Management of ARDS: including review of novel virus

台中榮總 呼吸治療科

詹明澄

Review Artic

Medical Progress

The Acute Respiratory Distress Syndrome

Lorraine B. Ware, M.D.,
and Michael A. Matthay, M.D.

THE acute respiratory distress syndrome is a common, devastating clinical syndrome of acute lung injury that affects both medical and surgical patients. Since the last review of this syndrome appeared in the *Journal*,[1] more uniform definitions have been devised and important advances have occurred in the understanding of the epidemiology, natural history, and pathogenesis of the disease, leading to the design and testing of new treatment strategies. This article provides an overview of the definitions, clinical features, and epidemiology of the acute respiratory distress syndrome and discusses advances in the areas of pathogenesis, resolution, and treatment.

HISTORICAL PERSPECTIVE AND DEFINITIONS

The first description of acute respiratory distress syndrome appeared in 1967, when Ashbaugh and colleagues described 12 patients with acute respiratory distress, cyanosis refractory to oxygen therapy,

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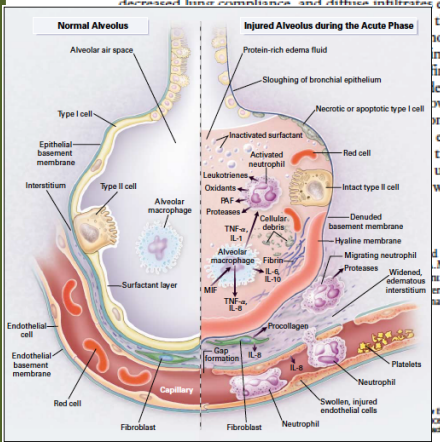

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Acute Respira

B. Taylor Thompson, M.D., Rachel

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This article was last updated on August 11, 2017, at NEJM.org.

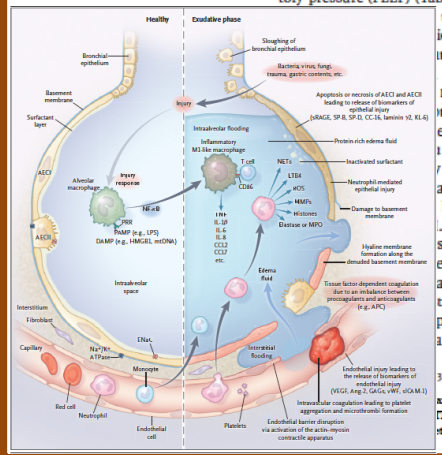
N Engl J Med 2017;377:562-72.
DOI: 10.1056/NEJMra1608077

IFTY YEARS AGO, ASHBAUGH
tachypnea, refractory hypox
ter infection or trauma.[1] Pr
veolar spaces of the lungs in 6 of
to be specific for the respiratory
adult (later changed to acute) res

Since ARDS was last reviewed
has been made in the care of af
with reductions in both incide
tively common and lethal or dis
involving 29,144 patients,[3] 10%
(ICU) and 23% of mechanically
subgroup of patients with severe
der are at high risk for cognitive
and persistent skeletal-muscle w

DEFINITION AN

Four major definitions of ARDS
the central features of the initial
lung permeability, edema, and in
care and no validated diagnostic
on clinical features and chest in
posed in 2012,[6] breaks with tr
based on the degree of hypoxem
tory pressure (PEEP) (Table 1). Th



REVIEW ARTICLE

CRITICAL CARE MEDICINE

Simon R. Finfer, M.D., and Jean-Louis Vincent, M.D., Ph.D., *Editors*

Ventilator-Induced Lung Injury

Arthur S. Slutsky, M.D., and V. Marco Ranieri, M.D.

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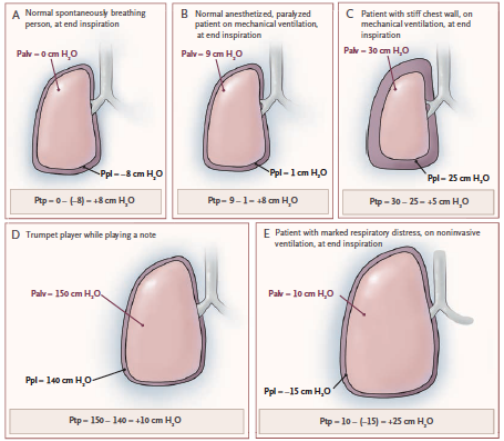
N Engl J Med 2013;369:2126-36.
DOI: 10.1056/NEJMra1208707

THE PURPOSE OF MECHANICAL VENTILATION IS TO REST THE RESPIRATORY muscles while providing adequate gas exchange. Ventilatory support proved to be indispensable during the 1952 polio epidemic in Copenhagen, decreasing mortality among patients with paralytic polio from more than 80% to approximately 40%.[1] Despite the clear benefits of this therapy, many patients eventually die after the initiation of mechanical ventilation, even though their arterial blood gases may have normalized.

This mortality has been ascribed to multiple factors, including complications of ventilation such as barotrauma (i.e., gross air leaks), oxygen toxicity, and hemodynamic compromise.[2,3] During the polio epidemic, investigators noted that mechanical ventilation could cause structural damage to the lung.[4] In 1967, the term "respirator lung" was coined to describe the diffuse alveolar infiltrates and hyaline membranes that were found on postmortem examination of patients who had undergone mechanical ventilation.[5] More recently, there has been a renewed focus on the worsening injury that mechanical ventilation can cause in previously damaged lungs and the damage it can initiate in normal lungs. This damage is characterized pathologically by inflammatory-cell infiltrates, hyaline membranes, increased vascular permeability, and pulmonary edema. The constellation of pulmonary consequences of mechanical ventilation has been termed ventilator-induced lung injury.

The concept of ventilator-induced lung injury is not new. In 1744, John Fothergill discussed a case of a patient who was "dead in appearance" after exposure to coal fumes and who was successfully treated by mouth-to-mouth resuscitation.[6] Fothergill noted that mouth-to-mouth resuscitation was preferable to using bellows because



ithout injury, as great a force as those of an-
ellows cannot always be determin'd." Fother-
it mechanical forces generated by bellows (i.e.,

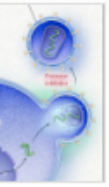
this century that the clinical importance of
Its was confirmed by a study showing that a
mize such injury decreased mortality among
istress syndrome (ARDS).[7] Given the clinical
g injury, this article will review mechanisms
and physiological consequences, and clinical
its effects.

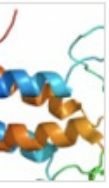
OLOGICAL FEATURES

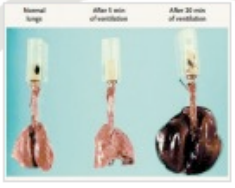
approximately 500 million breaths. For each
late the lungs comprises the pressure to over-
(a measure of the pressure gradient required

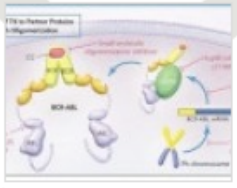
NOVEMBER 28, 2013

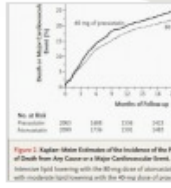
1812 PICK: AREAS OF MEDICINE SORT BY: MOST RELEVANT 1990 s 2012











1998 1999 2000 2001 2002 2003 2004

EDITORIAL

Happy 50th birthday ARDS!

Arthur S. Slutsky[1,2*], Jesús Villar[1,3,4] and Antonio Pesenti[5,6]

Intensive Care Medicine 2016 March

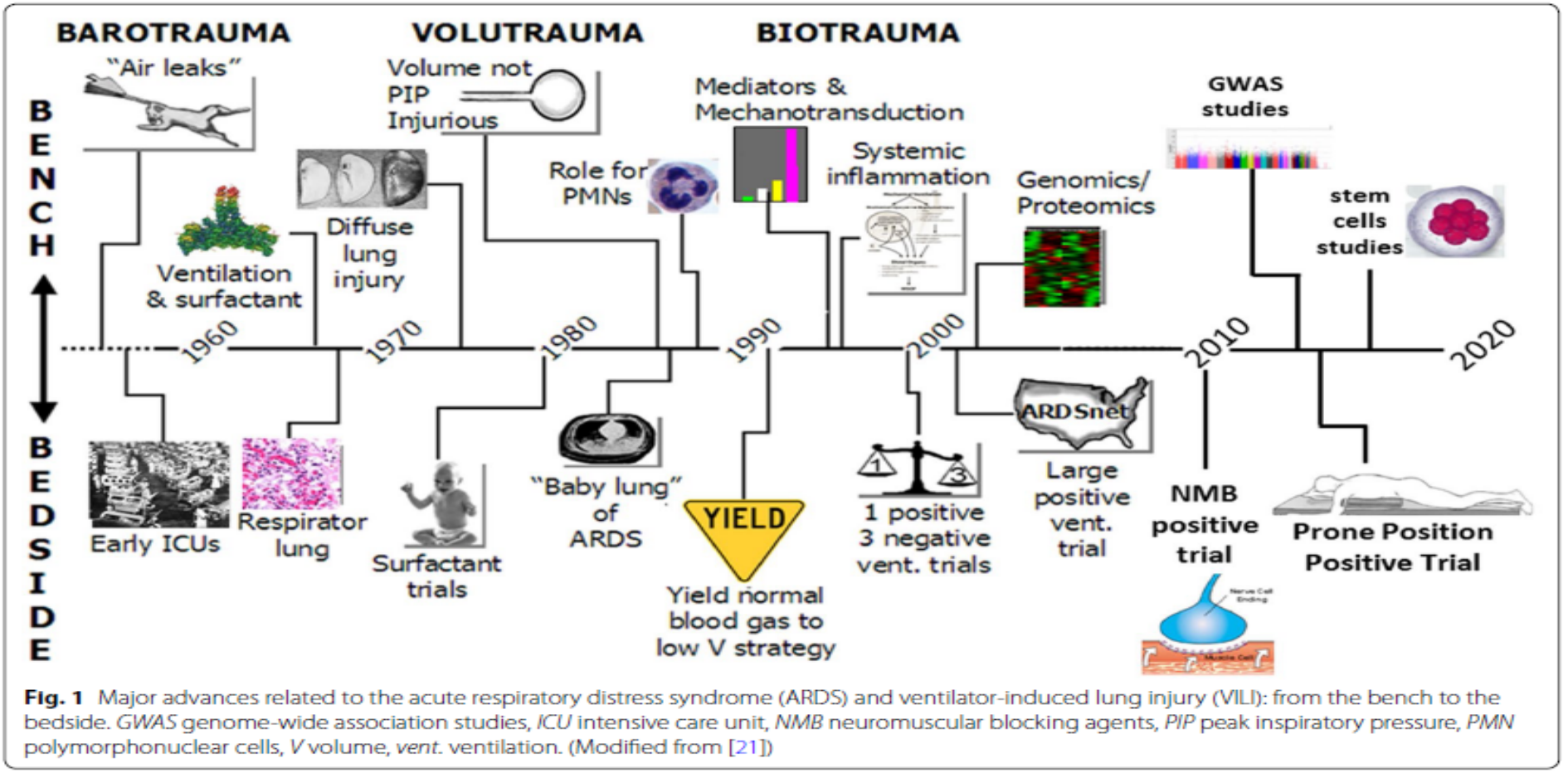


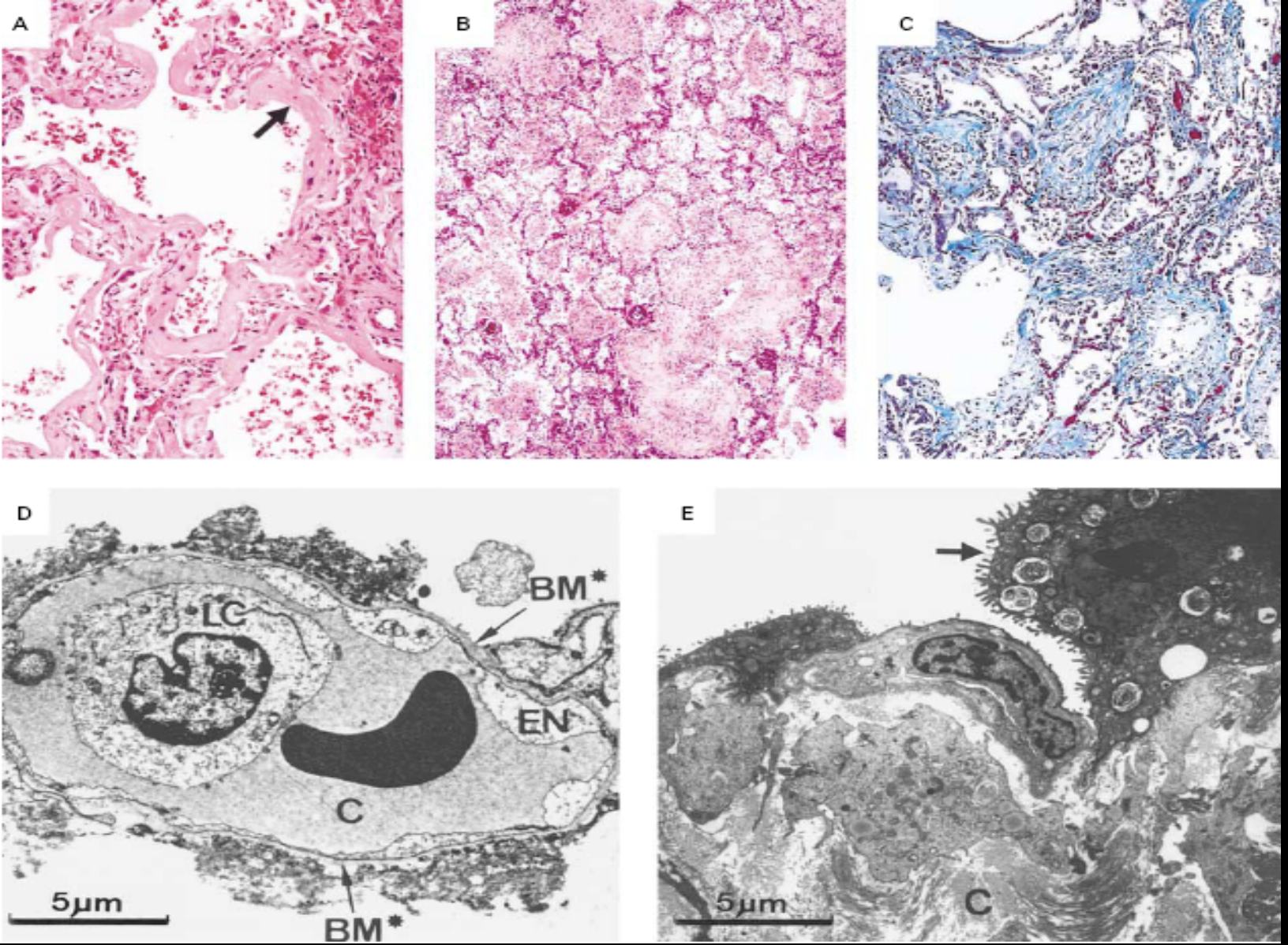
Fig. 1 Major advances related to the acute respiratory distress syndrome (ARDS) and ventilator-induced lung injury (VILI): from the bench to the bedside. *GWAS* genome-wide association studies, *ICU* intensive care unit, *NMB* neuromuscular blocking agents, *PIP* peak inspiratory pressure, *PMN* polymorphonuclear cells, *V* volume, *vent.* ventilation. (Modified from [21])

Berlin Definition

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_2O[c]
Moderate	100 mm Hg PaO_2/FIO_2 200 mm Hg with PEEP 5 cm H_2O
Severe	PaO_2/FIO_2 100 mm Hg with PEEP 5 cm H_2O

JAMA. 2012;307(23):5669



NEJM 2000

Common Causes of ARDS

Direct Lung Injury

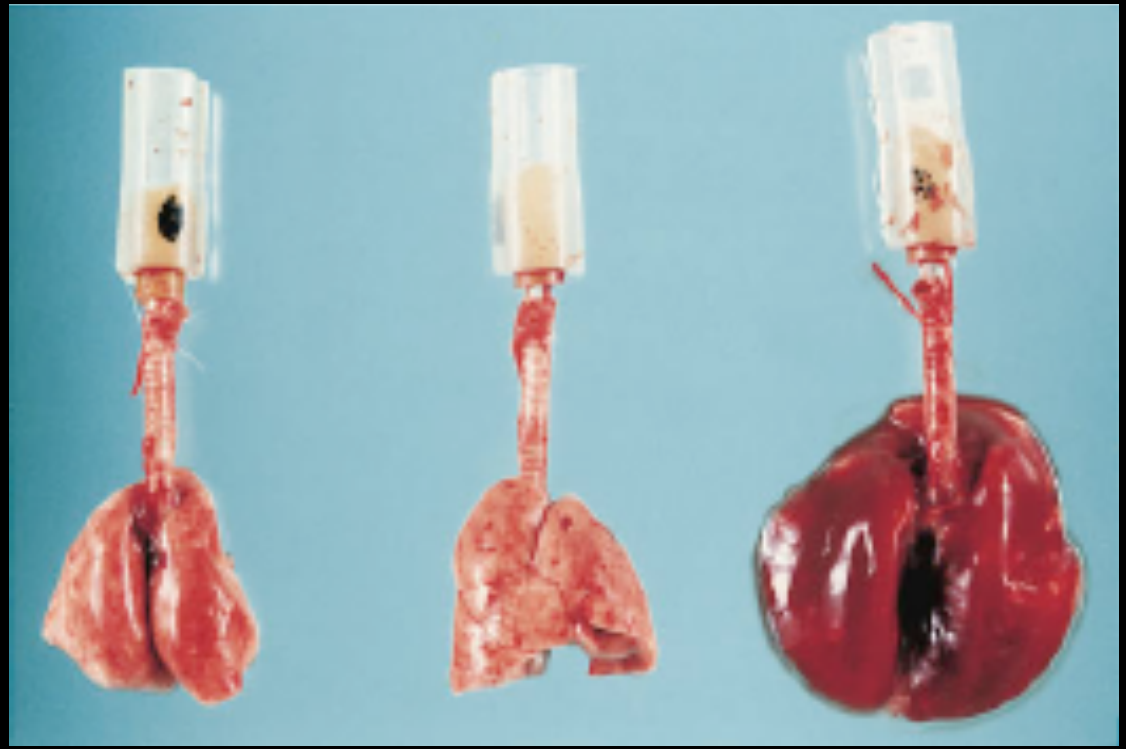
- Pneumonia
- Aspiration of gastric content
- Pulmonary contussion
- Fat embolism
- Near-drowning
- Inhalation injury
- Reperfusion injury after transplantation, pulmonary lobectomy

Indirect Lung Injury

- Sepsis
- Severe trauma with shock and multiple transfusion
- Cardiopulmonary bypass
- Drug overdose
- Acute pancreatitis
- Transfusion of blood prodcuts

Barotrauma, not Just Air Leak

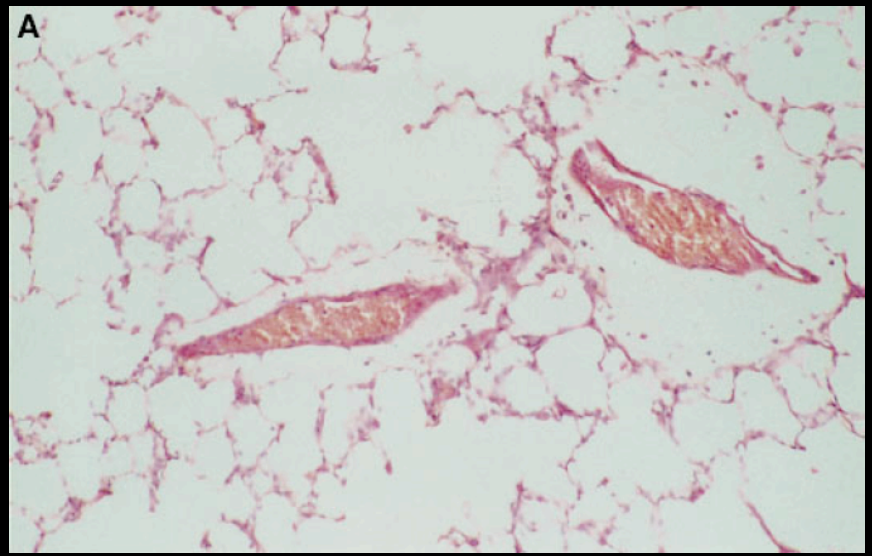
Normal 5 MIN 20 MIN



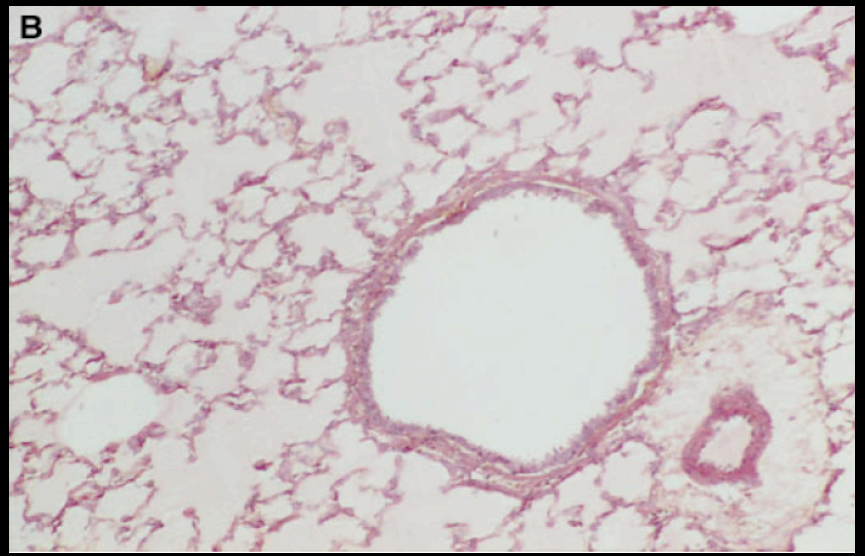
Peak Airway Pressure 45cm H_2O

VILI in Light Microscope

Perivascular cuffing
PC 45cmH_2O, 5ming

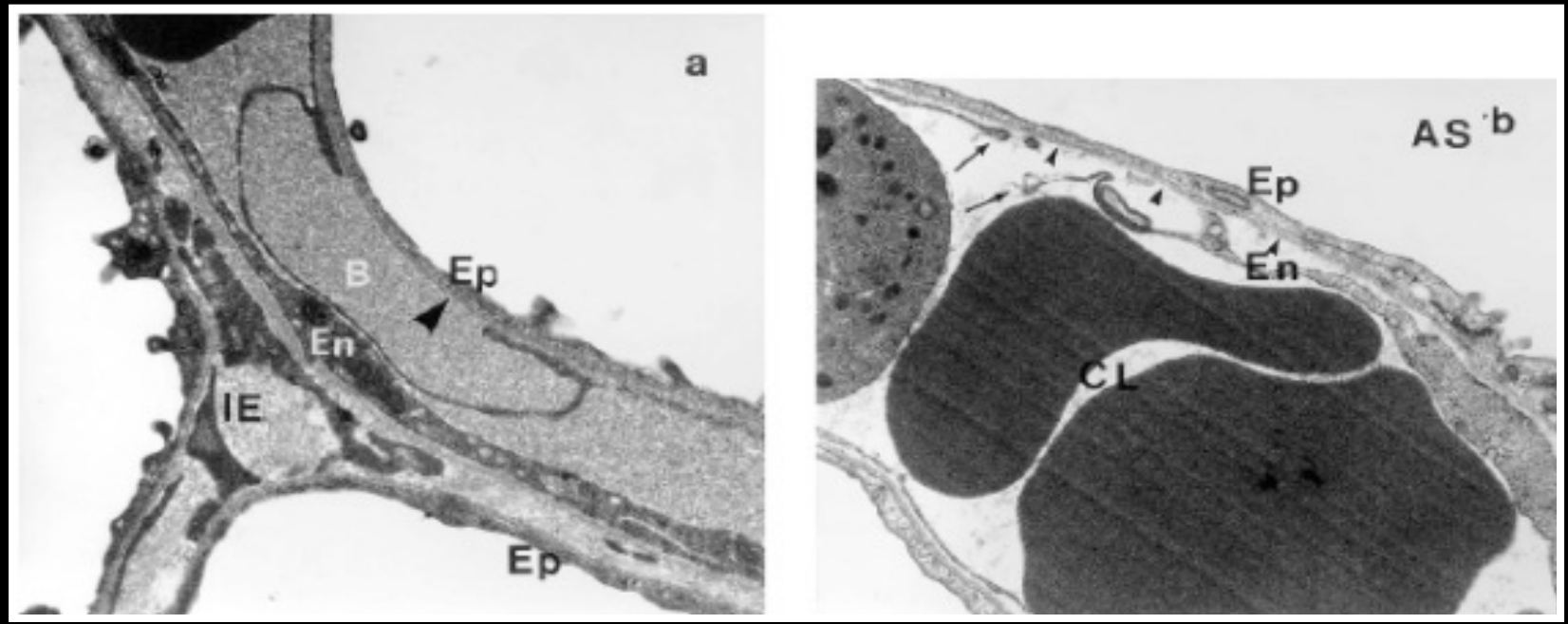


Alveolar edema
PC 45cm H_2O, 20min



AJRCCM 1998

Ultrastructural Change of Barotrauma



EP type I epithelium

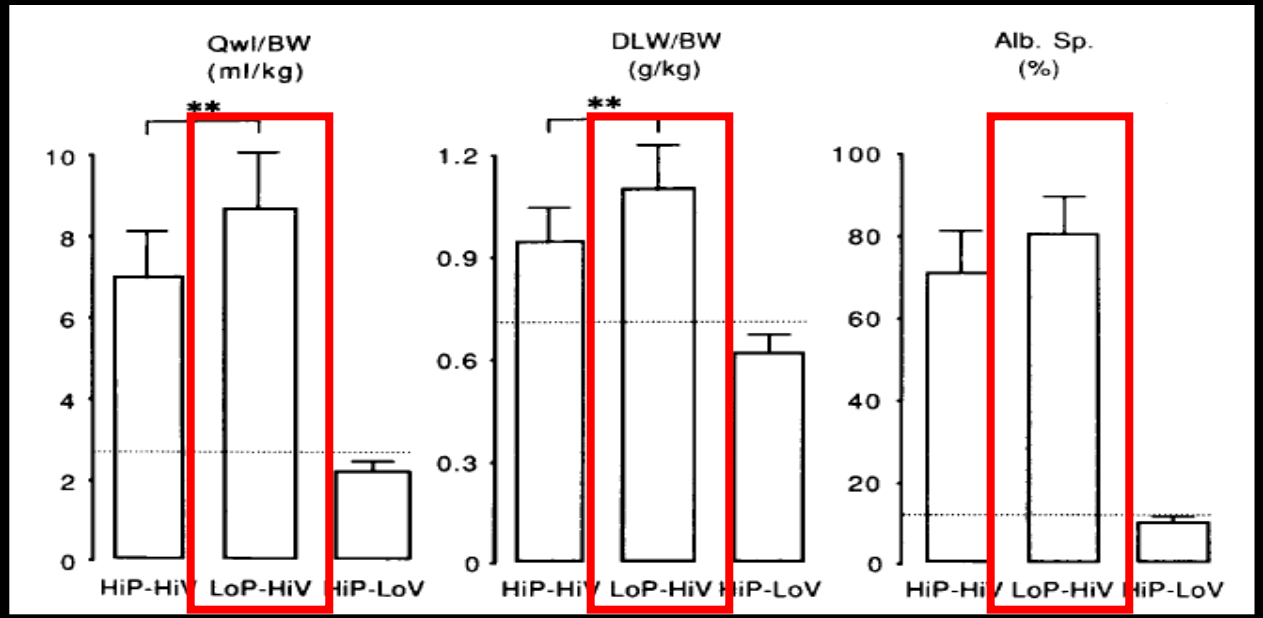
IE Interstitial edema

EN Endothelium

B Bleb

M. J. Tobin, Principles and Practice of Mechanical Ventilation, McGraw-Hill, New York. 793-811

Volutrauma



extravascular lung water content

bloodless dry lung weight

Distribution space of ^{125}I-labled albumin

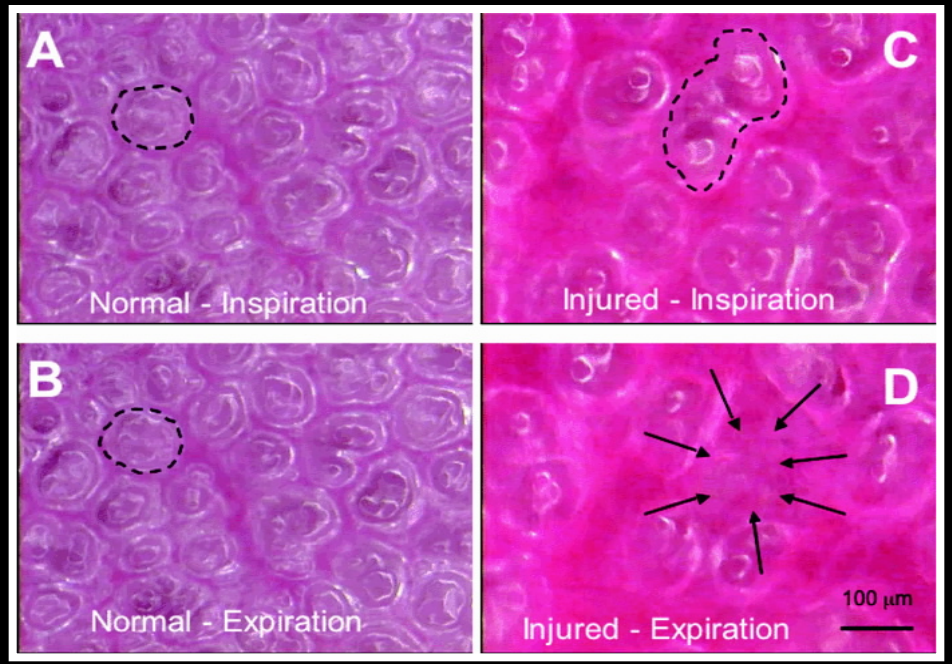
HiP-Hiv **High-pressure-high-volume**

LoP-HiV **Iron lung ventilation**

HiP-LoV **Thoracoabdominal strapping**

Deryfuss D, Am. Rev. Respir. Dis. 137: 1159-1164

Atelectrauma



- Opening collapsed airway requires relatively high forces and thus causes epithelium disruption.
- Ventilation at low lung volumes can inhibit production of surfactant and/or lead to surfactant being squeezed out of alveoli.
- Reexpansion of atelectatic regions can be associated with marked increase in regional stress.

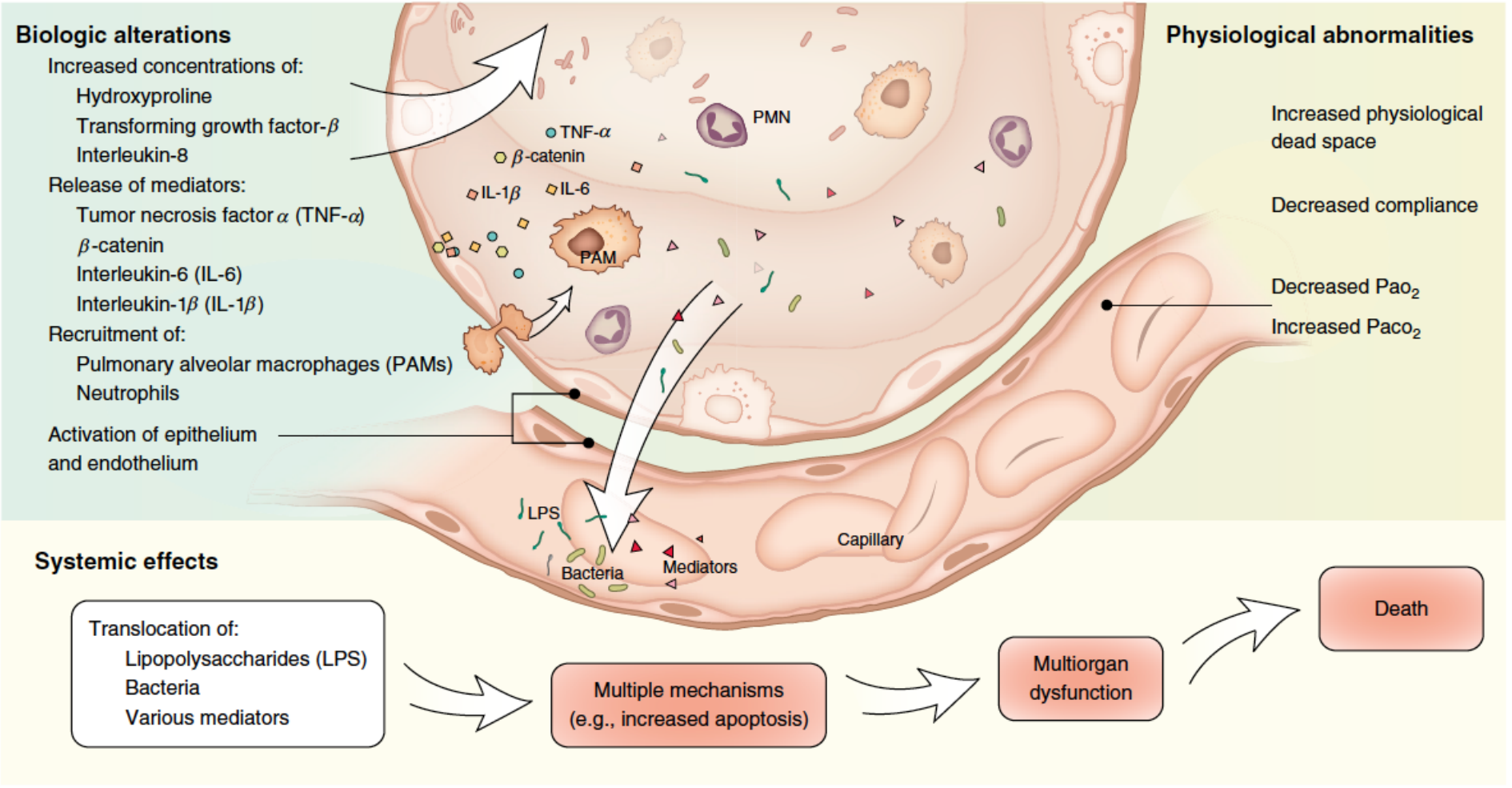
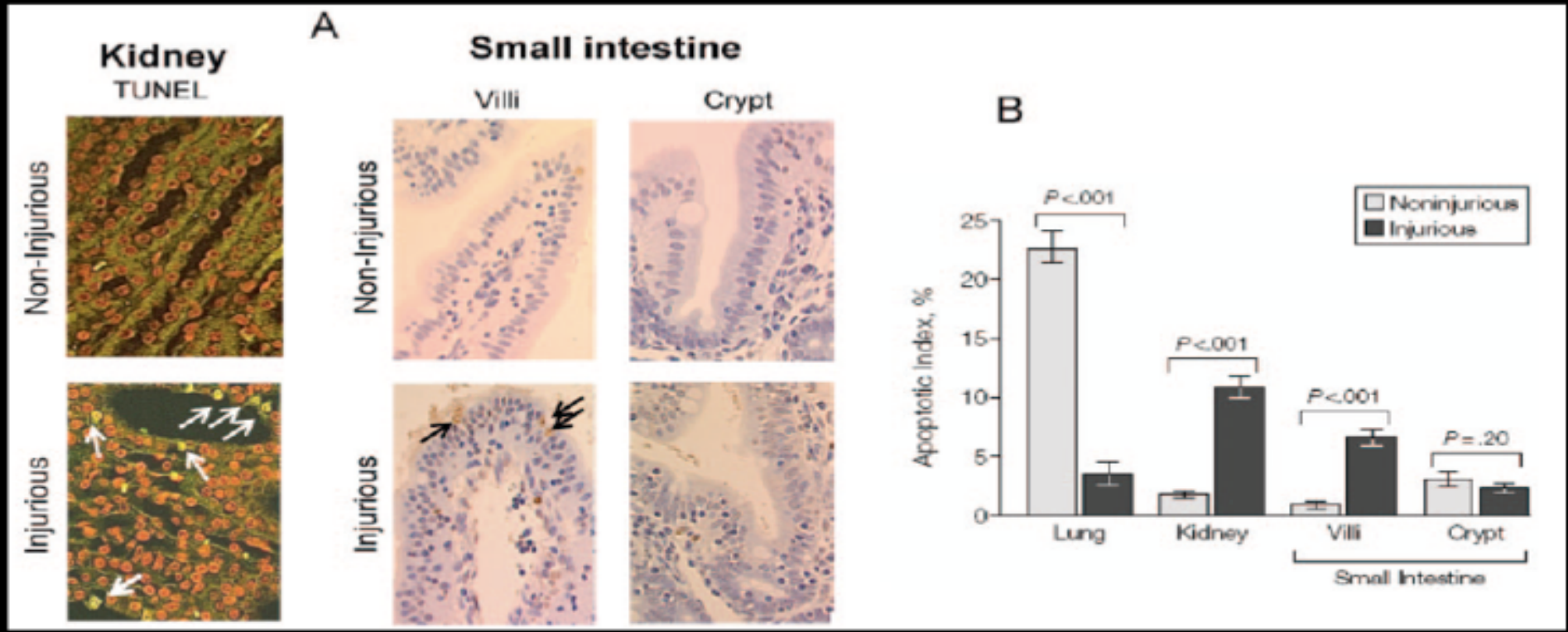


Figure 9. Alterations caused by ventilator-induced lung injury (VILI). Biologic, physiologic, and systemic effects caused by injurious ventilatory strategies. Further injury can be caused by mediators released into the lung. These mediators can recruit neutrophils into the lung or cause changes that can promote pulmonary fibrosis. VILI can also lead to increased alveolar–capillary permeability that in turn can facilitate translocation of mediators, bacteria, or lipopolysaccharides into the systemic circulation. These can then potentially lead to multiorgan dysfunction syndrome and death. PMN = polymorphonuclear leukocytes. Reprinted by permission from Reference 29.

Am J Respir Crit Care Med Vol 191, Iss 10, pp 1106–1115

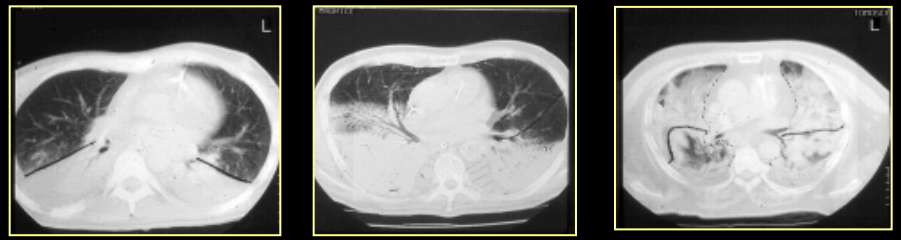
Injurious Ventilation Strategy Leads to Increased Epithelial Apoptosis



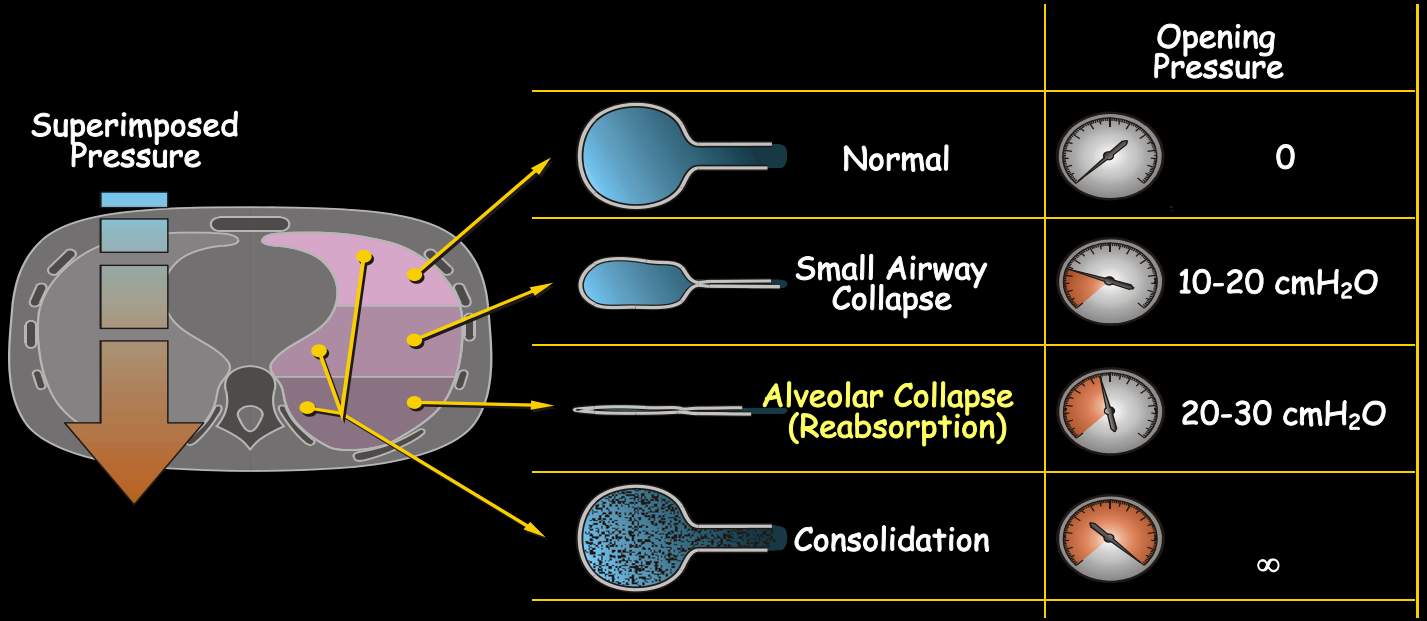
JAMA 2003;289(16):2104-2112

The ARDS Lung

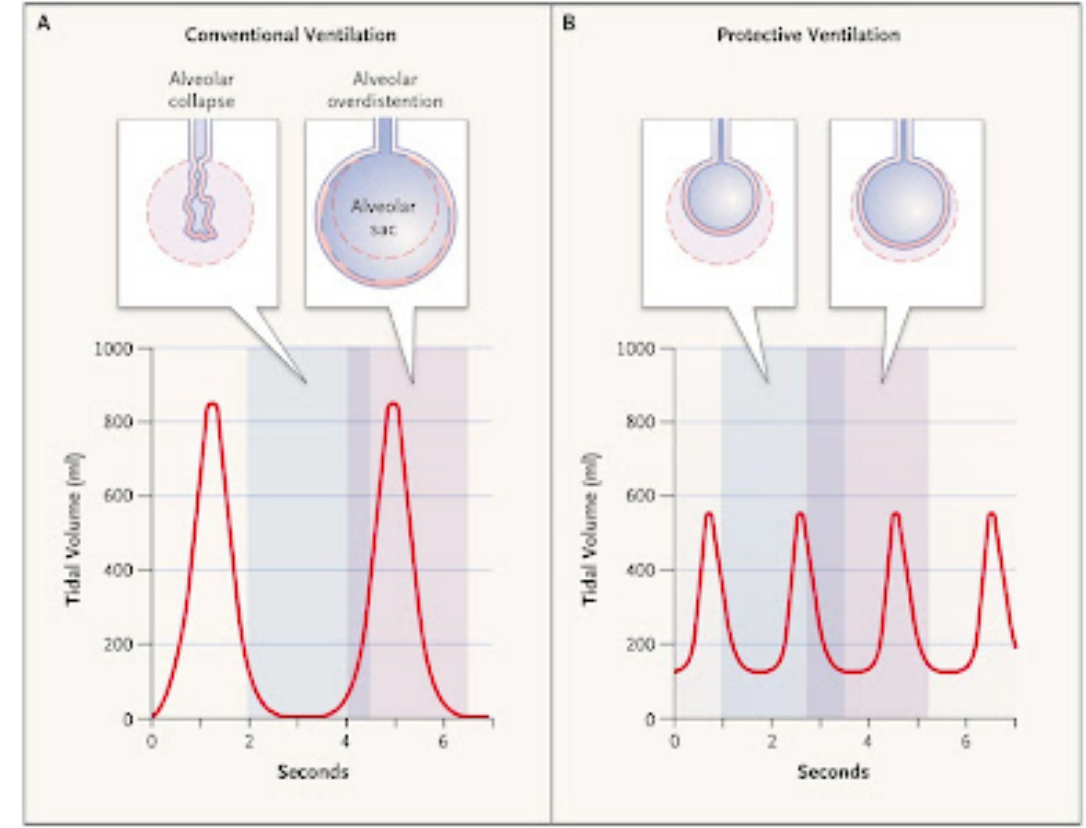
Gattinoni JAMA 1993, Pelosi AJRCCM 1994, Gattinoni AJRCCM 2002, Gattinoni ICM 2005



Rouby Intensive Care Med 2000



Protective Ventilation



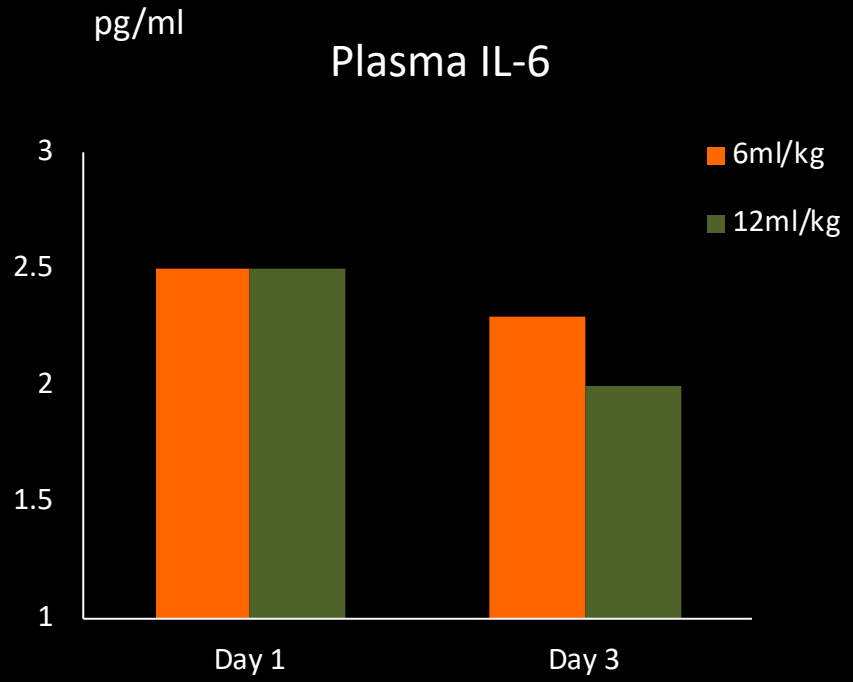
NEJM 2007

6 vs 12 ml/kg

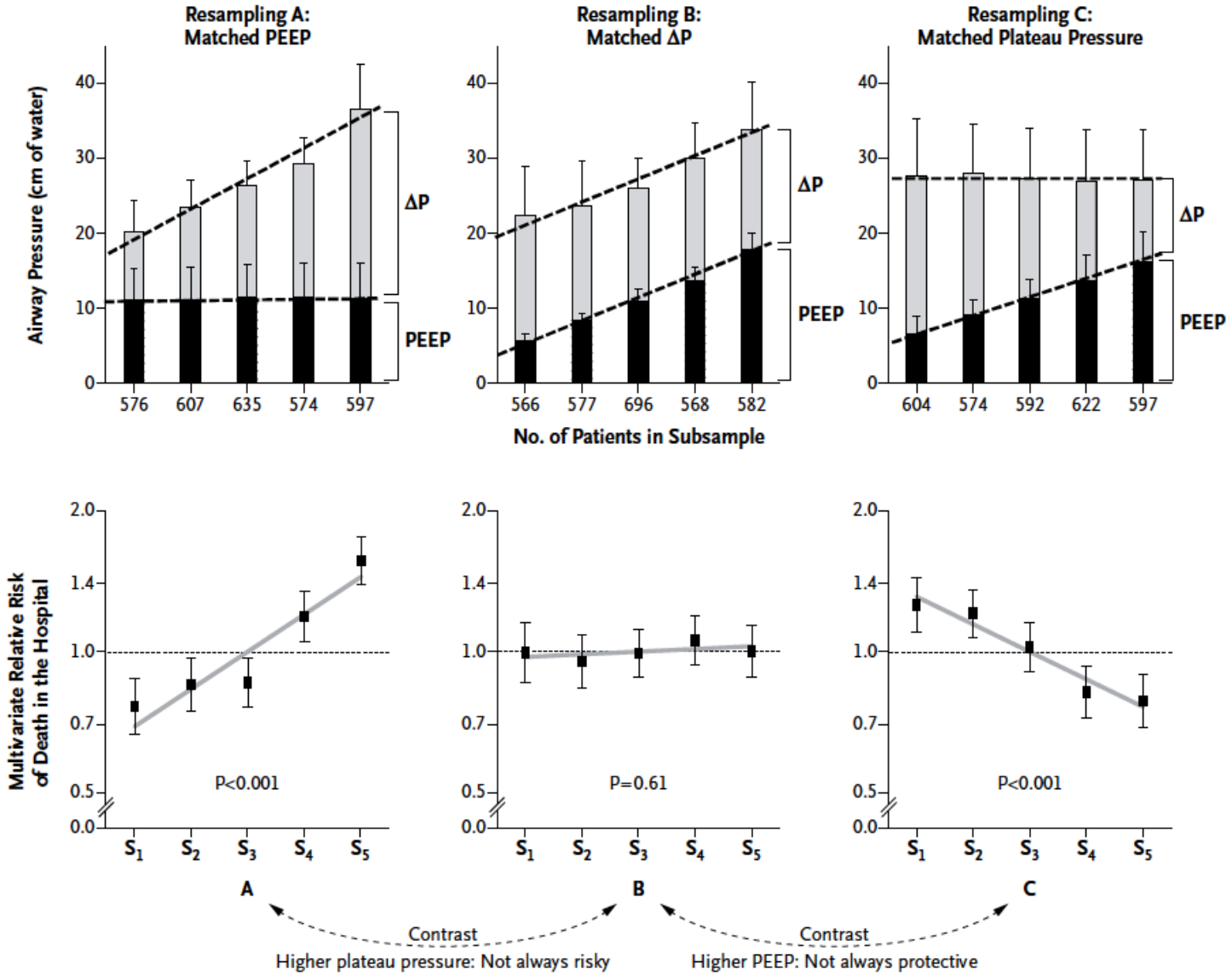
N Engl J Med 2000;342:1301-8

TABLE 4. MAIN OUTCOME VARIABLES.*

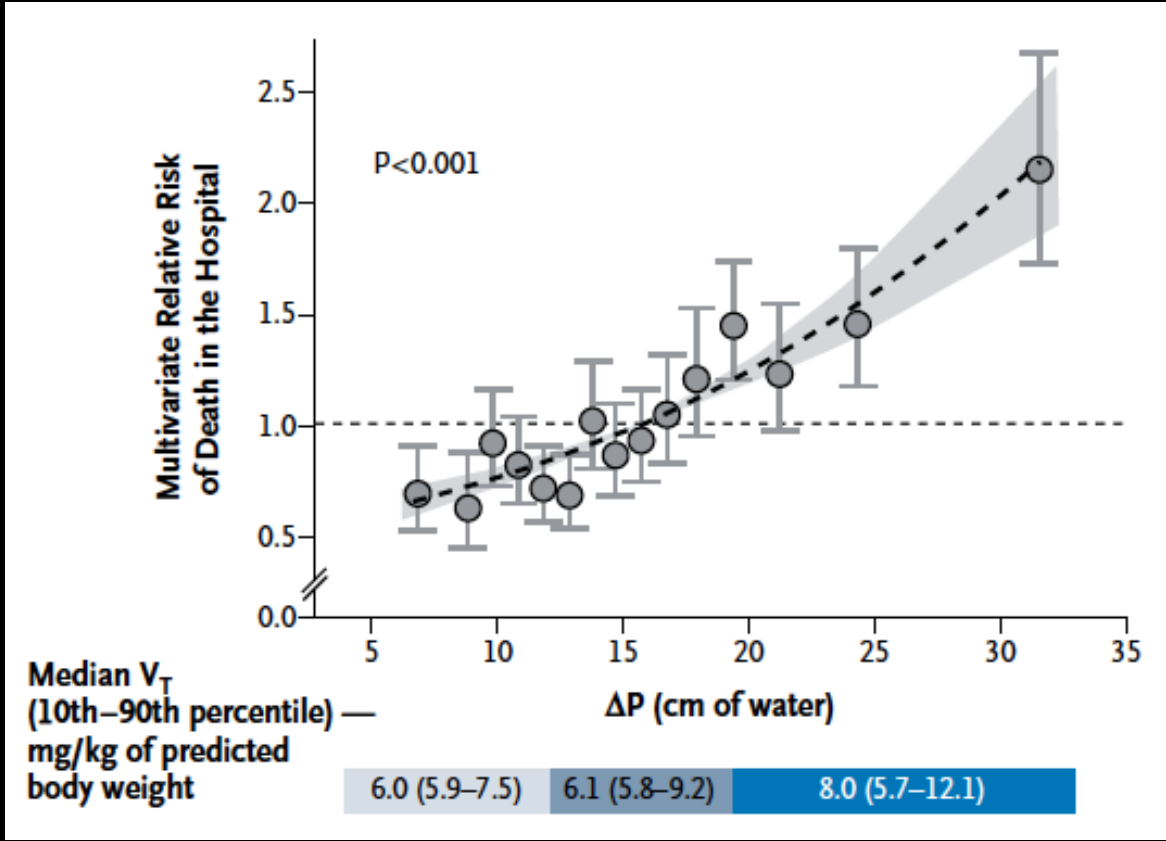
VARIABLE	GROUP RECEIVING LOWER TIDAL VOLUMES	GROUP RECEIVING TRADITIONAL TIDAL VOLUMES	P VALUE
Death before discharge home and breathing without assistance (%)	31.0	39.8	0.007
Breathing without assistance by day 28 (%)	65.7	55.0	<0.001
No. of ventilator-free days, days 1 to 28	12±11	10±11	0.007
Barotrauma,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



- The decrease was greater in the group treated with lower tidal volumes (P<0.001)
- The day 3 plasma interleukin-6 concentrations were also lower in this group (P=0.002).


Resampling A:
Matched PEEP
Resampling B:
Matched ΔP
Resampling C:
Matched Plateau Pressure
Airway Pressure (cm of water)
ΔP
PEEP
576 607 635 574 597
566 577 696 568 582
604 574 592 622 597
No. of Patients in Subsample
Multivariate Relative Risk of Death in the Hospital
P<0.001
P=0.61
P<0.001
A
B
C
Contrast
Higher plateau pressure: Not always risky
Contrast
Higher PEEP: Not always protective

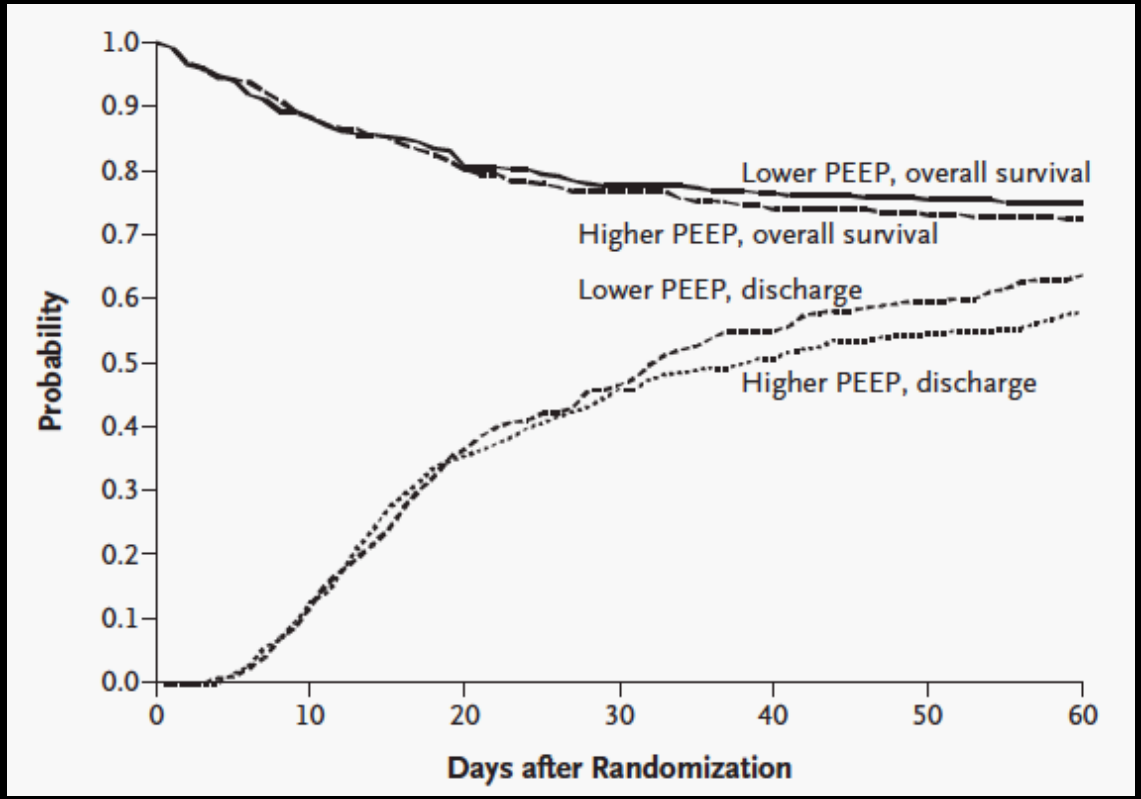
Driving pressure vs mortality



N Engl J Med 2015;372:747-55.

Higher vs Lower PEEP

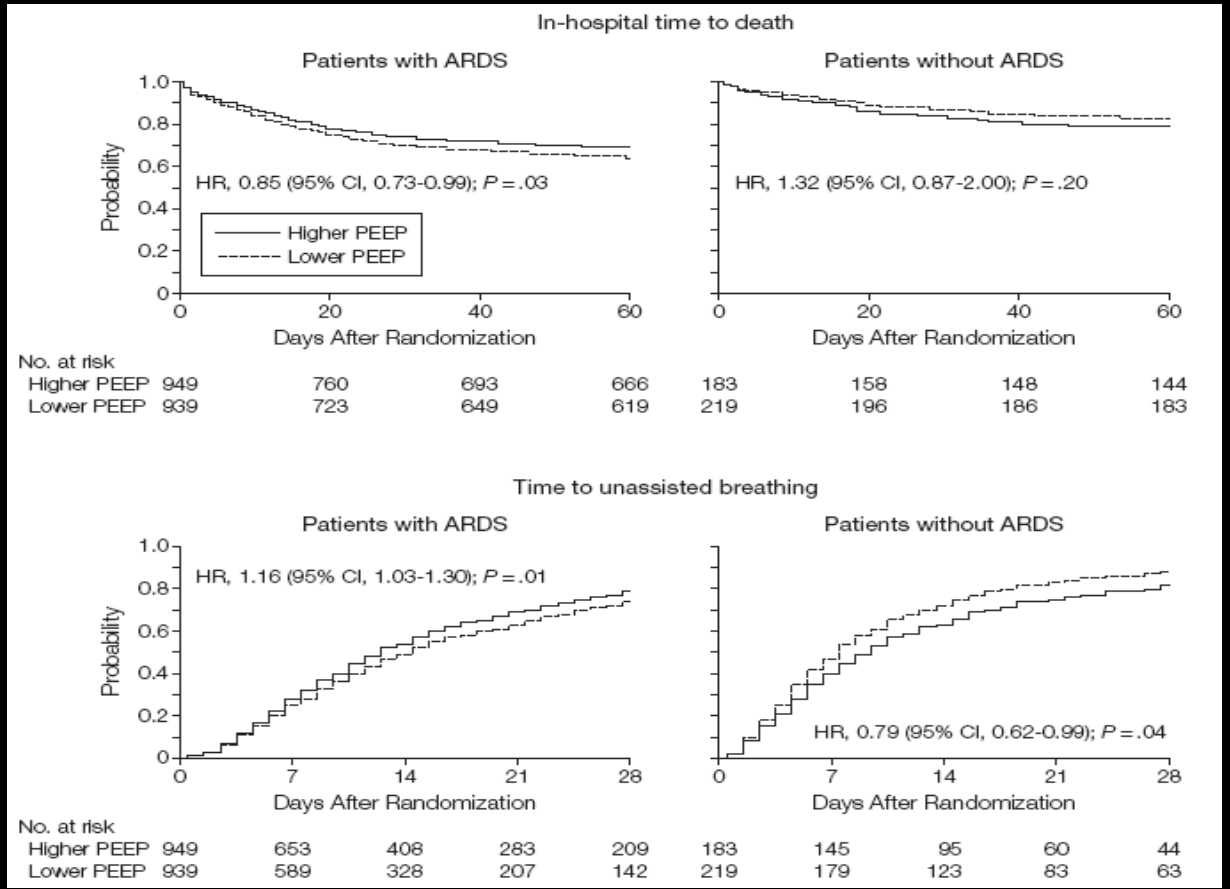
The National Heart, Lung, and Blood Institute ARDS Clinical Trials Network



N Engl J Med 2004;351:327-36.

Higher vs Lower PEEP

metaanalysis



JAMA. 2010;303(9):865-873

Corticosteroid for persistent ARDS

- Double-blind, randomized controlled, NHLBI ARDSNet
- 180 patients with ADRS for more than 7 days, methylprednisolone vs placebo
- No differences of mortality at 60 and 180 days.
- Methylprednisolone is associated with higher ventilator and shock free days at 28 days
- Higher mortality in methylprednisolone group at least 14 days of ARDS

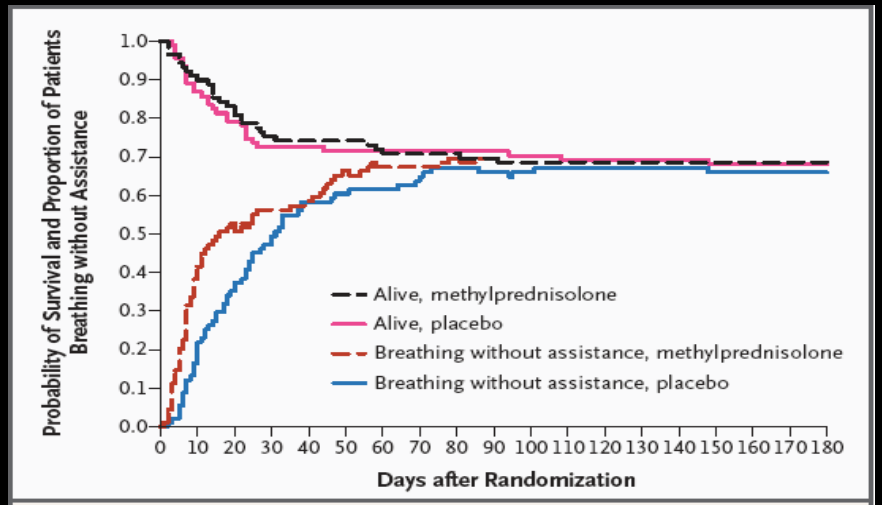


Figure 2. Probability of Survival and the Proportion of Patients with Persistent ARDS Who Became Able to Breathe without Assistance during the First 180 Days after Randomization.

At 180 days, 29 patients in the placebo group had died, 58 had been discharged home, and 4 had not been discharged home; the respective values in the methylprednisolone group were 28, 57, and 4. The status was known for all 180 patients at 180 days.

N Engl J Med 2006;354:1671-84.

Corticosteroid is associated with increased mortality in ARDS due to influenza pneumonia

Taiwan Severe Influenza Research Consortium

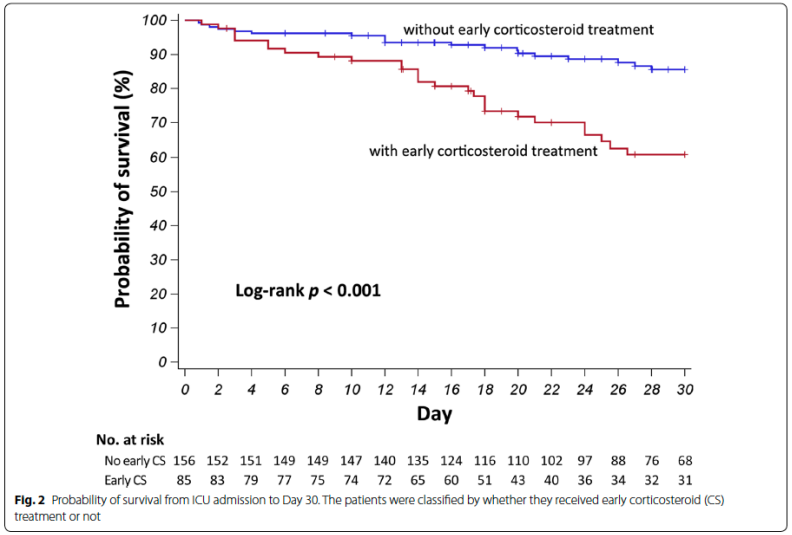


Fig. 2 Probability of survival from ICU admission to Day 30. The patients were classified by whether they received early corticosteroid (CS) treatment or not

Table 2 Univariate and multivariable analyses of factors associated with hospital mortality in patients with influenza-associated ARDS

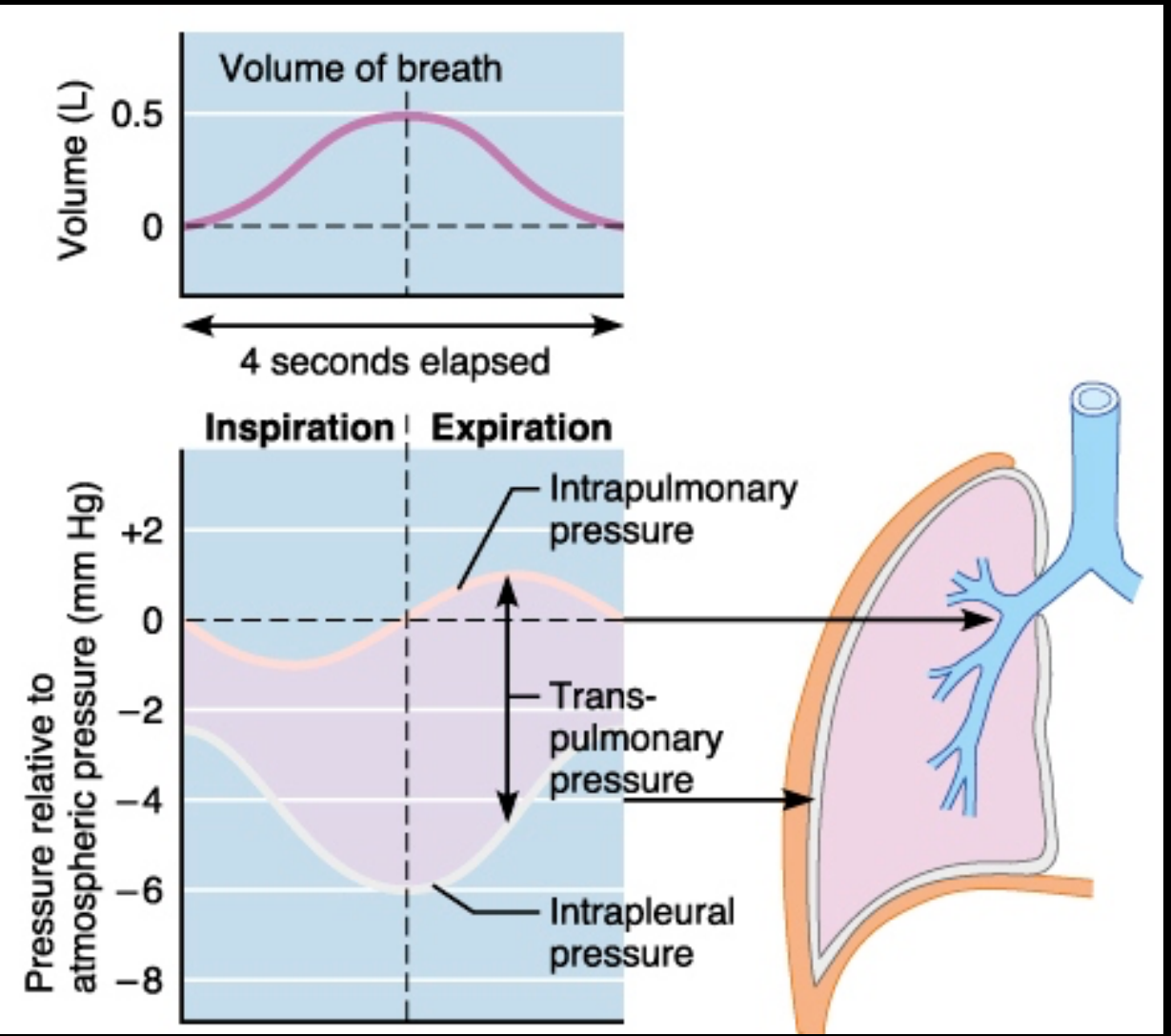
Variables	Univariate analysis[a]		Multivariable analysis[†]	
	OR (95% CI)	*p* value	Adjusted OR (95% CI)	*p* value
APACHE II score	1.11 (1.07–1.16)	< 0.001	1.12 (1.07–1.17)	*< 0.001*
PaO_2/FiO_2 ratio	0.99 (0.99–1.00)	0.007		
WBC	1.00 (1.00–1.00)	0.015		
Albumin, g/dL	0.55 (0.31–0.97)	0.039		
Malignancy	2.80 (1.27–6.18)	0.011	2.71 (1.06–6.90)	0.037
Influenza type A	0.50 (0.27–0.93)	0.028	0.38 (0.18–0.82)	0.013
ECMO	4.53 (2.25–9.14)	< 0.001	8.51 (3.52–20.55)	*< 0.001*
Vasopressor infusion	2.89 (1.59–5.25)	0.001		
Hemodialysis	2.54 (1.26–5.12)	0.009		
Early CS treatment	3.24 (1.80–5.81)	< 0.001	5.02 (2.39–10.54)	*< 0.001*

APACHE II Acute Physiology and Chronic Health Evaluation II, *ARDS* acute respiratory distress syndrome, *BMI* body mass index, *CI* confidence interval, *CS* corticosteroid, *ECMO* extracorporeal membrane oxygenation, FiO_2 fraction of inspired oxygen, PaO_2 partial pressure of arterial oxygen, *OR* odds ratio, *WBC* white blood cell

[a] The variable representing early CS treatment, basic demographic variables, and all clinical variables possibly associated with hospital mortality were analyzed in univariate logistic regression models

[†] We replaced missing values (APACHE II score in 4 patients, WBC count in 2 patients, and albumin in 40 patients) by the corresponding overall median values for the multivariable regression analysis. Variables associated with hospital mortality with a *p* value < 0.05 in univariate models were selected into the multivariable logistic regression model, using a stepwise algorithm with criteria of $p > 0.05$ for eliminating variables

Ann. Intensive Care (2020) 10:26



PEEP Guided by Esophageal Balloon

1. Optimal level of PEEP has been difficult to determine
2. Adjusting PEEP in according to lung and chest wall mechanics is achievable
3. Pao = flow x resistance + Vt/compliance
4. $P_{tp} = P_{aw} - P_{pleura}$ (P_{es})

Fluid management of ARDS

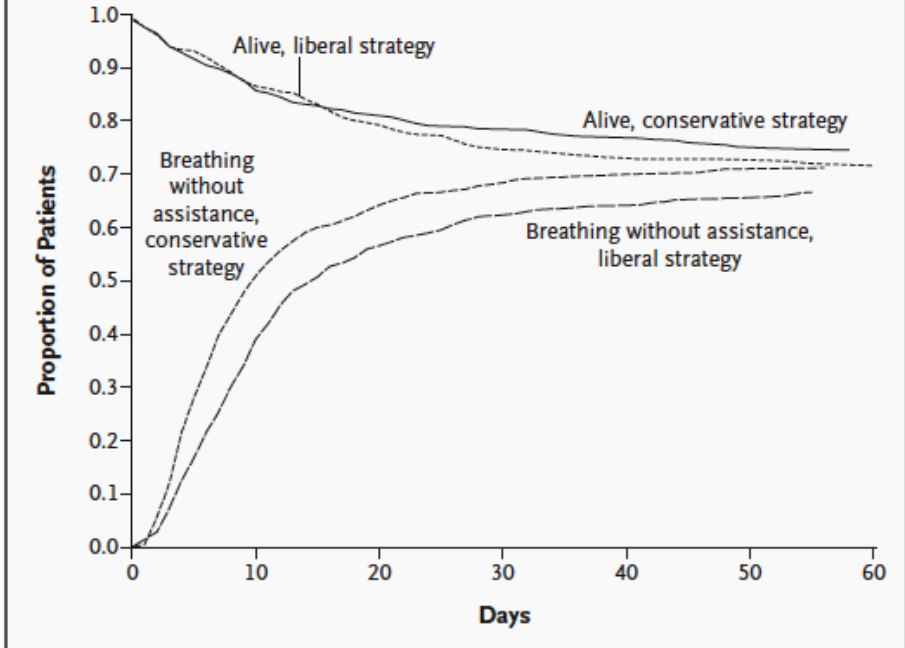
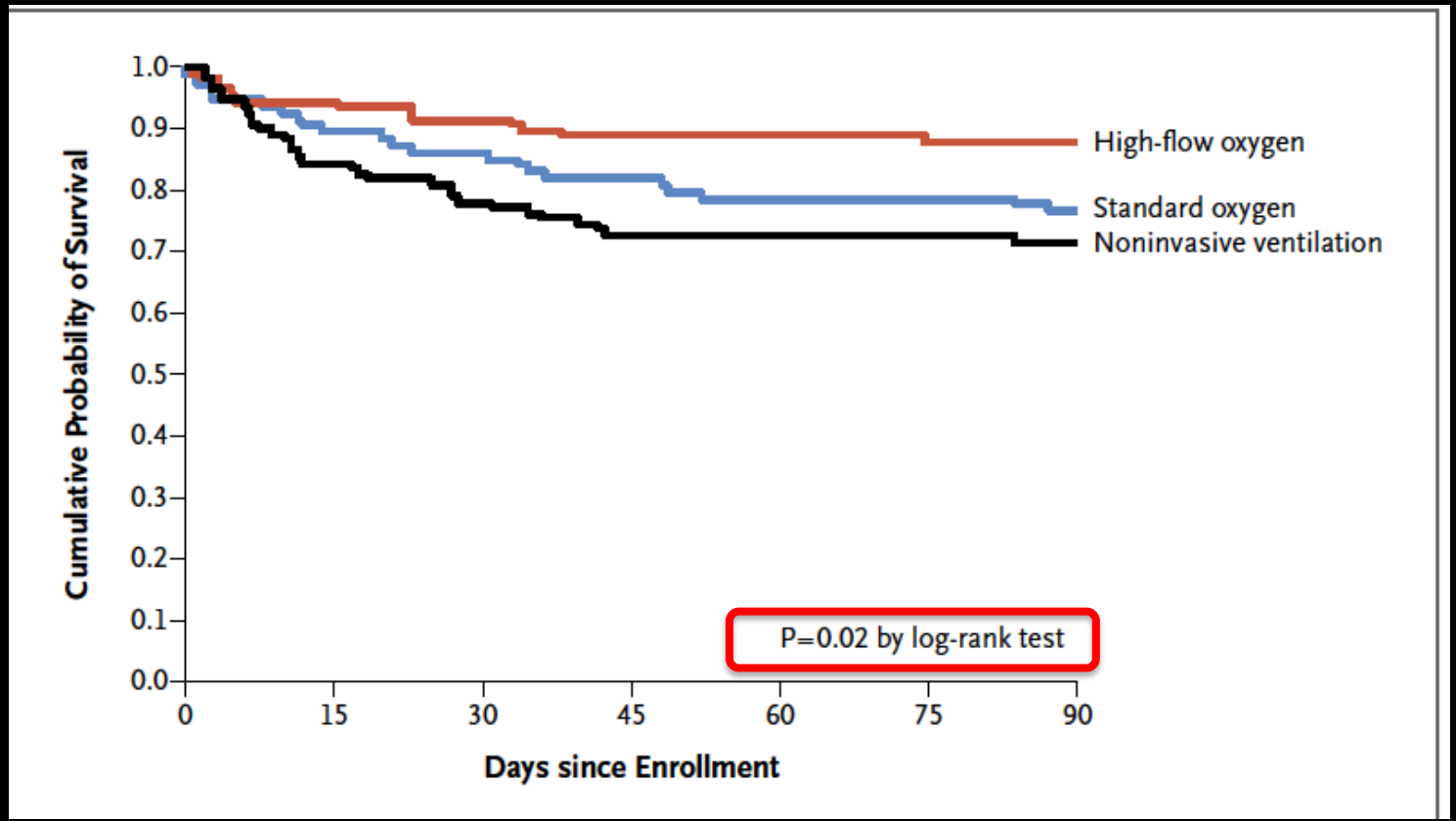


Figure 3. Probability of Survival to Hospital Discharge and of Breathing without Assistance during the First 60 Days after Randomization.

N Engl J Med 2006;354:2564-75.

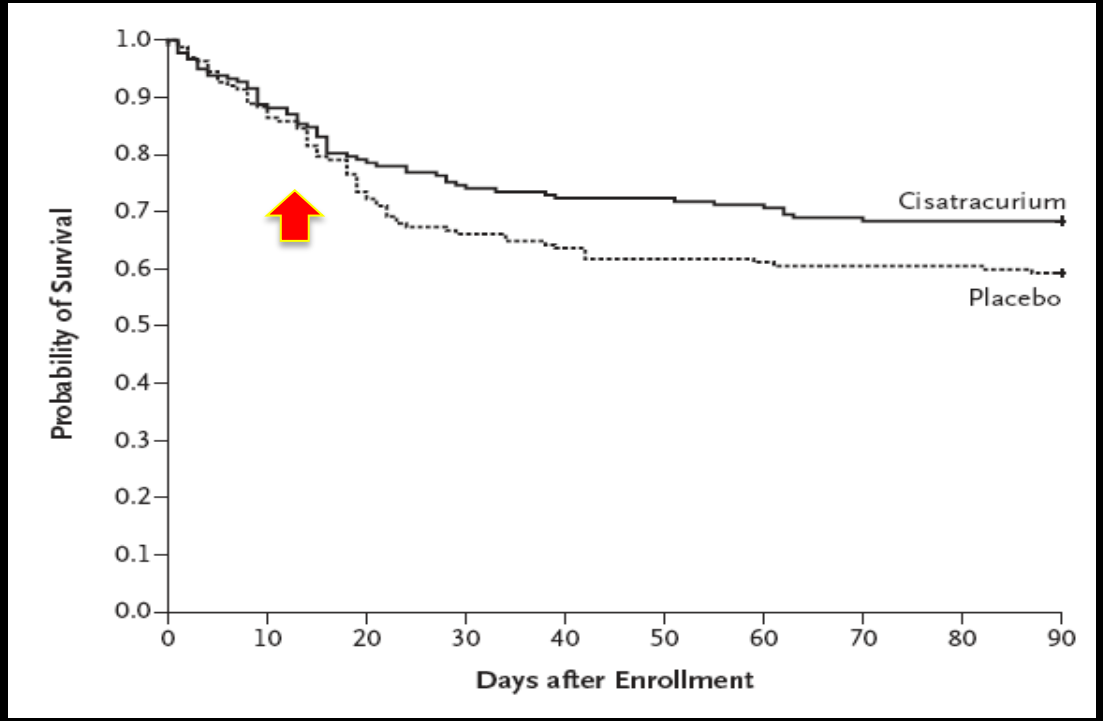
Nasal High Flow for Acute Hypoxemia



N Engl J Med 2015;372:2185-96.

Neuromuscular Blockade in Early ARDS

ACURASYS study

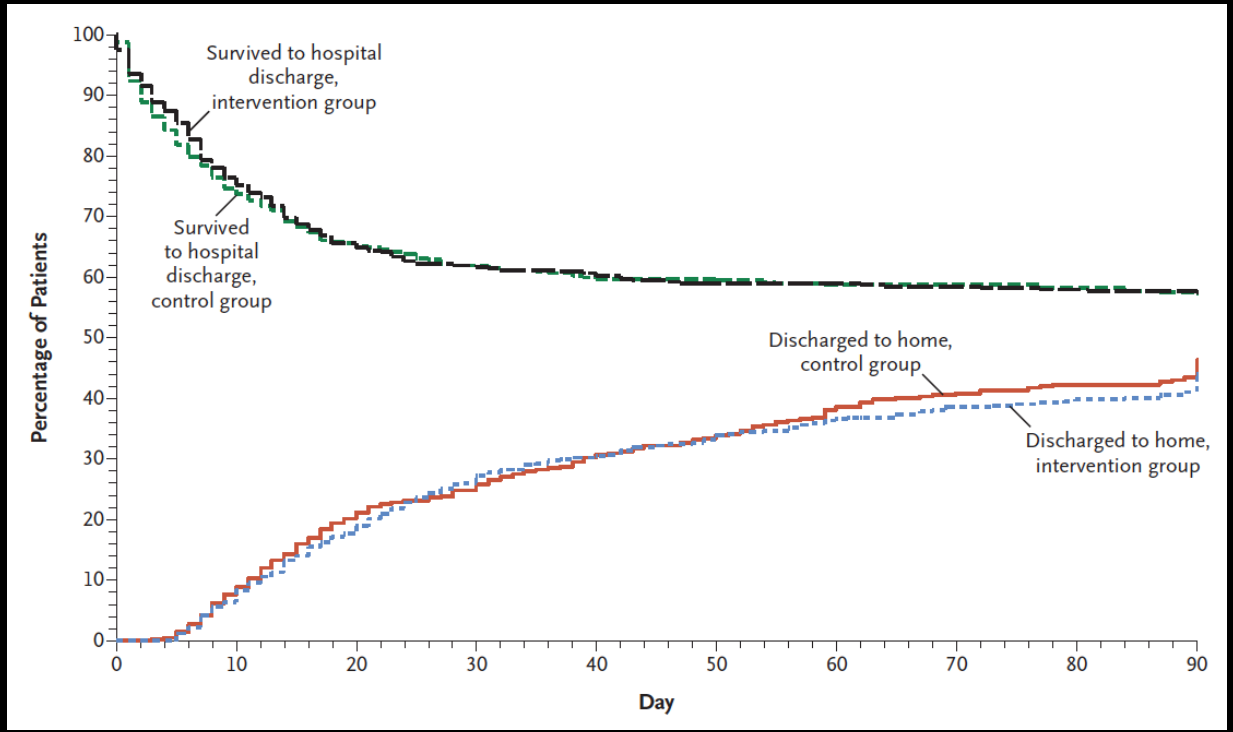


- Multi-center, double-blind, randomized controlled trial
- 340 patients with ARDS admitted to ICU within 48 hours
- Cisatracurium besylate v.s. placebl
- Hazard ratio of 90 days death in the cisatracurium v.s. placebo is 0.68 (95% CI, 0.48 to 0.98; P = 0.04),

N Engl J Med 2010;363:1107-16.

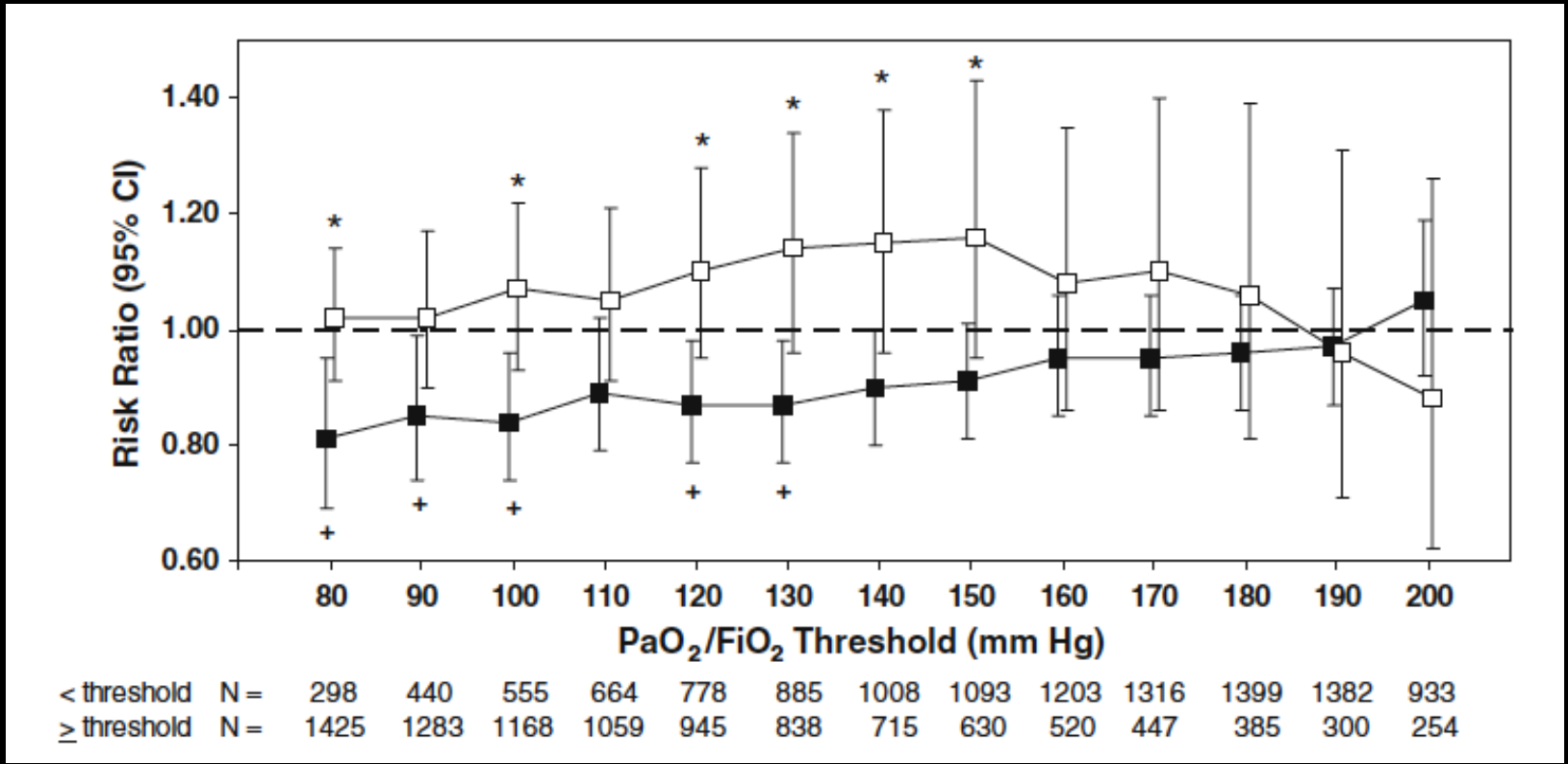
Early Neuromuscular Blockade in ARDS

ROSE trial, PETAL network



NEJM May 19, 2019

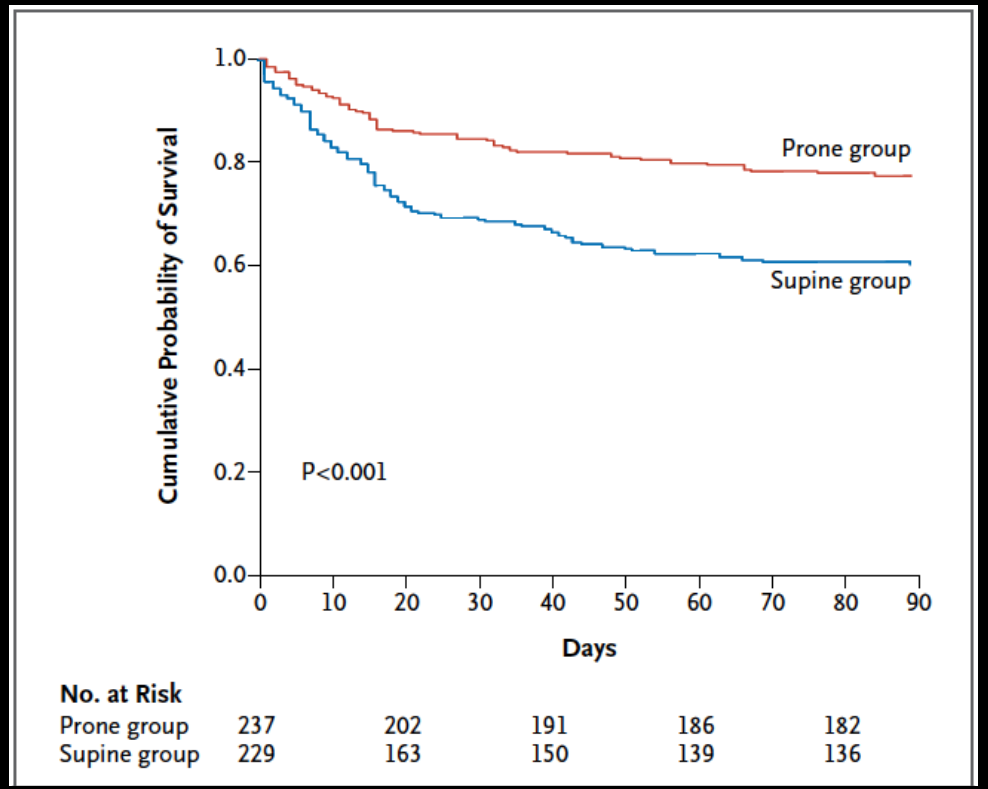
Mortality Benefits in Low P/F patients



Intensive Care Med (2010) 36:585–599

Prone positioning in severe ARDS

- Multicenter, prospective, randomized, controlled trial
- 446 patients
  - 237 prone, 229 supine
- Severe ARDS
  - P/F ratio < 150
  - $FiO_2 \geq 0.6$
  - PEEP ≥ 5 cm H_2O
- ≥ 16 hours/day



N Engl J Med 2013;368:2159-68.

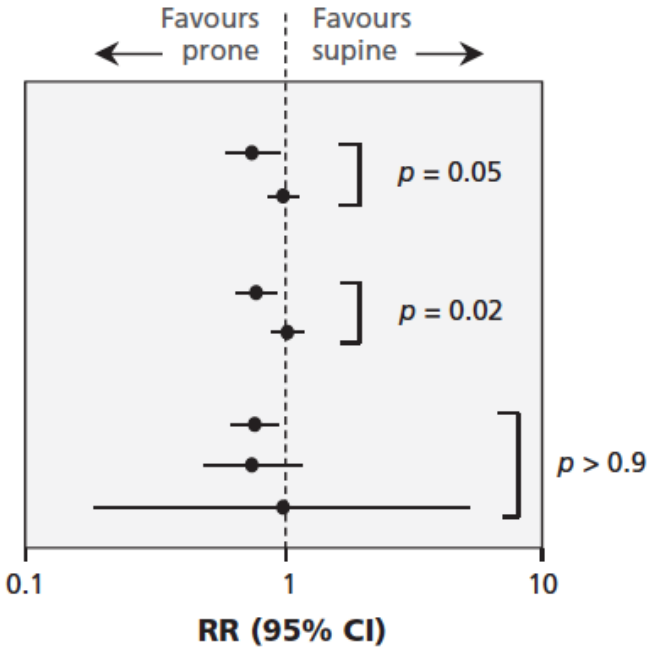
CMAJ

RESEARCH

CMAJ 2014. DOI:10.1503/cmaj.140081

Effect of prone positioning during mechanical ventilation on mortality among patients with acute respiratory distress syndrome: a systematic review and meta-analysis

Variable	No. of trials	Deaths, *n/N*		RR (95% CI)	I^2 value, %
		Prone	Supine		
Protective lung ventilation					
Mandated	6	154/510	209/506	0.74 (CI 0.59–0.95)	29
Not mandated	4	229/458	205/395	0.98 (CI 0.86–1.12)	0
Duration of prone positioning					
≥ 16 h/d	6	191/565	243/547	0.77(CI 0.64–0.92)	21
< 16 h/d	4	192/403	171/354	1.02 (CI 0.88–1.17)	0
Level of hypoxemia*					
Severe	6	75/210	102/209	0.76 (CI 0.61–0.94)	0
Moderate	6	75/274	102/268	0.74 (CI 0.48–1.16)	42
Mild	4	3/22	3/23	0.98 (CI 0.18–5.24)	0



ECMO for 2009 Influenza H1N1 Severe ARDS

Australia and New Zealand

JAMA. 2009;302(17):1888-1895

Table 3. Patient Outcomes[a]

Outcome Measure	2009 Influenza A(H1N1) Confirmed Infection (n = 53)	2009 Influenza A(H1N1) Suspected Infection (n = 15)	All Infections (N = 68)
Length of stay, median (IQR), d			
ICU	26 (16-35)	31 (15-38)	27 (16-37)
Hospital	35 (24-45)	40 (27-54)	39 (23-47)
Duration, median (IQR), d			
Mechanical ventilation	24 (13-31)	28 (13-34)	25 (13-34)
ECMO support	10 (7-14)	11 (10-16)	10 (7-15)
Survival at ICU discharge	38 (72)	10 (67)	48 (71)
Still in ICU	4 (8)	2 (13)	6 (9)
Survival at hospital discharge	22 (42)	10 (67)	32 (47)
Still in hospital[b]	14 (26)	2 (13)	16 (24)
Ambulant at hospital discharge[c]	21 (95)	10 (100)	31 (97)
Sa_{O_2} on room air at hospital discharge, median (IQR), %[c]	97 (95-98)	97 (95-98)	97 (95-98)
Discharge destination			
Died	11 (21)	3 (20)	14 (21)
Home	18 (34)	4 (27)	22 (32)
Other hospital	0	1 (7)	1 (1)
Rehabilitation facility	4 (8)	5 (33)	9 (13)
Cause of death[d]			
Hemorrhage	3 (27)	1 (33)	4 (29)
Intracranial hemorrhage	4 (36)	2 (66)	6 (43)
Infection	1 (9)	0	1 (7)
Intractable respiratory failure	3 (27)	1 (33)	4 (29)

Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial

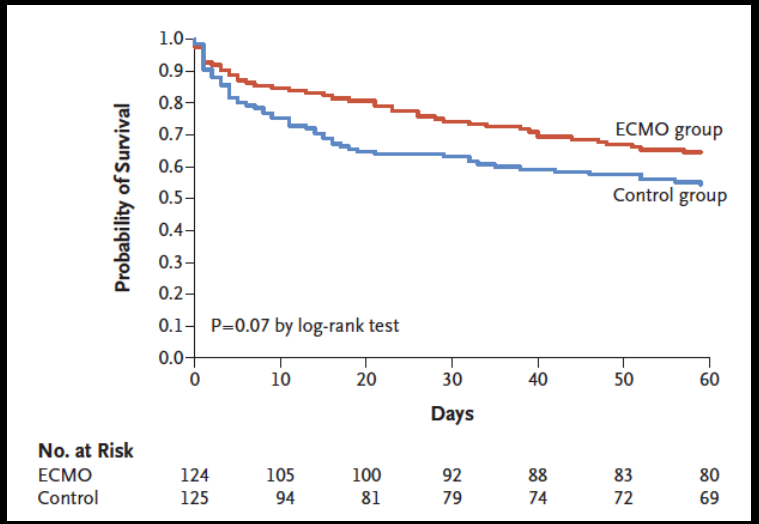
Giles J Peek, Miranda Mugford, Ravindranath Tiruvoipati, Andrew Wilson, Elizabeth Allen, Mariamma M Thalanany, Clare L Hibbert, Ann Truesdale, Felicity Clemens, Nicola Cooper, Richard K Firmin, Diana Elbourne, for the CESAR trial collaboration

- UK-based multi-center trial
- 180 patients,1:1 ratio, conventional vs ECMO
  - aged 18–65 years, severe (Murray score >3.0 or pH <7.20)
  - high pressure (>30 cm H_2O of PIP) or high FiO_2 (>0.8) ventilation for more than 7 days; intracranial bleeding; any other contraindication to limited heparinisation; or any contraindication to continuation of active treatment
- Survive to 6 months without disability
  - ECMO 63% (57/90) vs conventional 47% (41/87) (RR 0.69; 95% CI 0.05–0.97, p=0.03)

Lancet 2009; 374: 1351–63

Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome

A. Combes, D. Hajage, G. Capellier, A. Demoule, S. Lavoué, C. Guervilly, D. Da Silva, L. Zafrani, P. Tirot, B. Veber, E. Maury, B. Levy, Y. Cohen, C. Richard, P. Kalfon, L. Bouadma, H. Mehdaoui, G. Beduneau, G. Lebreton, L. Brochard, N.D. Ferguson, E. Fan, A.S. Slutsky, D. Brodie, and A. Mercat, for the EOLIA Trial Group, REVA, and ECMONet*



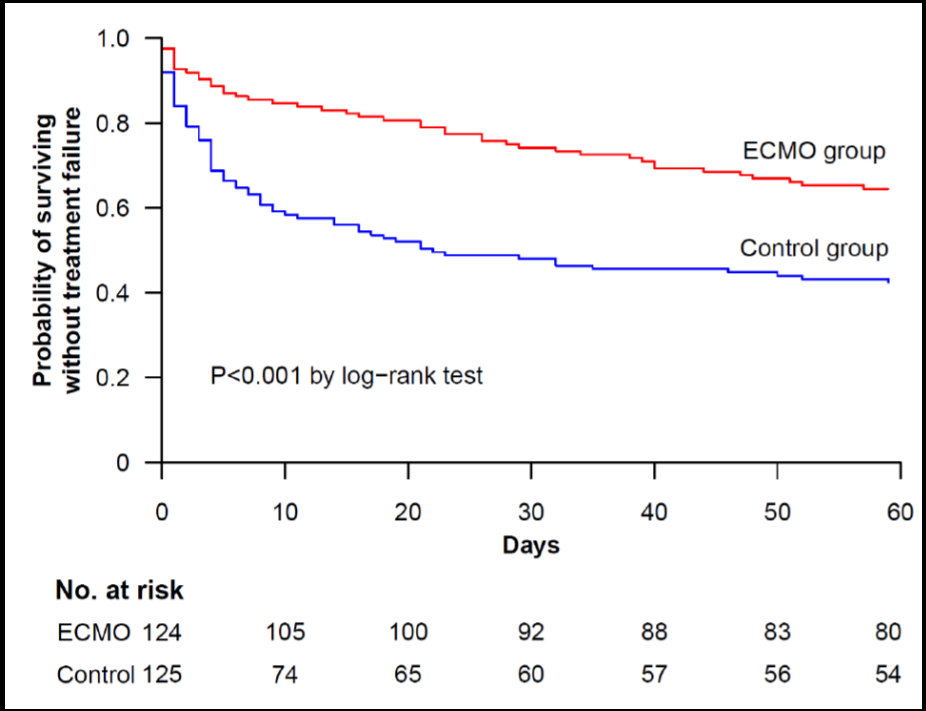
1. Very sick patients
   - P/F ratio < 80 mmHg
   - C_{RS} < 30 cmH_2O
   - Driving pressure > 16 cmH_2O
   - SOFA > 10
2. Strict study design
   - 100% ECMO in study group
   - Optimal care in control group
     - Low tidal volume, 90% prone, 100% NM blockade

The routine use of ECMO in patients with severe ARDS is not superior to the use of ECMO as a rescue maneuver in patients whose condition has deteriorated further.

N Engl J Med 2018; 378: 1965-75.

Survival Without Treatment Failure

Crossover to ECMO or Death for the Control Group and Death for the ECMO Group



1. Ethical consideration
2. 35(28%) in the control group crossover to ECMO
3. Crossover patients are sicker
   - Higher P_{plat}, ΔP, Lower compliance, more CXR infiltrates
4. High mortality (57%), without crossover (41%)

N Engl J Med 2018; 378: 1965-75.

“Prediction is very difficult, especially about the future”

Niels Bohr 1885-1962

Physics Nobel Price - 1922

Predictors for Prone Position Ventilation in Influenza-related ARDS

Table 3 Cox regression analysis of clinical variables associated with 60-day mortality in influenza pneumonia-related ARDS with prone positioning

Clinical variables	Univariate		Multivariate	
	Hazard ratio (95% CI)	*p* value	Hazard ratio (95% CI)	*p* value
APACHE II score	1.089 (1.035–1.147)	0.001*	1.042 (0.982–1.106)	0.178
PSI	1.015 (1.005–1.026)	0.003*	1.020 (1.009–1.032)	< 0.001*
Renal replacement therapy	5.355 (2.159–13.281)	0.000*	6.248 (2.245–17.389)	< 0.001*
Δ Peak airway pressure (cm H_2O)	1.143 (1.019–1.282)	0.022*	0.996 (0.822–1.208)	0.969
Δ Dynamic driving pressure (cm H_2O)	1.147 (1.008–1.305)	0.037*	1.372 (1.095–1.718)	0.006*
Δ Dynamic compliance (ml/cm H_2O)	0.925 (0.871–0.983)	0.011*	0.941 (0.872–1.015)	0.117

ARDS acute respiratory distress syndrome, *CI* confidence interval, *APACHE II* Acute Physical and Chronic Health Evaluation, *PSI* pneumonia severity index, *Δ* difference between before and after prone positioning 1 day

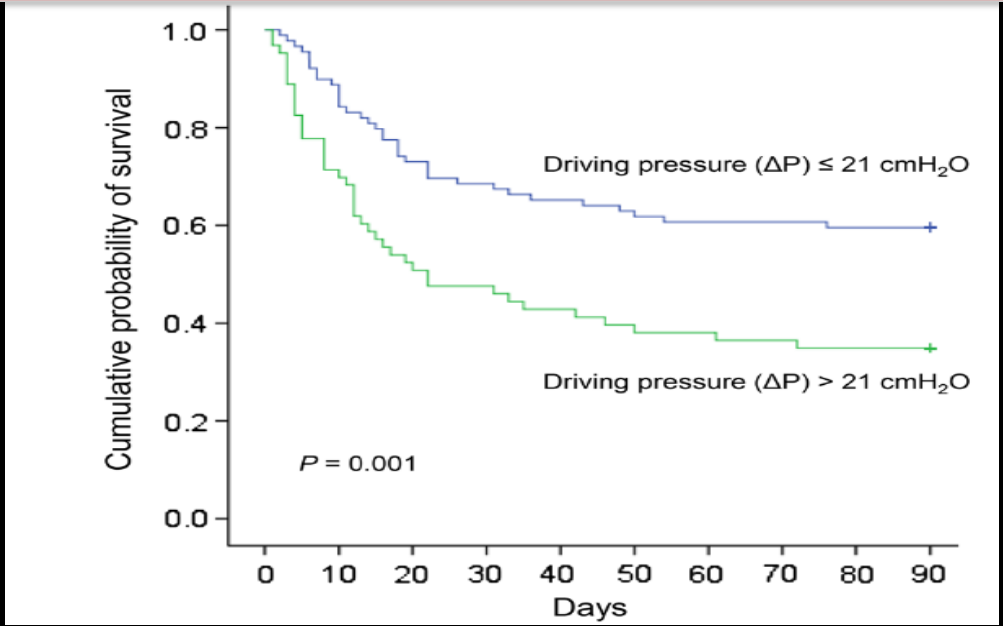
*$p < 0.05$

Kao et al. Ann. Intensive Care (2018) 8:94

Dynamic Driving Pressure for ARDS with ECMO

Table 2 Cox proportional hazards regression model with ICU mortality as outcome

Factors	Hazard ratio (95% CI)	*p* value
Multivariate analysis		
Immunocompromised	1.957 (1.216–3.147)	0.006
APACHE II score	1.039 (1.005–1.073)	0.023
ARDS duration before ECMO	1.002 (1.000–1.003)	0.029
Mean dynamic driving pressure from day 1 to 3 on ECMO	1.070 (1.026–1.116)	0.002



Chiu *et al. Ann. Intensive Care (2017) 7:12*

Lung Safe Study

Global Epidemiology of ARDS

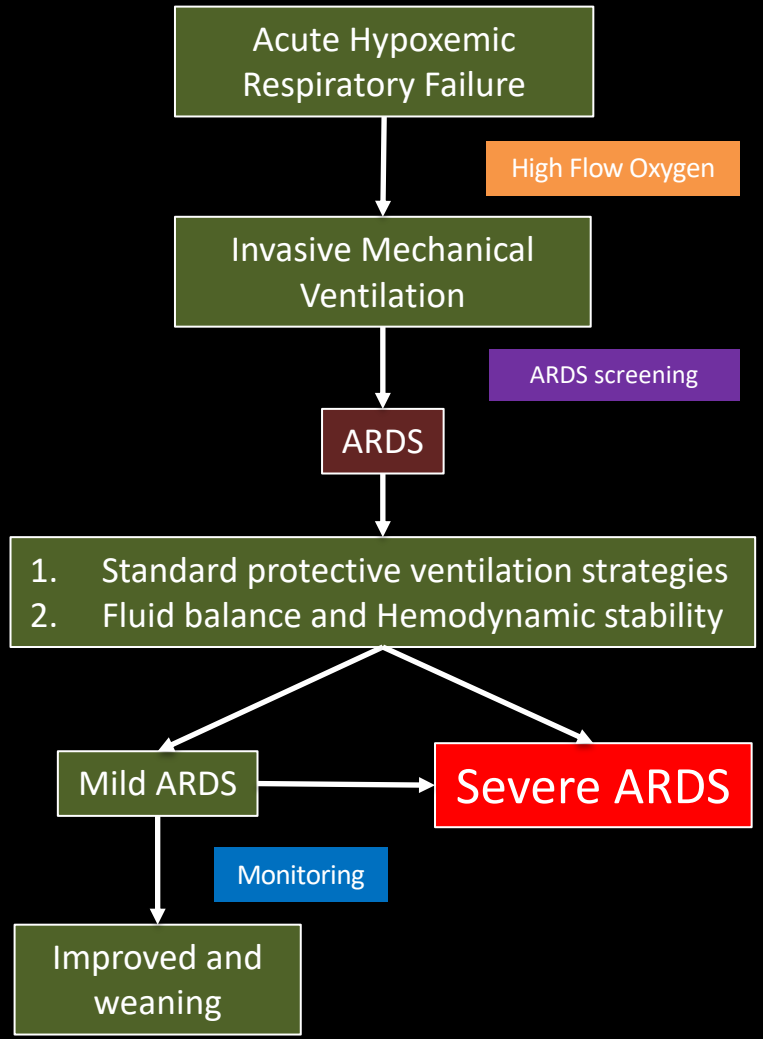
- International, multicenter, prospective cohort study in winter 2014
  - 459 ICUs from 50 countries
- 10.4% (3022/29144) of ICU admission and 23% of patients requiring MV fulfilled ARDS criteria.
- Underrecognized
  - Clinician recognition of ARDS only 60%
  - Clinician recognition of ARDS at the time of fulfillment of ARDS criteria was 34.0%
- Undertreated
  - Less than 2/3 Vt < 8 of mL/kg.
  - P_{plat} measured in 40.1%, whereas 82.6% PEEP < 12 cm H_2O.
  - Prone positioning was used in 16.3% of severe ARDS.
- High mortality
  - Hospital mortality, mild 34.9%, moderate 40.3%, severe 46.1%.

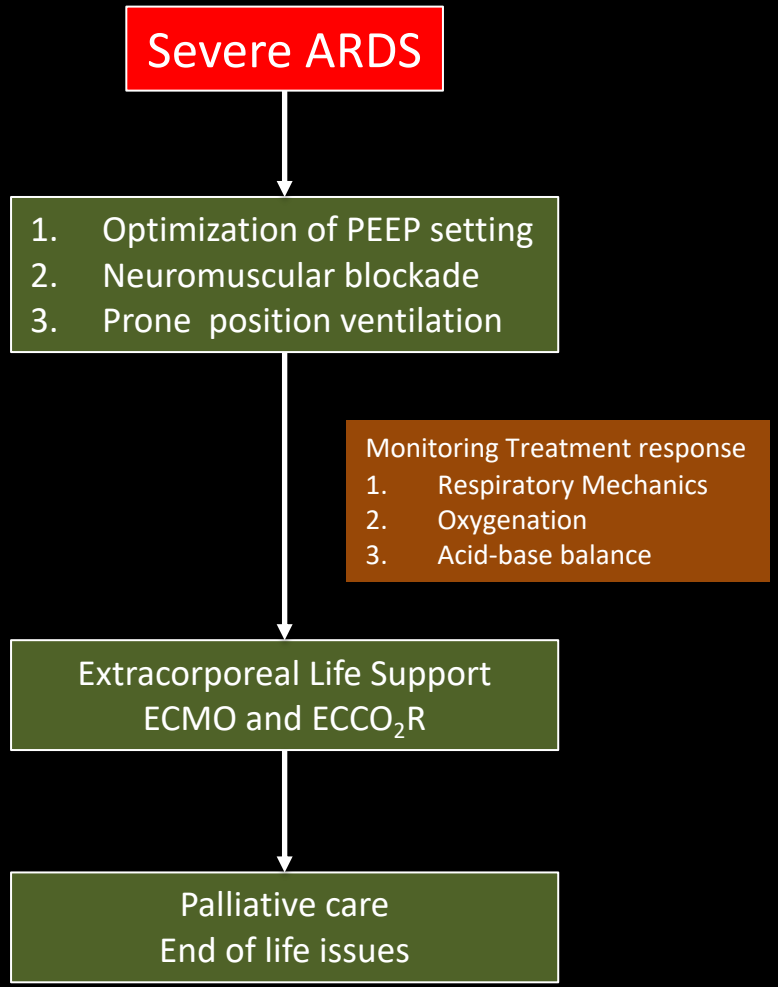
JAMA. 2016;315(8):788-800.

Table 3 Cox proportional hazard regression for 30-day mortality.

Characteristics	Univariate		Multivariate	
	HR (95% C.I.)	P value	HR (95% C.I.)	P value
Age, per 1 year increment	1.009 (0.991–1.027)	0.33	1.016 (0.992–1.041)	0.19
Sex				
Female	1 [Reference]		1 [Reference]	
Male	1.072 (0.663–1.819)	0.80	0.845 (0.452–1.581)	0.60
BMI, per 1 kg/m^2 increment	0.940 (0.889–0.994)	0.03	0.960 (0.892–1.034)	0.28
Cerebrovascular disease				
No	1 [Reference]		1 [Reference]	
Yes	2.165 (1.028–4.557)	0.04	0.899 (0.307–2.635)	0.85
PaO_2/FiO_2, per 1 increment	0.995 (0.990–1.000)	0.03	0.998 (0.992–1.004)	0.54
APACHE II, per 1 increment	1.087 (1.054–1.121)	<0.01	1.058 (1.014–1.105)	0.01
Lactate, per 1 mg/dl increment	1.014 (1.009–1.019)	<0.01	1.011 (1.004–1.018)	<0.01
ECMO				
No	1 [Reference]		1 [Reference]	
Yes	2.068 (1.211–3.529)	<0.01	1.096 (0.526–2.286)	0.81
Vasopressor-use				
No	1 [Reference]		1 [Reference]	
Yes	2.125 (1.225–3.683)	<0.01	1.896 (0.877–4.099)	0.10
Day-intubation V_T/PBW, per 1 mL/kg increment	1.250 (1.091–1.431)	<0.01	1.261 (1.072–1.484)	<0.01

Taiwan Severe Influenza Research Consortium.
Journal of the Formosan Medical Association (2018) xx, 1e8


Acute Hypoxemic Respiratory Failure
High Flow Oxygen
Invasive Mechanical Ventilation
ARDS screening
ARDS
1. Standard protective ventilation strategies
2. Fluid balance and Hemodynamic stability
Mild ARDS
Severe ARDS
Monitoring
Improved and weaning


Severe ARDS
1. Optimization of PEEP setting
2. Neuromuscular blockade
3. Prone position ventilation
Monitoring Treatment response
1. Respiratory Mechanics
2. Oxygenation
3. Acid-base balance
Extracorporeal Life Support
ECMO and ECCO2R
Palliative care
End of life issues