27]. If the subjects in a trial

c. A sub-phenotype is a distinct subgroup (of ARDS table). A secondary analysis of the observational LUNG-

Reproducibility of sub-phenotypes

over time [27]. If the subjects in a trial risk of the condition that the intervention

should also be reproducible in different populations. d. An **endotype** is a sub-phenotype with distinct

in prospective studies likely requires: (1) on-site, real-time testing and rapid results, and (2) operator independence.

Short term (up to day 90) mortality was found to be different between sub-phenotypes that are based on the following

Accuracy and repeatability of rapid classification

prior to diagnosing ARDS is likely appropriate. The length of this period remains uncertain.

Accurate classification of the sub-phenotype, as exemplified by the results of LITE trial [28]

Does sub-phenotyping alter patient response to an anti-inflammatory intervention in ARDS?

• Lung radiographic morphology (higher mortality in non-focal than in focal) [38]:

Pathophysiological pathways

tor settings, which could identify high-risk patients but may add further feasibility challenges.

sonalized treatment strategy; however, misclassified sub-phenotype resulting in misaligned treatment

[36], no heterogeneity of treatment effect was identified for the lung-inflammatory and hyper-inflammatory sub-

(higher mortality in upwards trajectory of ventilatory ratio and mechanical power than in steady-state)

Mortality attribution of each sub-phenotype

of measures of inflammation in ARDS. The relationship between these markers and response to injury

Question 2.3: What is the evidence for heterogeneity of treatment effect (predictive enrichment)

vastatin; however, these sub-phenotypes have not been reproduced in other populations [43].

Several research questions remain to be addressed in future studies, particularly regarding: (1) the stability of

Precision treatment improve ICU outcomes?

inflammatory and hyper-inflammatory sub-phenotypes and PEEP strategy adopted (higher vs lower PEEP/FiO₂)

of sub-phenotypes; (5) the quantification of the attributable mortality of each sub-phenotype; and (6) whether

AMERICAN THORACIC SOCIETY DOCUMENTS

**An Update on Marfan
Distress Syndrome**
An Official American

hypoxemia and bilateral radiographic infiltrates (1–4). More than 50 years have passed since its initial recognition, and its definition has evolved over time, with a recent suggestion that it be expanded to include intubated and nonintubated patients (5, see pp. 37–47 of this issue). ARDS management remains largely supportive, focusing on strategies intended to limit further lung injury, and high mortality rates persist, with those who survive often facing long-term impairments (6). In 2017, the American Thoracic Society (ATS) in





We suggest using **corticosteroids** for patients with ARDS.

syndrome (ARDS) (Figure 1). New recommendations in this guideline include: >12 hours per day in patients with severe ARDS (strong recommendation).

We suggest using **VV-ECMO** in selected patients with **severe** ARDS.

extracorporeal membrane oxygenation (VV-ECMO) in selected patients with a diverse group of patients with expertise in ARDS epidemiology, clinical trials.

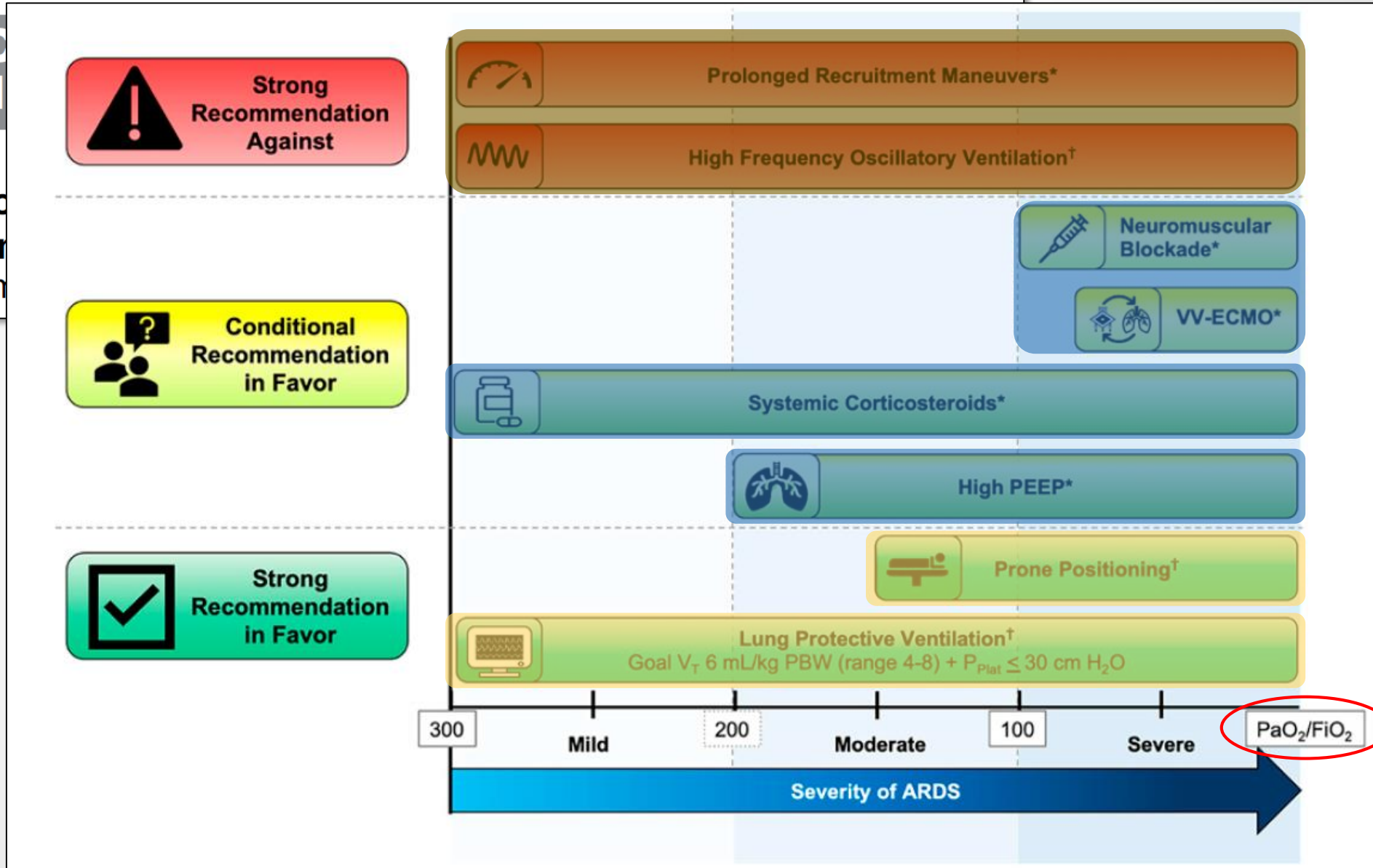
We suggest using **neuromuscular blockers** in patients with **early severe** ARDS.

low certainty of evidence). With regard to positive and negative definition has evolved over time, with a Development, and Evaluation (GRADE) methodology (8). We assigned panel





We suggest using **higher PEEP without lung recruitment** maneuvers than lower PEEP in patients with **moderate to severe** ARDS

low to moderate certainty). With regard to positive and negative definition has evolved over time, with a persist, with those who survive often facing conflicts of interest and financial relationships in accordance with ATS guidelines.

We recommend **against** using **prolonged LRMs** in patients with moderate to **severe** ARDS





Intervention	Population	Precautions	Practical considerations
 Corticosteroids	$PaO_2/FiO_2 \leq 300$	<ul style="list-style-type: none"> • May be associated with <u>increased risk of harm when initiated after > 14 days of mechanical ventilation</u> • <u>Monitor more closely for adverse effects</u> in patients with <u>immunosuppressed conditions</u>, <u>metabolic syndrome</u>, or known or increased risk of <u>fungal, parasitic, or mycobacterial infections</u> 	<ul style="list-style-type: none"> • <u>Optimal regimen, including type of corticosteroid, is unknown</u> • For patients with corticosteroid-responsive etiologies, regimen should be tailored to the specific condition • For other patients, regimens used in prior RCTs may be used • For patients that improve rapidly, <u>consider discontinuation at time of extubation</u>
 VV-ECMO	$PaO_2/FiO_2 < 80$ or $pH < 7.25$ with $pCO_2 \geq 60$	<p>Conditions associated with increased risk for futility of treatment</p> <ul style="list-style-type: none"> • <u>Irreversible etiology</u> of respiratory failure • <u>Mechanical ventilation > 7 days</u> • <u>Immunosuppression</u> • <u>Multi-organ failure</u> • <u>Older age</u> • <u>Systemic bleeding</u> or other contraindication to anticoagulation • Chronic medical condition and <u>life expectancy <1yr</u> • <u>CNS hemorrhage</u> or irreversible and incapacitating <u>CNS pathology</u> 	<ul style="list-style-type: none"> • <u>Less invasive therapies, including lung protective ventilation, prone positioning, and neuromuscular blockade, should be initiated prior to ECMO consideration</u> • Resource limitations should be considered, with an emphasis on maximizing access for patients most likely to benefit from ECMO • For patients meeting these criteria at hospitals without ECMO capabilities, <u>consider transfer to ECMO centers when feasible</u>
 NMBAs	<p>Early ARDS (≤ 48 hours of MV) with $PaO_2/FiO_2 \leq 100$</p>	<ul style="list-style-type: none"> • <u>Unknown</u> and potentially increased incidence of <u>neuromuscular weakness</u> with <u>infusions of > 48 hours duration</u> • Use caution in patients with prior neuromuscular conditions 	<ul style="list-style-type: none"> • <u>Reduced mortality when compared to deep sedation</u>. No mortality benefit when compared to light sedation • May have greater utility in patients with <u>ventilator dyssynchrony</u> not mitigated by ventilator changes • Either bolus dosing or continuous infusion may be appropriate • <u>Consider cessation after 48 hours</u> or earlier for patients that are improving rapidly • Cisatracurium most frequently used in clinical trials; optimal agent unknown
 High PEEP	$PaO_2/FiO_2 \leq 200$	<ul style="list-style-type: none"> • <u>Respiratory mechanics, hemodynamics, and response to PEEP</u> should be <u>continuously monitored</u> • Use additional caution in patients with severe hemodynamic instability or increased risk of barotrauma • Prolonged recruitment maneuvers should be avoided 	<ul style="list-style-type: none"> • <u>Optimal strategy is unknown</u>; selected strategy should be tailored to clinician expertise • Potential strategies may include <u>oxygenation-based titration</u> or titration to <u>maximal compliance</u> or <u>maximal safe plateau pressure</u> • Deleterious clinical response to higher PEEP (i.e. worsened oxygenation, dead space, compliance, or hemodynamics) should prompt re-evaluation of PEEP level



Variation in Early Management in Moderate to Severe ARDS in

The NEW ENGLAND JOURNAL of MEDICINE



For numbered affiliations see end of article.

Correspondence for this iteration to: Bram Rochweg bram.rochweg@gmail.com; Beverley Hunt beverley.hunt@gstt.nhs.uk; Miriam Stegemann miriam.stegemann@charite.de; Gordon Guyatt guyatt@mcmaster.ca

Additional material is published online only. To view please visit the journal online


Cite this as: *BMJ* 2020;370:m3379 <http://dx.doi.org/10.1136/bmj.m3379>

Intensive Care Med (2021) 47:521–537
<https://doi.org/10.1007/s00134-021-06394-2>

SYSTEMATIC REVIEW

Corticosteroids in COVID-19 and non-COVID-19 ARDS: a systematic review and meta-analysis



Dipayan Chaudhuri^{1,2} , Kiyoka Sasaki¹, Aram Karkar¹, Sameer Sharif¹, Kimberly Lewis^{1,2}, Manoj J. Mammen³, Paul Alexander², Zhikang Ye², Luis Enrique Colunga Lozano², Marie Warrer Munch⁴, Anders Perner⁴, Bin Du⁵, Lawrence Mbuagbaw^{2,6}, Waleed Alhazzani^{1,2}, Stephen M. Pastores⁷, John Marshall⁸, François Lamontagne⁹, Djillali Annane¹⁰, Gianfranco Umberto Meduri¹¹ and Bram Rochweg^{1,2,12*}

ABSTRACT
UPDATES

Clinical trials based on one RCT comparing the drug with nirmatrelvir/ritonavir. The structure of the

ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies



Steroid?

No Comment

No Recommendation in 2017

GLUCOCORTICOIDS

Our approach to the use of systemic glucocorticoid therapy in patients with ARDS is discussed in the sections below.

Indications — Glucocorticoids can be administered in the following patients:

- **Patients with ARDS who also have additional conditions that benefit from systemic glucocorticoid therapy** — This includes the following:
 - ARDS that has been precipitated by a steroid-responsive process (eg, acute eosinophilic pneumonia, organizing pneumonia). (See "Idiopathic acute eosinophilic pneumonia", section on 'Treatment' and "Cryptogenic organizing pneumonia", section on 'Treatment'.)
 - ARDS associated with refractory septic shock. (See "Glucocorticoid therapy in septic shock in adults".)
 - ARDS associated with coronavirus disease 2019 (COVID-19). (See "COVID-19: Management in hospitalized adults", section on 'Dexamethasone and other glucocorticoids'.)
 - ARDS associated with community-acquired pneumonia. (See "Treatment of community-acquired pneumonia in adults who require hospitalization", section on 'Adjunctive glucocorticoids'.)

Regimens — When glucocorticoids are used for other steroid-responsive conditions that are associated with ARDS, we follow the protocol typically used for that etiology. (See 'Indications' above.)

When glucocorticoid therapy is used for ARDS itself, commonly used regimens include:

- Dexamethasone 20 mg IV once daily for five days, then 10 mg once daily for five days [40].
- Methylprednisolone 1 mg/kg/day in divided doses for 14 days, followed by a taper for a total of 21 to 28 days (using ideal body weight dosing) [39].

Many experts prefer shorter courses based upon indirect data from patients with community-acquired pneumonia (200 mg of hydrocortisone daily for seven days) and COVID-19-related ARDS (6 mg of dexamethasone for 10 days). These protocols are discussed in detail separately (see "Treatment of community-acquired pneumonia in adults who require hospitalization", section on 'Adjunctive glucocorticoids' and "COVID-19: Management in hospitalized adults", section on 'Dexamethasone and other glucocorticoids'). Earlier tapering after cessation of mechanical ventilation is also reasonable.

The agents used (eg, methylprednisolone, hydrocortisone, dexamethasone) and dosing regimens varied somewhat in the available clinical trials. However, the efficacy of the different regimens appears to be generally similar [41].

AMERICAN THORACIC DOCUMENTS

An Update on Management of Acute Distress Syndrome An Official American Thoracic Society

Evidence summary. Corticosteroids were evaluated in 19 RCTs including 2,790 patients (20–35). Pooled analysis demonstrated that corticosteroids probably decrease mortality ($n = 17$ studies; RR, 0.84; 95% CI, 0.73–0.96; moderate certainty) (20–33) and may reduce the duration of mechanical ventilation ($n = 9$ studies; mean difference (MD), 4 d less; 95% CI, –5.5 to –2.5; low certainty) (22, 24–27, 30, 34, 35) and the length of hospital stay ($n = 4$ studies; MD, 8 d shorter; 95% CI, –13 to –3; low certainty) (22, 25, 35), although the effect on the length of ICU stay is uncertain ($n = 4$ studies; MD, 0.8 d shorter; 95% CI, –4.1 to +5.7; very low certainty) (21, 22, 25, 34). With regard to safety outcomes, corticosteroids probably increase the risk of serious hyperglycemia ($n = 6$ studies; RR, 1.11; 95% CI, 1.01–1.23; moderate certainty) (22, 23, 26, 27, 30), may increase the risk of gastrointestinal bleeding ($n = 5$ studies; RR, 1.20; 95% CI, 0.43–3.34; low certainty) (20, 23, 26), and have an uncertain effect on neuromuscular weakness ($n = 2$ studies; RR, 0.85; 95% CI, 0.62–1.18; very low certainty) (22, 25).





EXTRACORPOREAL LIFE SUPPORT

Q1 In adult patients with severe ARDS or COVID-19 does veno-venous extracorporeal membrane oxygenation (VV-ECMO) compared with conventional ventilation improve outcomes?

1 We recommend that patients with severe ARDS not due to COVID-19 as defined by the EOLIA trial eligibility criteria, should be treated with ECMO in an ECMO centre which meets defined organisational standards, adhering to a management strategy similar to that used in the EOLIA trial.



MODERATE LEVEL OF EVIDENCE

2 This recommendation applies also to severe ARDS from COVID-19.



LOW LEVEL OF EVIDENCE

Q2 In adult patients with ARDS, does extracorporeal carbon dioxide removal (ECCO₂R) compared with conventional ventilation improve outcomes?

1 We recommend against the use of ECCO₂R for the treatment of ARDS not due to COVID-19 to prevent mortality outside of randomized controlled trials.



HIGH LEVEL OF EVIDENCE

2 This recommendation applies also to severe ARDS from COVID-19.



MODERATE LEVEL OF EVIDENCE

ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies



NMBA?

NEUROMUSCULAR BLOCKING AGENTS

Q1 Does the *routine* use of a continuous infusion of neuromuscular blocking agents (NMBA) in patients with moderate to severe ARDS not due to COVID-19 or moderate to severe ARDS due to COVID-19 reduce mortality?

1 We **recommend against** the *routine* use of continuous infusions of NMBA to reduce mortality in patients with moderate to severe ARDS not due to COVID-19.

MODERATE LEVEL OF EVIDENCE

2 We are **unable to make a recommendation** for or against the *routine* use of continuous infusions of NMBA to reduce mortality in patients with moderate to severe ARDS due to COVID-19.

NO EVIDENCE

ESICM guidelines on acute respiratory



POSITIVE END-EXPIRATORY PRESSURE AND RECRUITMENT MANEUVERS

PEEP?

Q1 In patients with ARDS undergoing invasive mechanical ventilation, does routine positive end-expiratory pressure (PEEP) titration using a higher PEEP/FiO₂ strategy compared to a lower PEEP/FiO₂ strategy reduce mortality?

1 We are **unable to make a recommendation** for or against routine PEEP titration with a higher PEEP/FiO₂ strategy versus a lower PEEP/FiO₂ strategy to reduce mortality in patients with ARDS.

2 This statement applies also to ARDS from COVID-19.

Q2 In patients with ARDS undergoing invasive mechanical ventilation, does routine PEEP titration based principally on respiratory mechanics compared to PEEP titration based principally on a standardized PEEP/FiO₂ table reduce mortality?

1 We are **unable to make a recommendation** for or against PEEP titration guided principally by respiratory mechanics, compared to PEEP titration based principally on PEEP/FiO₂ strategy, to reduce mortality in patients with ARDS.

2 This statement applies also to ARDS from COVID-19.

HIGH LEVEL OF EVIDENCE

MODERATE LEVEL OF EVIDENCE

HIGH LEVEL OF EVIDENCE

MODERATE LEVEL OF EVIDENCE

AMERICAN THORACIC SOCIETY DOCUMENTS

An Update on Management of Adult Patients with Distress Syndrome

An Official Am

Evidence summary. This recommendation was based on evidence from two meta-analyses. The first was a recently published network meta-analysis comparing the relative effects of different PEEP strategies using a Bayesian analysis framework; 18 RCTs with 4,646 participants with moderate to severe ARDS were included (75). Compared with lower PEEP, **higher PEEP** without LRMs probably **reduced mortality** ($n = 4$ trials, 1,162 patients; RR, 0.77; 95% credible interval [CrI],

0.60–0.96; high certainty) (76–79), improved **oxygenation** (MD Pa_{O₂}/F_{I_{O₂} ratio 63.7 mm Hg higher; 95% CrI, 51.5–75.9 mm Hg; high certainty), and possibly **increased ventilator-free days** (MD, 1.3 d more; 95% CI, 2.5 d fewer to 4.3 d more; low certainty). The impact on barotrauma was uncertain (RR, 1.13; 95% CrI, 0.87–1.86; very low certainty). Compared with higher PEEP without LRMs, higher PEEP with prolonged LRMs probably increased mortality (RR, 1.37; 95% CrI, 1.04–1.81; moderate certainty), whereas strategies involving higher PEEP with brief LRMs or esophageal pressure-guided PEEP titration may have no effect on mortality (RR, 1.07; 95% CrI, 0.79–1.48; low certainty; and RR, 1.00; 95% CrI, 0.65–1.54; moderate certainty, respectively). The second meta-analysis was a prior meta-analysis of individual patient data that included three RCTs with 2,299 patients with ARDS and demonstrated that higher PEEP probably **improved survival** compared with lower PEEP in patients with moderate to severe ARDS (RR, 0.90; 95% CI, 0.81–1.00; $P = 0.049$), but possibly **increased mortality in patients with mild ARDS** (adjusted RR, 1.29; 95% CI, 0.91–1.83; $P = 0.02$) (80).}



NIH NHLBI ARDS Clinical Network
Mechanical Ventilation Protocol Summary

INCLUSION CRITERIA: Acute onset of

1. $PaO_2/FiO_2 \leq 300$ (corrected for altitude)
2. Bilateral (patchy, diffuse, or homogeneous) infiltrates consistent with pulmonary edema
3. No clinical evidence of left atrial hypertension

PART I: VENTILATOR SETUP AND ADJUSTMENT

1. Calculate predicted body weight (PBW)
Males = $50 + 2.3 [\text{height (inches)} - 60]$
Females = $45.5 + 2.3 [\text{height (inches)} - 60]$
2. Select any ventilator mode
3. Set ventilator settings to achieve initial $V_T = 8 \text{ ml/kg PBW}$
4. Reduce V_T by 1 ml/kg at intervals ≤ 2 hours until $V_T = 6 \text{ ml/kg PBW}$.
5. Set initial rate to approximate baseline minute ventilation (not $> 35 \text{ bpm}$).
6. Adjust V_T and RR to achieve pH and plateau pressure goals below.

ARDS Network is cited as the source.

OXYGENATION GOAL: PaO_2 55-80 mmHg or SpO_2 88-95%

Use a minimum PEEP of 5 cm H_2O . Consider use of incremental FiO_2 /PEEP combinations such as shown below (not required) to achieve goal.

Lower PEEP/higher FiO_2

FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12

FiO_2	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	14	14	14	16	18	18-24

Higher PEEP/lower FiO_2

FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5
PEEP	5	8	10	12	14	14	16	16

FiO_2	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	18	20	22	22	22	24

PLATEAU PRESSURE GOAL: $\leq 30 \text{ cm H}_2O$

Check Pplat (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or V_T .

If Pplat $> 30 \text{ cm H}_2O$: decrease V_T by 1ml/kg steps (minimum = 4 ml/kg).

If Pplat $< 25 \text{ cm H}_2O$ and $V_T < 6 \text{ ml/kg}$, increase V_T by 1 ml/kg until Pplat $> 25 \text{ cm H}_2O$ or $V_T = 6 \text{ ml/kg}$.

If Pplat < 30 and breath stacking or dys-synchrony occurs: may increase V_T in 1ml/kg increments to 7 or 8 ml/kg if Pplat remains $\leq 30 \text{ cm H}_2O$.





ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping



ar **Q3** In patients with ARDS undergoing invasive mechanical ventilation, does use of prolonged high-pressure recruitment maneuvers (RMs), compared to not using prolonged high-pressure RMs, reduce mortality?

1 We **recommend against** use of prolonged high-pressure RMs (defined as airway pressure maintained ≥ 35 cmH₂O for at least one minute) to reduce mortality of patients with ARDS.



MODERATE LEVEL OF EVIDENCE

2 This recommendation applies also to ARDS from COVID-19.



LOW LEVEL OF EVIDENCE

Q4 In patients with ARDS undergoing invasive mechanical ventilation, does *routine* use of brief high-pressure RMs, compared to no use of brief high-pressure RMs, reduce mortality?

1 We **suggest against routine use of brief high-pressure RMs** (defined as airway pressure maintained ≥ 35 cmH₂O for less than one minute) to reduce mortality in patients with ARDS.



HIGH LEVEL OF EVIDENCE

2 This suggestion applies also to ARDS from COVID-19.



MODERATE LEVEL OF EVIDENCE

Q1 In non-mechanically ventilated patients with acute respiratory failure (ARHF) not due to cardiogenic pulmonary edema, does high flow nasal oxygen (HFNO) compared to conventional oxygen therapy reduce mortality or intubation?

Q1 In adult patients with ARDS and COVID-19 related ARDS, does low tidal volume ventilation compared to a higher tidal volume strategy reduce mortality?

POSITIVE END-EXPIRATORY PRESSURE AND RECRUITMENT MANEUVERS

1 W
ca
co

Q1 In patients with ARDS undergoing invasive mechanical ventilation, does routine positive end-expiratory pressure (PEEP) titration using a higher PEEP/ FiO_2 strategy compared to a lower PEEP/ FiO_2 strategy reduce mortality?

2 Th

1 We are **unable to make a recommendation** for or against routine PEEP titration with a higher PEEP/ FiO_2 strategy versus a lower PEEP/ FiO_2 strategy to reduce mortality in patients with ARDS.

? HIGH LEVEL OF EVIDENCE

3 W
CO

4 Th

2 This statement applies also to ARDS from COVID-19.

? MODERATE LEVEL OF EVIDENCE

Q2 In
pu
no

Q2 In patients with ARDS undergoing invasive mechanical ventilation, does routine PEEP titration based principally on respiratory mechanics compared to PEEP titration based principally on a standardized PEEP/ FiO_2 table reduce mortality?

1 W
co
or
pu

1 We are **unable to make a recommendation** for or against PEEP titration guided principally by respiratory mechanics, compared to PEEP titration based principally on PEEP/ FiO_2 strategy, to reduce mortality in patients with ARDS.

? HIGH LEVEL OF EVIDENCE

2 W
of

3 No
co

2 This statement applies also to ARDS from COVID-19.

? MODERATE LEVEL OF EVIDENCE



PRONE POSITIONING

Q1 In intubated patients with ARDS, does prone position compared to supine position reduce mortality?

1 We **recommend** using prone position as compared to supine position for patients with moderate-severe ARDS (defined as $\text{PaO}_2/\text{FiO}_2 < 150$ mmHg and $\text{PEEP} \geq 5$ cmH_2O , despite optimization of ventilation settings) to reduce mortality.



HIGH LEVEL OF EVIDENCE

2 This recommendation applies also to ARDS from COVID-19.



MODERATE LEVEL OF EVIDENCE

Q2 In patients started to

1 We **recom** mechanical which low $\text{PaO}_2/\text{FiO}_2$ sessions (

2 This recom

Q3 In non intubated patients with AHRF, does awake prone positioning (APP) as compared to supine positioning reduce intubation or mortality?

1 We **suggest** awake prone positioning as compared to supine positioning for non-intubated patients with COVID-19-related AHRF to reduce intubation.



LOW LEVEL OF EVIDENCE

2 We are **unable to make a recommendation** for or against APP for non-intubated patients with COVID-19-related AHRF to reduce mortality.



MODERATE LEVEL OF EVIDENCE

3 We are **unable to make a recommendation** for patients with AHRF failure not due to COVID-19.



NO EVIDENCE

AMERICAN THORACIC SOCIETY DOCUMENTS

An Update on Management of Distress Syndrome An Official American Thoracic Society Statement

Justification and implementation considerations. Although higher PEEP was consistently associated with lower mortality in patients with moderate to severe ARDS, the panel issued a conditional recommendation because of a high level of heterogeneity among higher PEEP strategies in the included RCTs. For patients with mild ARDS, there were insufficient data to make a recommendation on PEEP strategy because these patients were excluded from the network meta-analysis, but there appears to be no benefit of high PEEP versus low PEEP, and there is a potential trend toward harm (80). With regard to prolonged LRMs, the





대한중환자의학회 부산·울산·경남지회

제7회 대한중환자의학회 부산·울산·경남지회

연수강좌

일자: 2024년 6월 8일 (토요일)

장소: 부산대학교병원 E동 9층 대강당

평점: 대한의사협회 및 중환자의학 세부전문의 3평점

프로그램

08:50-09:00 — 인사말

지회장: 동아대학교병원 마취통증의학과 이승철

SESSION 1 — 좌장: 양산부산대학교병원 호흡기내과 김윤성

09:00-09:30 — Update of guideline : Airway management

부산대학교병원 호흡기알레르기내과 류완호

09:30-10:00 — Update of guideline : fever in critically ill patients

창원경상국립대학교병원 호흡기내과 허이레

10:00-10:30 — Recent update of ARDS guideline

해운대백병원 호흡기내과 장지훈

SESSION 2 — 좌장: 동아대학교병원 마취통증의학과 이승철

11:00-11:30 — The current status of sepsis in Korea and the latest trends
in sepsis treatment

서울아산병원 호흡기내과 현동곤

11:30-12:00 — Clinical research utilizing National Health Insurance Data

분당서울대학교병원 마취통증의학과 송인애

12:00-12:30 — Nutritional therapy in critically ill patients

삼성서울병원 중환자의학과 고령은

12:30-12:40 — 경품추첨 및 폐회



대한중환자의학회 부산·울산·경남지회 2019년 제4회 연수강좌

일시: 2019년 5월 28일 (토요일) 장소: 부산대학교병원 오송기반(4동) 1층 대강당

일시: 2019년 5월 1일(토) 장소: 부산대학교병원 오송기반(5동) 5층 대강당 주최: 대한중환자의학회 부산·울산·경남지회



2024년 6월 8일



대한중환자의학회 부산·울산·경남지회

제7회 대한중환자의학회
부산·울산·경남지회

2024

연수강좌

일자: 2024년 6월 8일 (토요일)

장소: 부산대학교병원 E동 9층 대강당

평점: 대한의사협회 및 중환자의학 세부전문의 3평점

