I Can Fix The Lung with the Ventilator?

Pro/Con Debate

St. Louis Shock Symposium

November 20th 2021

Pratik Sinha MB ChB PhD FFICM FRCEM

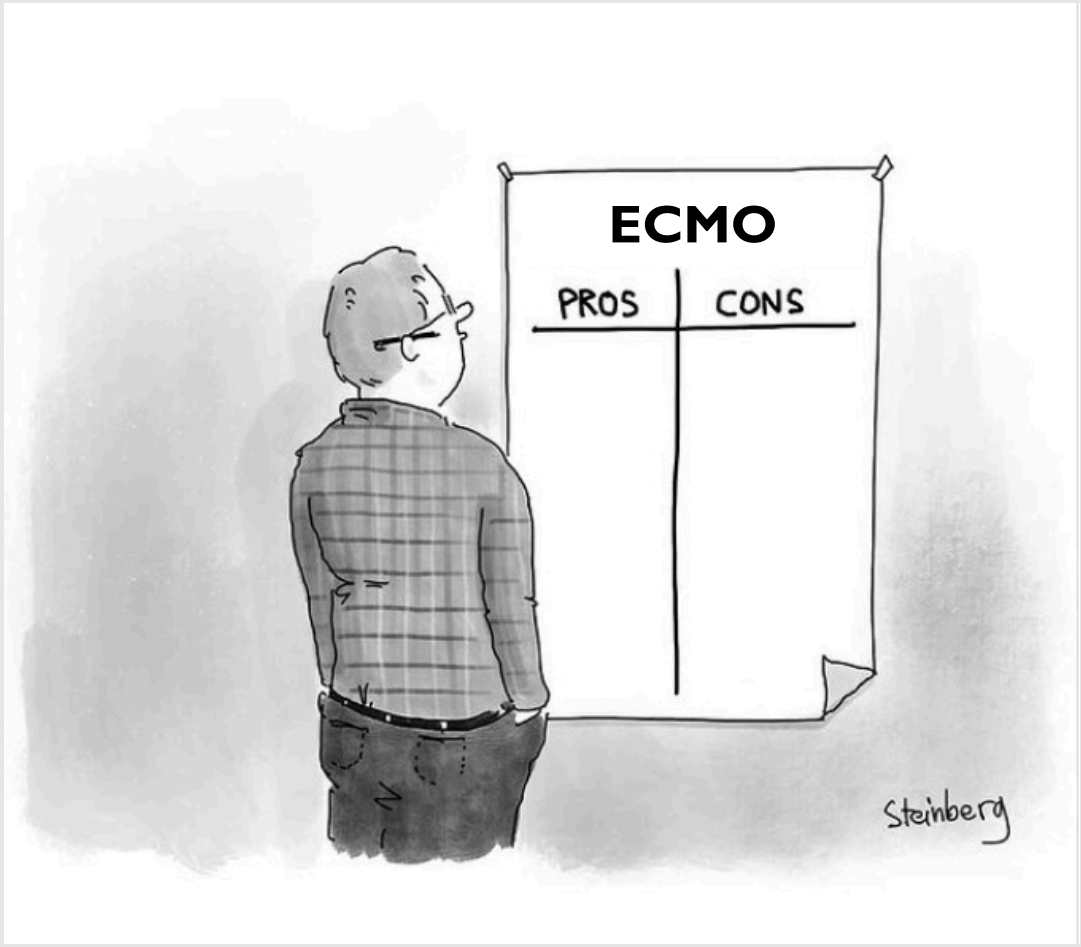
Assistant Professor

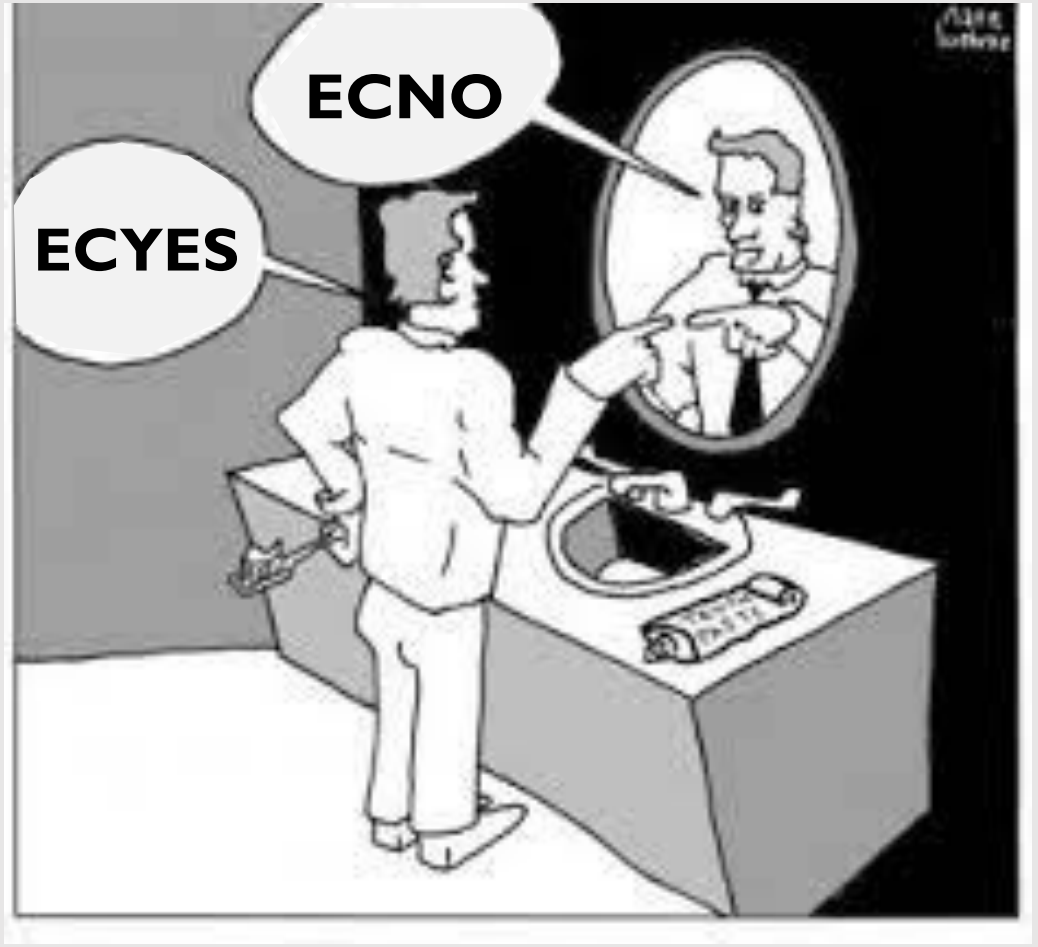
Department of Anesthesia

Washington University

~~I have no disclosures~~

I am a big proponent of ECMO in ARDS


ECMO
PROS
CONS
Steinberg

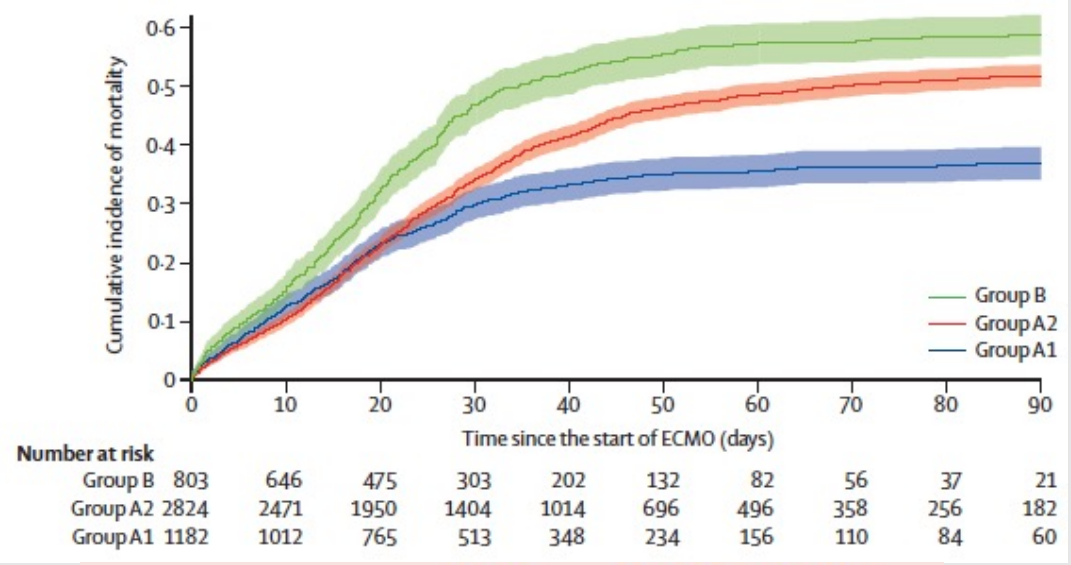

ECNO
ECYES


ECMO
PROS
Cool
CONS
Bleeding
Pneumothorax
Thrombosis
Expensive
Definitive evidence of efficacy lacking

Extracorporeal membrane oxygenation for COVID-19: evolving outcomes from the international Extracorporeal Life Support Organization Registry

Lancet 2021; 398: 1230–38

Ryan P Barbaro, Graeme MacLaren*, Philip S Boonstra, Alain Combes, Cara Agerstrand, Gail Annich, Rodrigo Diaz, Eddy Fan, Katarzyna Hryniewicz, Roberto Lorusso, Matthew L Paden, Christine M Stead, Justyna Swol, Theodore J Iwashyna†, Arthur S Slutsky†, Daniel Brodie†, for the Extracorporeal Life Support Organization*

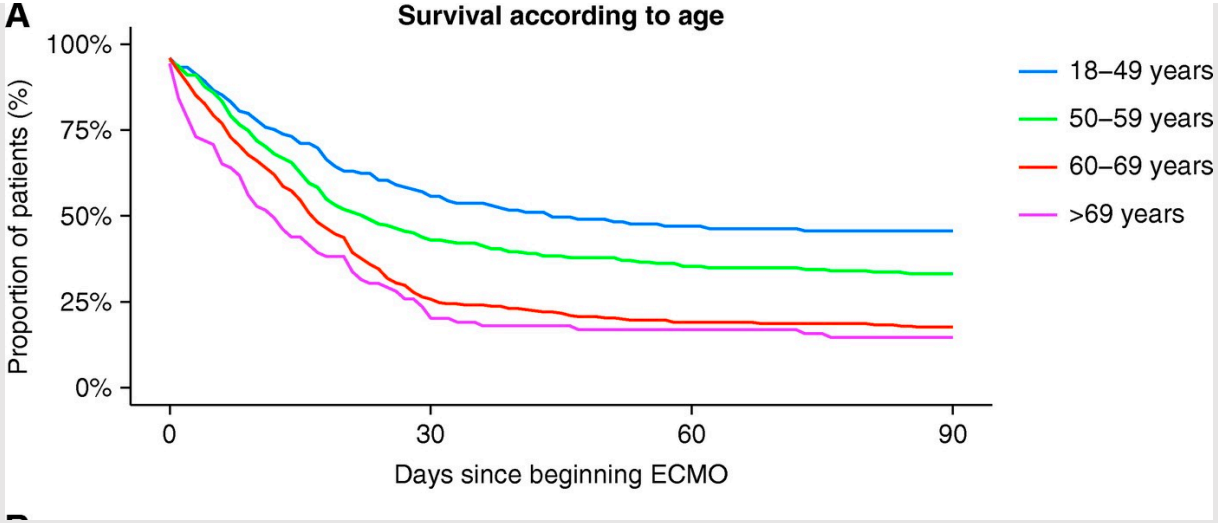


	Group A1	Group A2	Group B
Last known patient status	1182	2824	806
Discharged			
To home or acute rehabilitation	376 (32%)	623 (22%)	190 (24%)
To long-term acute care or unspecified location	128 (11%)	329 (12%)	71 (9%)
To another hospital	212 (18%)	301 (11%)	47 (6%)

American Journal of Respiratory and Critical Care Medicine

High In-Hospital Mortality Rate in Patients with COVID-19 Receiving Extracorporeal Membrane Oxygenation in Germany: A Critical Analysis

Christian Karagiannidis [1,2]*, Stephan Strassmann [1,2], Michaela Merten [1,2], Thomas Bein [3], Wolfram Windisch [1,2], Patrick Meybohm [4], and Steffen Weber-Carstens [5]



Objectives

- Cost of mechanical ventilation in severe ARDS
- Advances in ventilation management in ARDS
- The future of ARDS ventilation

Ibsen and the Polio Epidemic and the birth of Intensive Care

TABLE III—MORTALITY-RATES

Group	Period of admission	No. of cases	Died	Died within three days
I	July 24–Aug. 25	31	27 (87 %)	19 (70 %)
II	Aug. 26–Sept. 8	50	26 (52 %)	7 (27 %)
III	Sept. 8–Sept. 23	50	24 (48 %)	8 (33 %)
IV	Sept. 23–Oct. 5	50	19 (38 %)	10 (53 %)
V	Oct. 6–Oct. 21	50	13 (26 %)	7 (54 %)
VI	Oct. 21–Nov. 6	50	18 (36 %)	10 (55 %)
	Total II–VI	250	100 (40 %)	42 (42 %)

NNT = 2

Lassen Lancet 1953

Does Mechanical Ventilation save lives?

Yes

Can I "**Fix**" the ARDS Lungs with a Ventilator?

NO

Can I "**Fix**" the ARDS Lungs with ECMO?

NO

Aims of Ventilatory Management in ARDS

- Provide the **optimal** physiological conditions using the **least aggressive** interventions to allow the **greatest** recovery [patient-centric goals]
    - Scope of statement: Acute- prevent death; Chronic- return to full function

- **Treat the cause**

- Mindful- what is the cost of intervention?

Cost of Mechanical Ventilation

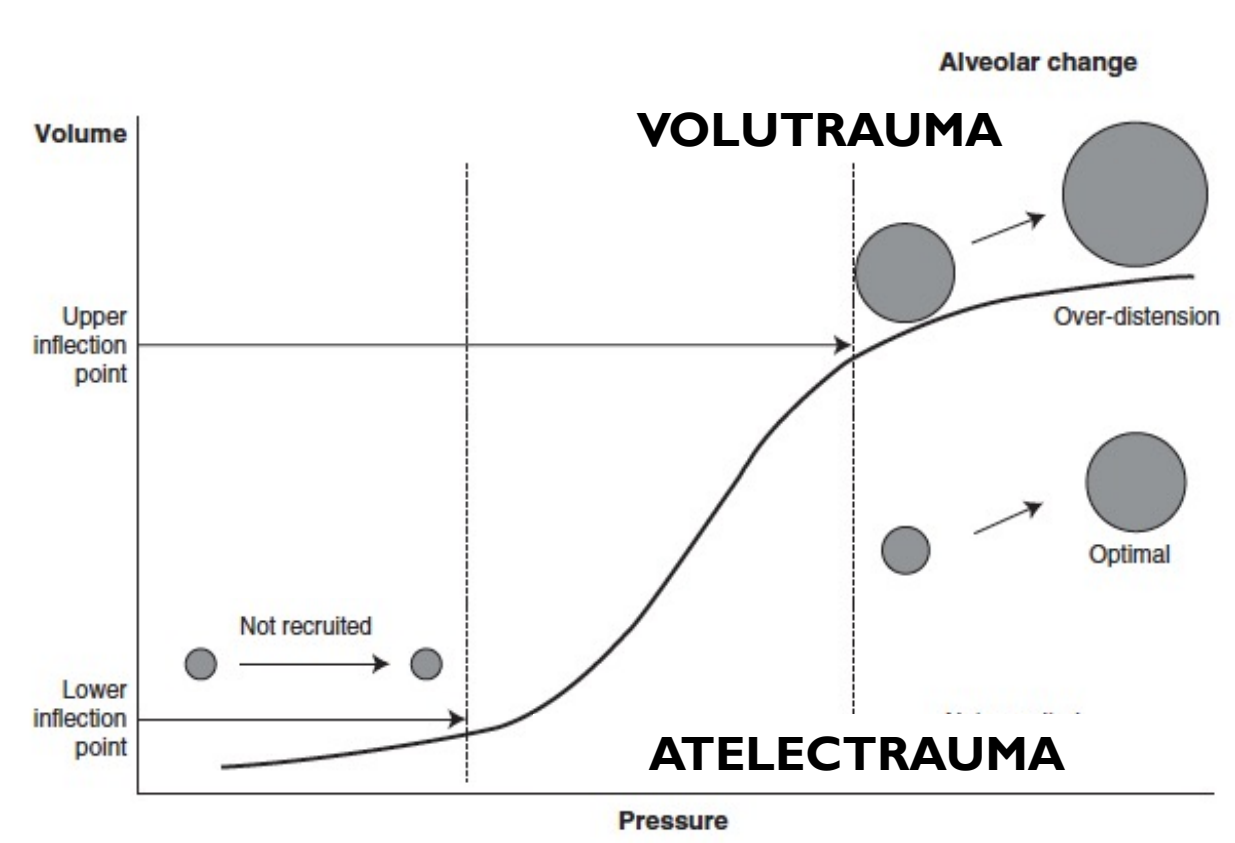
British Journal of Anaesthesia 101 (4): 446–57 (2008)
doi:10.1093/bja/aen240

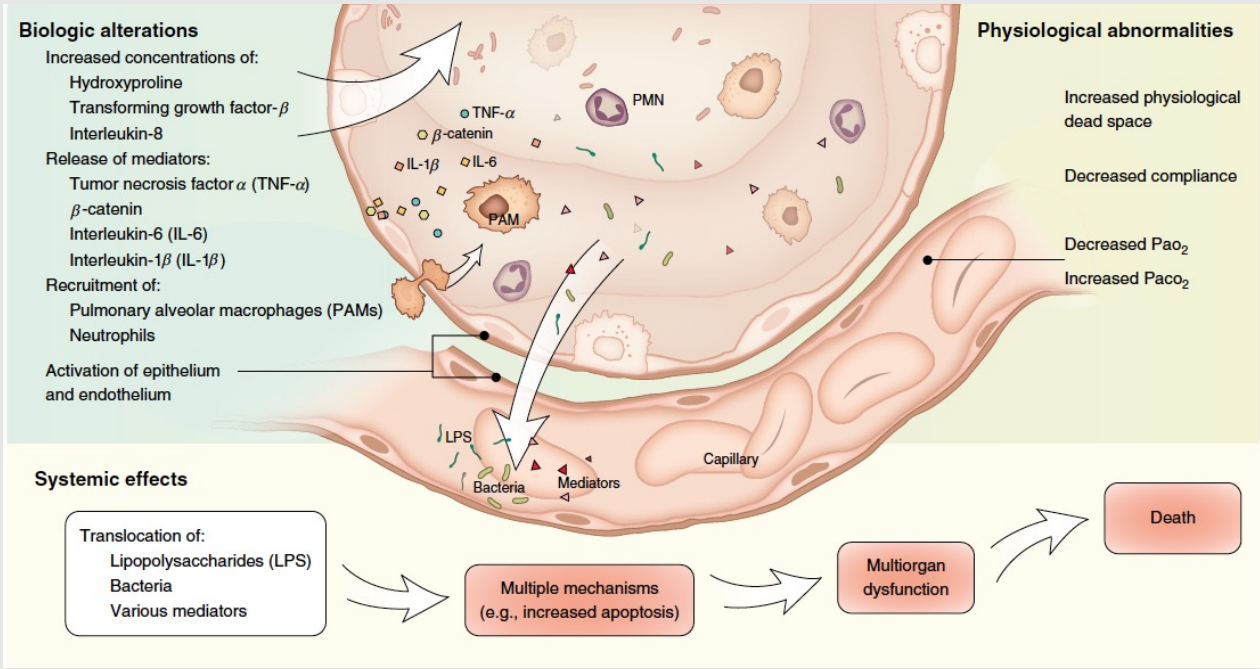
BJA

REVIEW ARTICLE

Positive pressure ventilation: what is the real cost?

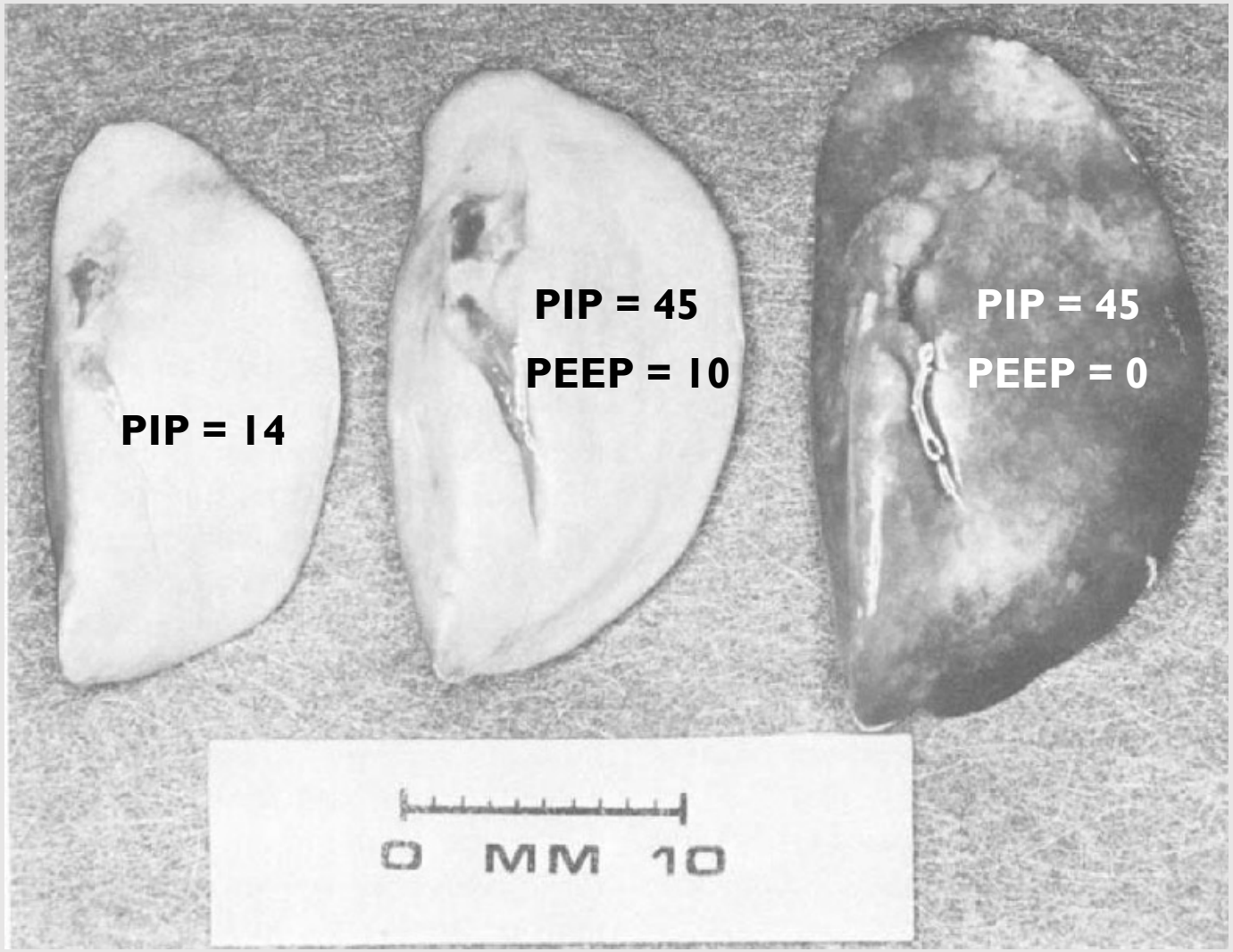
N. Soni* and P. Williams





Slutsky AJRCCM 2015

VILI



Webb and Thierney AJRD 1974

Other Cots of Positive Pressure Ventilation?

- Barotrauma
- Cardiovascular
  - Reduced venous return
  - Increased SVR
  - Right heart failure
- VAP
  - Reduced lymphatic drainage
- O_2 Toxicity

Can I Minimise Damage to the ARDS Lungs with a Ventilator?

Pro/Con Debate

St. Louis Shock Symposium

November 20th 2021

Pratik Sinha MB ChB PhD FFICM FRCEM

Assistant Professor

Department of Anesthesia

Washington University

Advances in ventilation management in ARDS

NARRATIVE REVIEW

Current and evolving standards of care for patients with ARDS

Mario Menk[1,2], Elisa Estenssoro[3,4], Sarina K. Sahetya[5], Ary Serpa Neto[6,7,8], Pratik Sinha[9], Arthur S. Slutsky[10], Charlotte Summers[11], Takeshi Yoshida[12], Thomas Bein[13] and Niall D. Ferguson[14,15*]

Intensive Care Med
https://doi.org/10.1007/s00134-020-06299-6

Lung Protective Ventilation

n = 432 **6.2** mL/KG

n = 439 **11.8** mL/KG

The New England Journal of Medicine

VOLUME 342 MAY 4, 2000 NUMBER 18

VENTILATION WITH LOWER TIDAL VOLUMES AS COMPARED WITH TRADITIONAL TIDAL VOLUMES FOR ACUTE LUNG INJURY AND THE ACUTE RESPIRATORY DISTRESS SYNDROME

THE ACUTE RESPIRATORY DISTRESS SYNDROME NETWORK*

VARIABLE	GROUP RECEIVING LOWER TIDAL VOLUMES	GROUP RECEIVING TRADITIONAL TIDAL VOLUMES	P VALUE
Death before discharge home and breathing without assistance (%)	31.0	39.8	0.007
Breathing without assistance by day 28 (%)	65.7	55.0	<0.001
No. of ventilator-free days, days 1 to 28	12±11	10±11	0.007
Barotrauma, days 1 to 28 (%)	10	11	0.43
No. of days without failure of nonpulmonary organs or systems, days 1 to 28	15±11	12±11	0.006

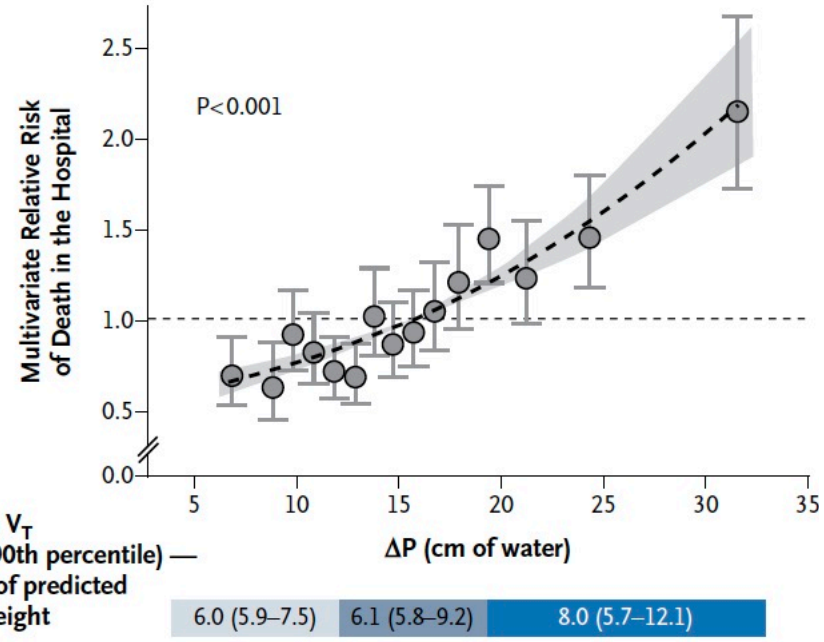
Low Tidal Volume is the Standard of Practice in ARDS

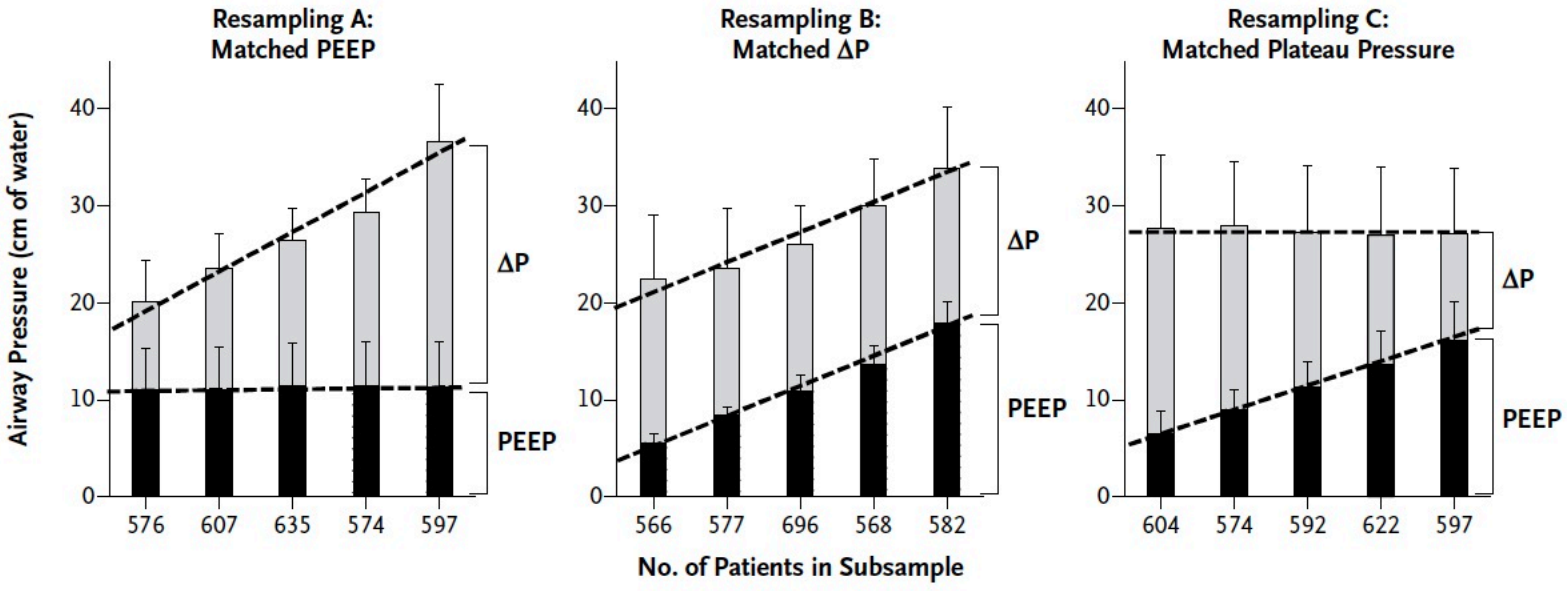
Driving Pressure and Survival in the Acute Respiratory Distress Syndr

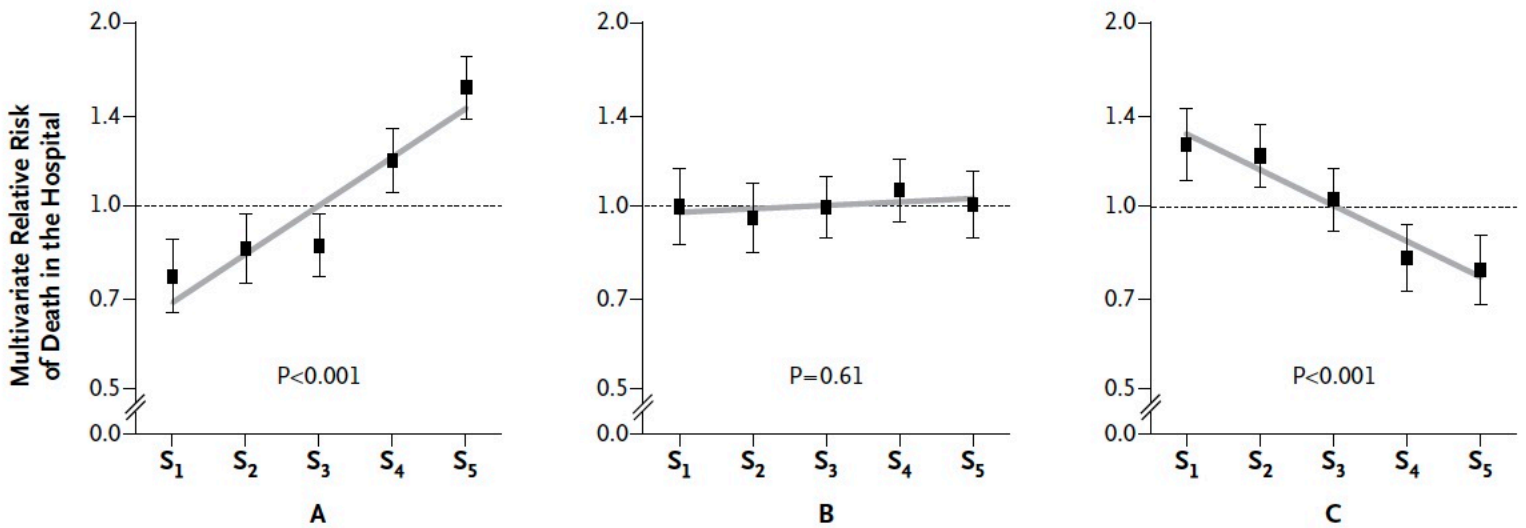
Marcelo B.P. Amato, M.D., Maureen O. Meade, M.D., Arthu
Laurent Brochard, M.D., Eduardo L.V. Costa, M.D., David A.
Thomas E. Stewart, M.D., Matthias Briel, M.D., Daniel Talm
Alain Mercat, M.D., Jean-Christophe M. Richard
Carlos R.R. Carvalho, M.D., and Roy G. Brower,

N ENGL J MED 372;8 NEJM.ORG FEBRUARY 19, 2015

DP should be maintained around 15-18 cmH_2O







Also Rans

- PEEP titration- No current evidence for specific strategy
- High frequency oscillation- out
- Open lung ventilation- out
- APRV- No RCT evidence

Negative Trials:

- High PEEP vs Low PEEP (ALVEOLI NEMJ 2006)
- Open Lung Ventilation (ART JAMA 2017)
- Oesophageal Pressure-Guided ventilation (EPVENT-2 JAMA 2019)
- High-Frequency oscillation (OSCAR and OSCILLATE NEMJ 2013)

Adjuvant Approaches

Prone-Positioning: PROSEVA

Prone-positioning is the Standard of Practice in moderate-severe ARDS

$PaO_2/FiO_2 \leq$ 150 mmHg

41% vs 24%

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 6, 2013 VOL. 368 NO. 23

Prone Positioning in Severe Acute Respiratory Distress Syndrome

Claude Guérin, M.D., Ph.D., Jean Reignier, M.D., Ph.D., Jean-Christophe Richard, M.D., Ph.D., Pascal Beuret, M.D., Arnaud Gacouin, M.D., Thierry Boulain, M.D., Emmanuelle Mercier, M.D., Michel Badet, M.D., Alain Mercat, M.D., Ph.D., Olivier Baudin, M.D., Marc Clavel, M.D., Delphine Chatellier, M.D., Samir Jaber, M.D., Ph.D., Sylvène Rosselli, M.D., Jordi Mancebo, M.D., Ph.D., Michel Sirodot, M.D., Gilles Hilbert, M.D., Ph.D., Christian Bengler, M.D., Jack Richecoeur, M.D., Marc Gainnier, M.D., Ph.D., Frédérique Bayle, M.D., Gael Bourdin, M.D., Véronique Leray, M.D., Raphaele Girard, M.D., Loredana Baboi, Ph.D., and Louis Ayzac, M.D., for the PROSEVA Study Group*

Table 3. Primary and Secondary Outcomes According to Study Group.*

Outcome	Supine Group (N=229)	Prone Group (N=237)	Hazard Ratio or Odds Ratio with the Prone Position (95% CI)	P Value
Mortality — no. (% [95% CI])				
At day 28				
Not adjusted	75 (32.8 [26.4–38.6])	38 (16.0 [11.3–20.7])	0.39 (0.25–0.63)	<0.001
Adjusted for SOFA score†			0.42 (0.26–0.66)	<0.001
At day 90				
Not adjusted	94 (41.0 [34.6–47.4])	56 (23.6 [18.2–29.0])	0.44 (0.29–0.67)	<0.001
Adjusted for SOFA score†			0.48 (0.32–0.72)	<0.001
Successful extubation at day 90 — no./total no. (% [95% CI])	145/223 (65.0 [58.7–71.3])	186/231 (80.5 [75.4–85.6])	0.45 (0.29–0.70)	<0.001
Ventilation-free days				
At day 28	10±10	14±9		<0.001
At day 90	43±38	57±34		<0.001

NM Blockade: ACURSYS

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 16, 2010 VOL. 363 NO. 12

Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome

Laurent Papazian, M.D., Ph.D., Jean-Marie Forel, M.D., Arnaud Gacouin, M.D., Christine Penot-Ragon, Pharm.D., Gilles Perrin, M.D., Anderson Loundou, Ph.D., Samir Jaber, M.D., Ph.D., Jean-Michel Arnal, M.D., Didier Perez, M.D., Jean-Marie Seghboyan, M.D., Jean-Michel Constantin, M.D., Ph.D., Pierre Courant, M.D., Jean-Yves Lefrant, M.D., Ph.D., Claude Guérin, M.D., Ph.D., Gwenaël Prat, M.D., Sophie Morange, M.D., and Antoine Roch, M.D., Ph.D., for the ACURASYS Study Investigators*

$PaO_2/FiO_2 \leq$ 150 mmHg

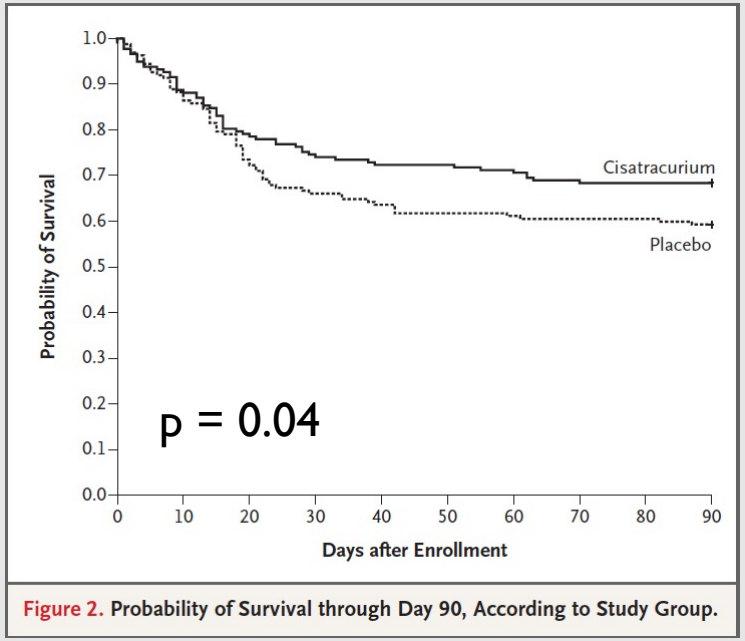


Figure 2. Probability of Survival through Day 90, According to Study Group.

Table 3. Secondary Outcomes, According to Study Group.*

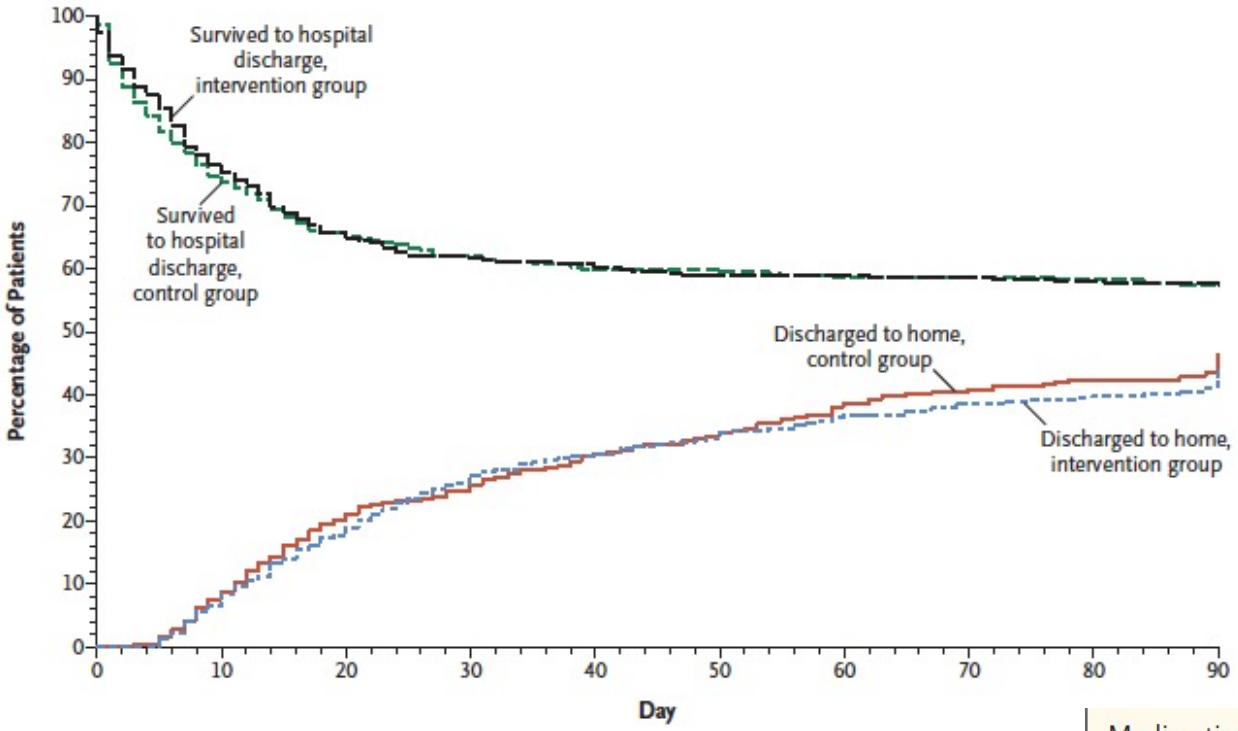
Outcome	Cisatracurium (N=177)	Placebo (N=162)	Relative Risk with Cisatracurium (95% CI)	P Value
Death — no. (% [95% CI])				
At 28 days	42 (23.7 [18.1–30.5])	54 (33.3 [26.5–40.9])	0.71 (0.51–1.00)	0.05
In the ICU	52 (29.4 [23.2–36.5])	63 (38.9 [31.7–46.6])	0.76 (0.56–1.02)	0.06
In the hospital	57 (32.2 [25.8–39.4])	67 (41.4 [34.1–49.1])	0.78 (0.59–1.03)	0.08
No. of ventilator-free days†				
From day 1 to day 28	10.6±9.7	8.5±9.4		0.04
From day 1 to day 90	53.1±35.8	44.6±37.5		0.03

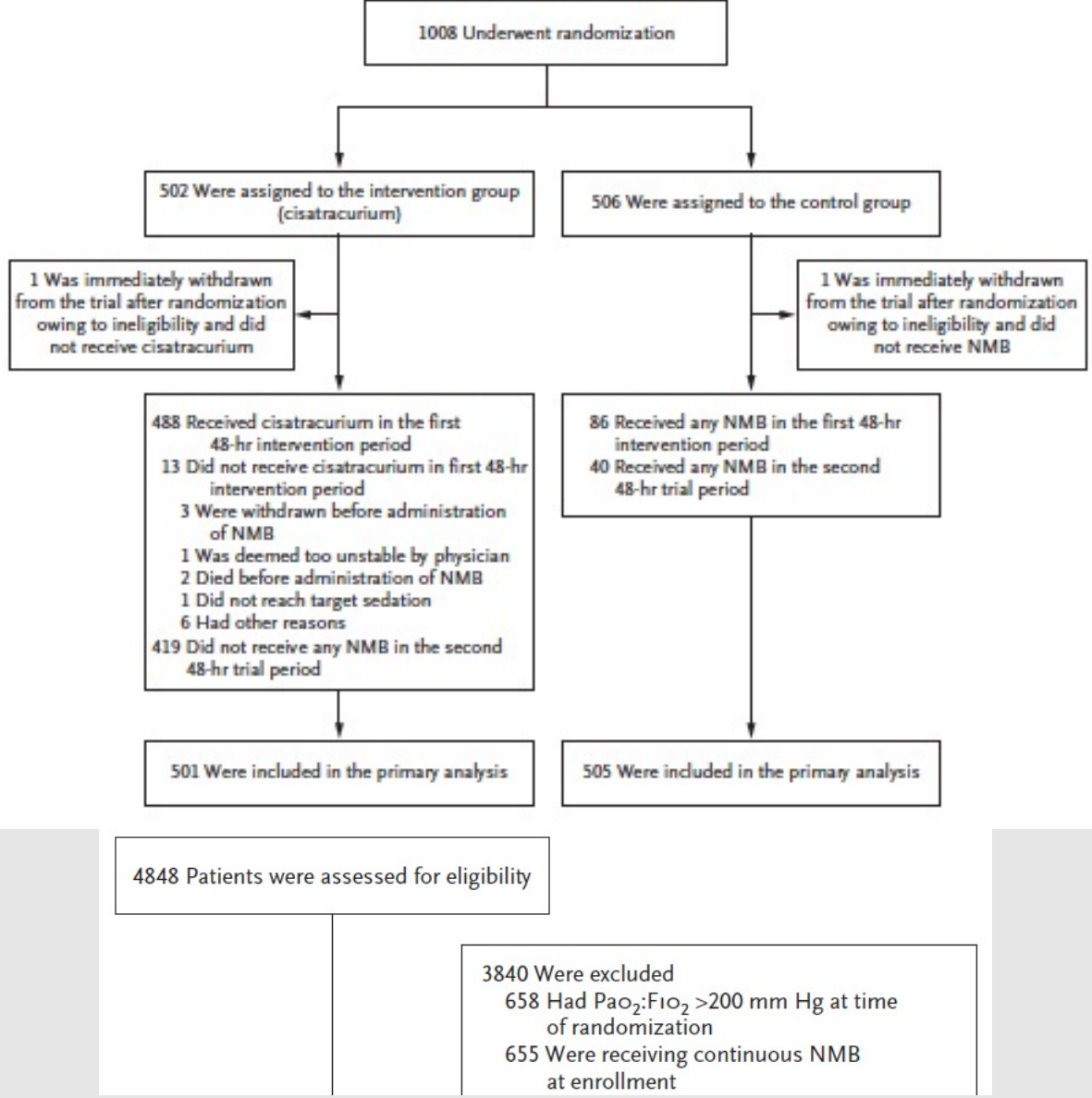
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 23, 2019 VOL. 380 NO. 21

Early Neuromuscular Blockade in the Acute Respiratory Distress Syndrome

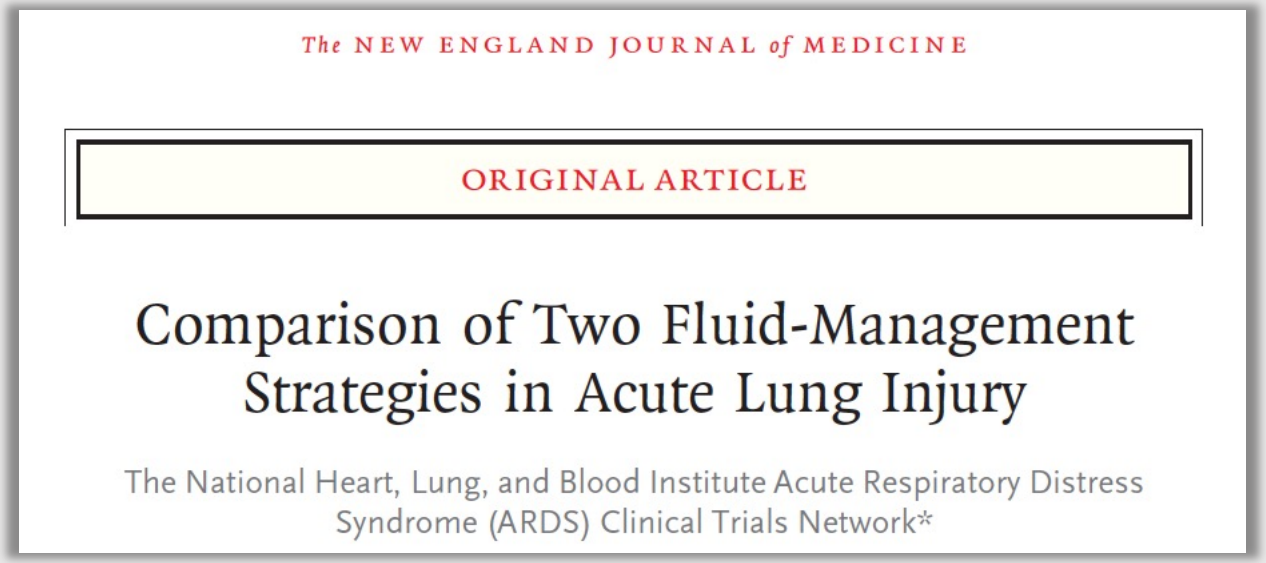
The National Heart, Lung, and Blood Institute PETAL Clinical Trials Network*





Median time from eligibility to randomization (IQR) — hr	8.2 (4.0–16.4)	6.8 (3.3–14.5)
Neuromuscular blockade use between meeting inclusion criteria and randomization — no./total no. (%)	55/484 (11.4)	50/484 (10.3)

Conservative vs Liberal Fluid Therapy



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Comparison of Two Fluid-Management Strategies in Acute Lung Injury

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*

n = 503

-0.1L

(Day 7)

n = 497

+ 7L

(Day 7)

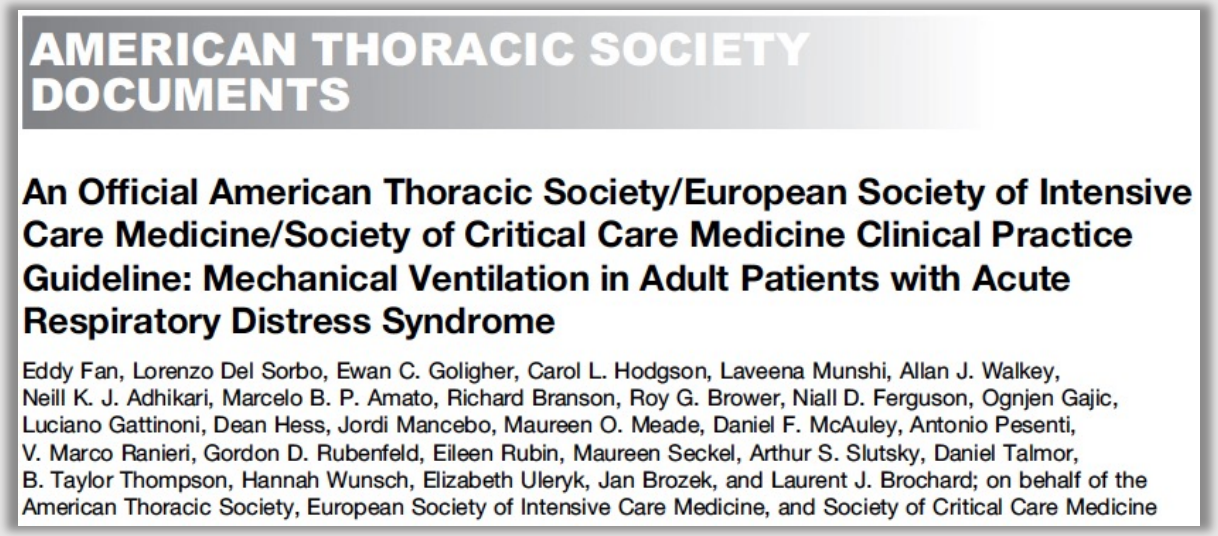
Outcome	Conservative Strategy	Liberal Strategy	P Value
Death at 60 days (%)	25.5	28.4	0.30
Ventilator-free days from day 1 to day 28†	14.6±0.5	12.1±0.5	<0.001
ICU-free days†			
Days 1 to 7	0.9±0.1	0.6±0.1	<0.001
Days 1 to 28	13.4±0.4	11.2±0.4	<0.001

Some Evidence to Suggest Conservative Fluid Management May be Beneficial

Also Rans

- Recruitment Maneuvers- No evidence
- Inhaled vasodilators- Make the PaO_2 look better
  - Think about why and what is the cost?
- Corticosteroids- some evidence but more needed

Summary of Supportive Care



AMERICAN THORACIC SOCIETY DOCUMENTS

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

Eddy Fan, Lorenzo Del Sorbo, Ewan C. Goligher, Carol L. Hodgson, Laveena Munshi, Allan J. Walkey, Neill K. J. Adhikari, Marcelo B. P. Amato, Richard Branson, Roy G. Brower, Niall D. Ferguson, Ognjen Gajic, Luciano Gattinoni, Dean Hess, Jordi Mancebo, Maureen O. Meade, Daniel F. McAuley, Antonio Pesenti, V. Marco Ranieri, Gordon D. Rubenfeld, Eileen Rubin, Maureen Seckel, Arthur S. Slutsky, Daniel Talmor, B. Taylor Thompson, Hannah Wunsch, Elizabeth Uleryk, Jan Brozek, and Laurent J. Brochard; on behalf of the American Thoracic Society, European Society of Intensive Care Medicine, and Society of Critical Care Medicine

Intervention	Recommendation	My Practice
Low Tidal Volume Ventilation		
Prone-Positioning		
High-Frequency Ventilation		
Higher PEEP vs Lower PEEP		
Recruitment Maneuvers		
ECMO		
Neuromuscular Blockade		

The Future of Ventilation

Avoid Ventilation

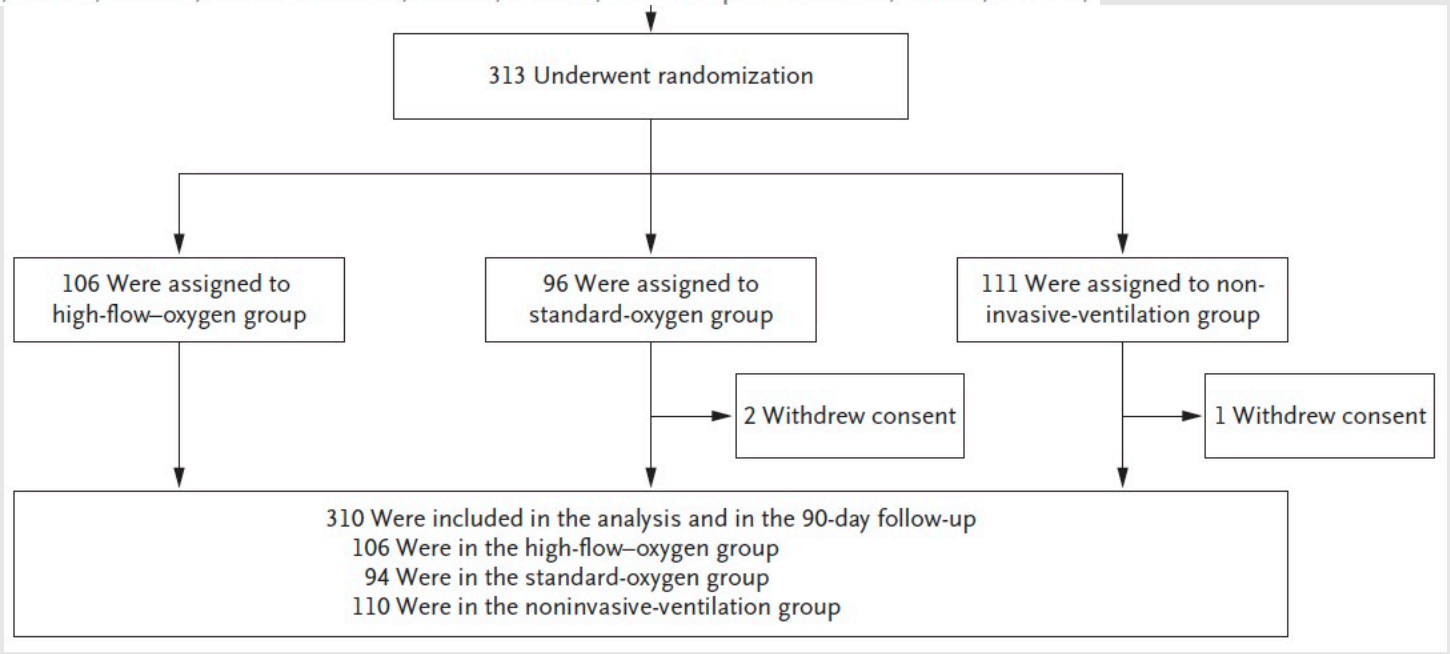
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 4, 2015 VOL. 372 NO. 23

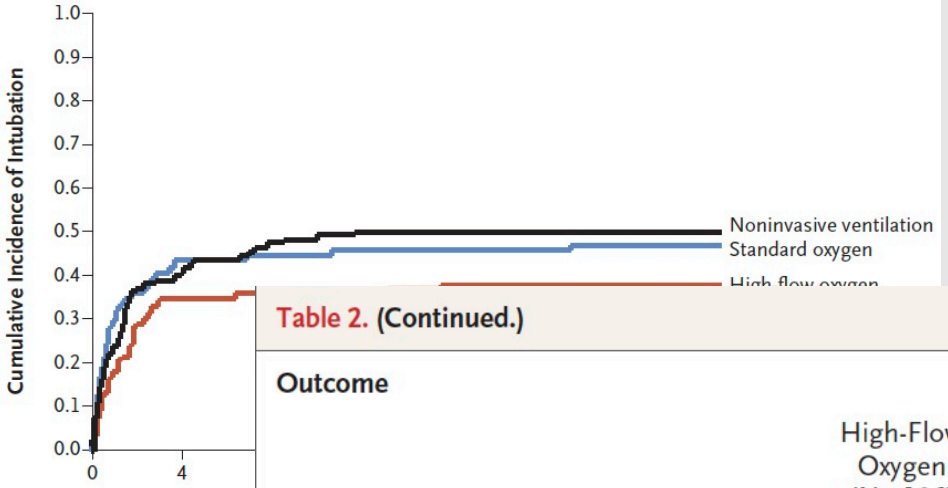
High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure

Jean-Pierre Frat, M.D., Arnaud W. Thille, M.D., Ph.D., Alain Mercat, M.D., Ph.D., Christophe Girault, M.D., Ph.D.,

Consecutive patients who were 18 years of age or older were enrolled if they met all four of the following criteria: a respiratory rate of more than 25 breaths per minute, a ratio of the partial pressure of arterial oxygen (PaO_2) to the FIO_2 of 300 mm Hg or less while the patient was breathing oxygen at a flow rate of 10 liters per minute or more for at least 15 minutes, a partial pressure of arterial carbon dioxide ($PaCO_2$) not higher than 45 mm Hg, and an absence of clinical history of underlying chronic respiratory failure. FIO_2 was measured

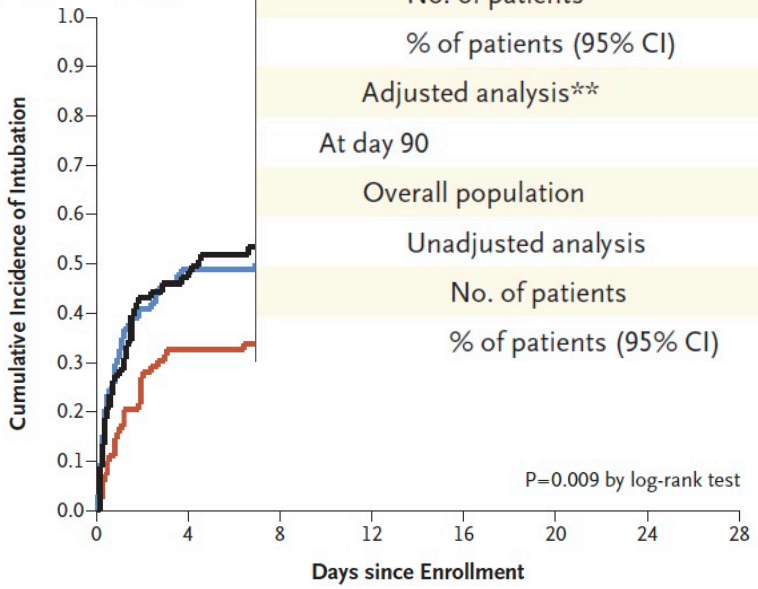


A Overall Population



No. at Risk		
High-flow oxygen	106	68
Standard oxygen	94	52
Noninvasive ventilation	110	64

B Patients with a Pao_2:Fio_2 ≤200 mm Hg



No. at Risk								
High-flow oxygen	83	55	54	54	53	53	53	53
Standard oxygen	74	37	35	34	34	34	33	33
Noninvasive ventilation	81	41	34	32	32	32	32	32

Table 2. (Continued.)

Outcome	Study Group			P Value†	Odds Ratio or Hazard Ratio (95% CI)	
	High-Flow Oxygen (N=106)	Standard Oxygen (N=94)	Noninvasive Ventilation (N=110)		Standard Oxygen vs. High-Flow Oxygen	Noninvasive Ventilation vs. High-Flow Oxygen
Death						
In ICU						
Unadjusted analysis				0.047	1.85 (0.84–4.09)	2.55 (1.21–5.35)
No. of patients	12	18	27			
% of patients (95% CI)	11 (6–19)	19 (12–28)	25 (17–33)			
Adjusted analysis**	—	—	—	—	2.55 (1.07–6.08)	2.60 (1.20–5.63)
At day 90						
Overall population						
Unadjusted analysis				0.02	2.01 (1.01–3.99)	2.50 (1.31–4.78)
No. of patients	13	22	31			
% of patients (95% CI)	12 (7–20)	23 (16–33)	28 (21–37)			

Personalized Mechanical Ventilation in ARDS

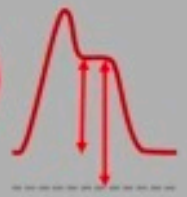
1

RATIONALE
Regulate ventilatory parameters based on close monitoring of targeted physiologic variables, intervention responses and individual integrated goals.

2

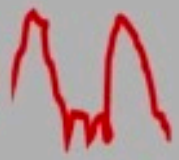
TIDAL VOLUME
Low V_T (4-6 ml/Kg PBW) is a standard of care. Personalized targeting requires evaluation of EELV and IC, AI and closed-loop systems may provide better monitoring.

3



DRIVING AND PLATEAU PRESSURE
Low ΔP (< 13 cmH_2O) is a target in most patients. ΔP could help individualize V_T and PEEP levels. P_{PLAT} should be kept below 27 cmH_2O.

4



TRANSPULMONARY PRESSURE
P_L estimated on esophageal pressure can be used to titrate ventilation, but requires correct physiological interpretation.

5

MECHANICAL POWER
Mechanical power is a summary variable including recognized determinants of VILI.

6

ALVEOLAR RECRUITMENT
The identification of recruitable patients and estimation of recruitment are essential to individualize recruitment strategies.

7

GAS-EXCHANGE
Gas-exchange including oxygenation is commonly targeted to set ventilation. However, dead space, ventilatory ratio and oxygen transport should be considered.

8

LUNG IMAGING
Computed tomography remains the gold standard. Lung ultrasound and electrical impedance tomography are promising bedside tools.

9

PHENOTYPES
Patient stratification according to biological phenotypes is promising, but translation into clinical practice requires further research.

10

LIMITS OF PHYSIOLOGICAL GAIN
When applying physiological manipulations, clinicians should consider the uncertainty surrounding their effect on patient-centered outcomes

Pelosi et al Critical Care 2020

Mortality at Day 90 (ALVEOLI) Differential Treatment Response to PEEP Strategy was observed in ARDS phenotypes

Model AUC: 0.94

Model	Hypoinflammatory Phenotype			Hyperinflammatory Phenotype			P-Value interaction term (Tx and Phenotype)
	Overall	Low PEEP	High PEEP	Overall	Low PEEP	High PEEP	
Clinical-Classifier Model	20%	**15%**	**24%**	45%	**53%**	**39%**	**0.006**

Calfee LRM 2014

Sinha et al AJRCCM 2020

Differential Response to PEEP were Observed in ARDS in Phenotypes (In-Hospital Mortality in LUNG SAFE; N = 2813)

PEEP Group	Hypoinflammatory	Hyperinflammatory	P value
Low PEEP (N = 943)	31%	64%	0.016
High PEEP (N = 992)	34%	55%	

Maddali et al Lanc Resp Med (2021 in press)

Summary

- Evidence-based approaches have allowed gentler ventilatory strategies for mechanical ventilation
- Outcomes are improving
- More bespoke approaches should be trialled in patients with ARDS

Can We Minimise Damage to the ARDS Lungs with a Ventilator?

Thank You

Twitter: *@progdoctalk*
Email: p.sinha@wustl.edu

Washington University School of Medicine in St. Louis
Department of Anesthesiol
Division of Clinical and Translational Resea