Optimal Strategies for Management of ARDS

台中榮總 呼吸治療科

詹明澄

Review Articles

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

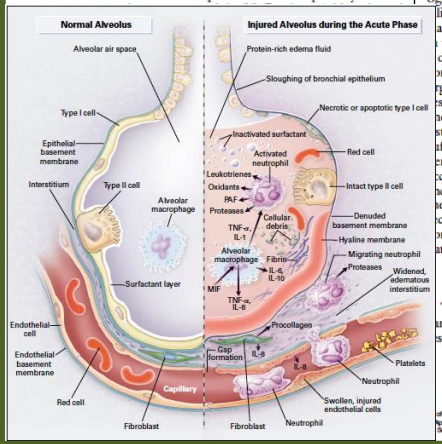
The first description of acute respiratory distress

based on the level of positive
the ratio of the partial pressu
the fraction of inspired oxyge
pliance, and the degree of
chest radiographs.[4] Other fac
sessment were the inciting cl
presence or absence of nonpu
tion (Table 1). Although the l
tem has been widely used to
lung injury in both clinical r
als, it cannot be used to predi
the first 24 to 72 hours after
respiratory distress syndrom
clinical usefulness.[6,7] When th
four to seven days after the
scores of 2.5 or higher may
plicated course with the ne
chanical ventilation.[8]

In 1994, a new definition w
American–European Consen
mittee (Table 1).[5] The consen
advantages. First, it recogniz
clinical lung injury varies: p
hypoxemia (as defined by a r
sure of arterial oxygen to the
ygen of 300 or less) are consid
injury, and those with more
defined by a ratio of 200 or
have the acute respiratory dist
gnition of patients with acu
itate earlier enrollment of a
al trials. Second, the defini
the clinical setting. Howeve
disadvantage, since factors
ome, such as the underlying
rgan systems are affected,
ssed.[6,7,9-11] In addition, the
nce of bilateral infiltrates on
stent with the presence of p
fficiently specific to be app
erienced clinicians.[12,13] Never
cceptance of both the 199
nd the 1988 lung-injury scori
e standardization of clinical
commend that clinicians r
onsensus definition to allow
atients with patients enrolle

CLINICAL, PATH AND RADIOGRAPH

The definitions discussed
arly in the course of acute lu
spiratory distress syndrome.



REVIEW AR

Jeffrey M. Drazen,

Acute Respiratory D

B. Taylor Thompson, M.D., Rachel C. Chambers

FIFTY YEARS AGO, ASHBAUGH AND COLL
tachypnea, refractory hypoxemia, and d
ter infection or trauma.[1] Prominent hya
veolar spaces of the lungs in 6 of the 7 patien
to be specific for the respiratory distress syn
adult (later changed to acute) respiratory dis

Since ARDS was last reviewed in the Jour
has been made in the care of affected patie
with reductions in both incidence and mor
tively common and lethal or disabling syn
involving 29,144 patients,[3] 10% of all patie
(ICU) and 23% of mechanically ventilated
subgroup of patients with severe ARDS was
der are at high risk for cognitive decline, dep
and persistent skeletal-muscle weakness.[4,5]

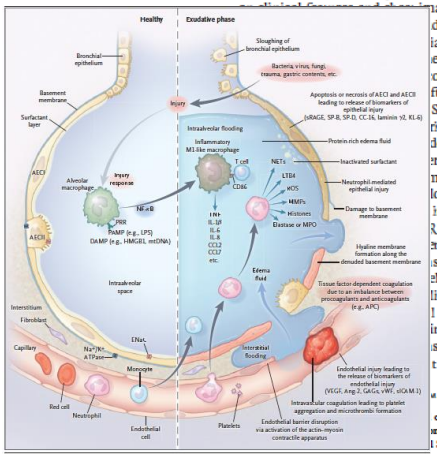
From the Division of Pulmonary and Critical Care, Department of Medicine, Massachusetts General Hospital, and Harvard Medical School — both in Boston (B.T.T.); Centre for Inflammation and Tissue Repair, the Division of Medicine, University College London, London (R.C.C.); and the Divisions of Nephrology and Critical Care Medicine, University of California San Francisco, San Francisco (K.D.L.). Address reprint requests to Dr. Thompson at the Division of Pulmonary and Critical Care, Department of Medicine, Massachusetts General Hospital, Bulfinch Bldg., Suite 148, 55 Fruit St., Boston, MA 02114, or at thompson.taylor@mgh.harvard.edu.

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

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

DEFINITION AND PATHO

Four major definitions of ARDS have evolve
the central features of the initial description
lung permeability, edema, and inflammation
care and no validated diagnostic biomarkers



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.

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.

From the Keenan Research Center, Li Ka Shing Knowledge Institute, St. Michael's Hospital, and the Department of Medicine and Interdepartmental Division of Critical Care Medicine, University of Toronto — both in Toronto (A.S.S.); and Dipartimento di Anestesia e Medicina degli Stati Critici, Ospedale S. Giovanni Battista Molinette, Università di Torino, Turin, Italy (V.M.R.). Address reprint requests to Dr. Slutsky at St. Michael's Hospital, 30 Bond St., Toronto, ON M5B 1W8, Canada, or at slutskya@smh.ca.

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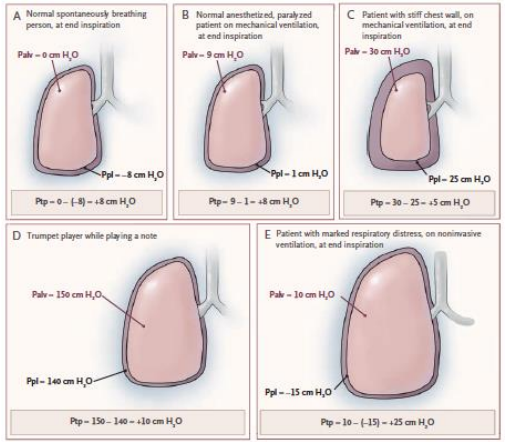
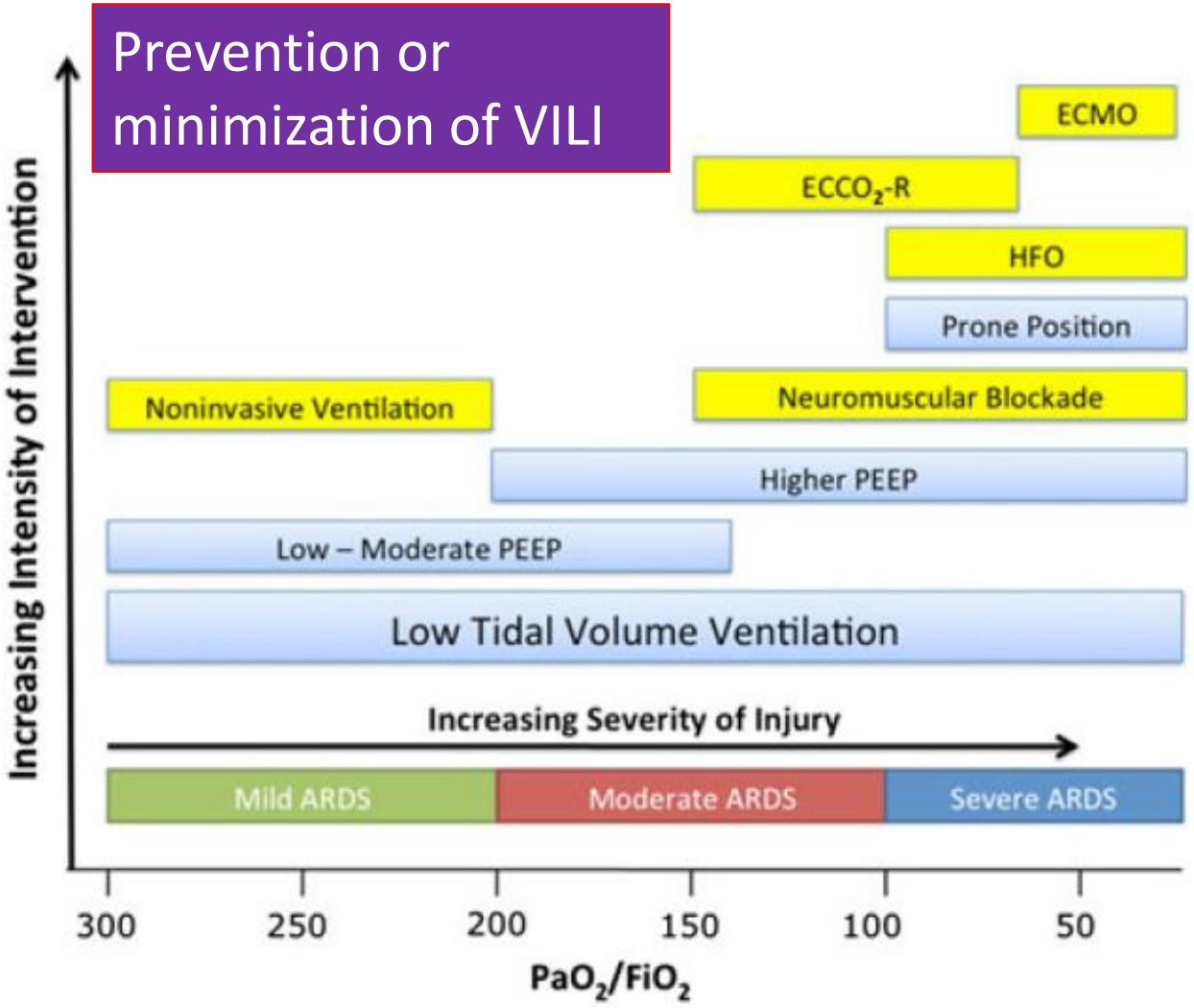
N Engl J Med 2013;369:2126-36.
DOI: 10.1056/NEJMra1208707



L FEATURES



Therapeutic options for ARDS

Intensive Care Med (2012) 38:1573–1582

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.

Mild ARDS in Lung Safe Study

Among 580 patients with initial mild ARDS, 18% (103 of 580) continuously improved, 36% (210 of 580) had persisting mild ARDS, and 46% (267 of 580) worsened in the first week after ARDS onset.

	Nonworsening, N = 313	Worsening, N = 267	*P* value	N
Outcome				
Clinician recognition of ARDS, No. (%)	146 (46.6)	146 (54.7)	0.065	580
Decision of withholding or withdrawing life-sustaining treatments, No. (%)	44 (14.1)	61 (22.8)	0.008	580
Duration of mechanical ventilation, median (IQR), days	5 (3, 11)	11 (6, 18)	< 0.001	550
Ventilator-free days, median (IQR), days	22 (6, 25)	9 (0, 20)	< 0.001	550
ICU length of stay, median (IQR), days	9 (5, 17)	14 (8, 22)	< 0.001	580
ICU mortality, No. (%)	53 (16.9)	89 (33.3)	< 0.001	580
Hospital length of stay, median (IQR), days	20 (11, 38)	19 (11, 37)	0.950	564
Hospital mortality, No. (%)	73 (23.5)	99 (37.4)	< 0.001	576

Anesthesiology 2019; 130:263–83

Timing of Low Tidal Volume Ventilation and Intensive Care Unit Mortality in Acute Respiratory Distress Syndrome

A Prospective Cohort Study

Dale M. Needham[1,2,3,4], Ting Yang[4], Victor D. Dinglas[1,2], Pedro A. Mendez-Tellez[1,5], Carl Shanholtz[6], Jonathan E. Sevransky[7], Roy G. Brower[2], Peter J. Pronovost[1,4,5], and Elizabeth Colantuoni[1,8]

[1]Outcomes After Critical Illness and Surgery Group, [2]Division of Pulmonary and Critical Care Medicine, School of Medicine, [3]Department of Physical Medicine and Rehabilitation, School of Medicine, [4]Armstrong Institute for Patient Safety and Quality, [5]Department of Anesthesiology and Critical Care Medicine, School of Medicine, and [8]Department of Biostatistics, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland; [6]Division of Pulmonary and Critical Care Medicine, University of Maryland, Baltimore, Maryland; and [7]Division of Pulmonary, Allergy and Critical Care, Emory University School of Medicine, Atlanta, Georgia

Main Result:

An increase of 1 ml/kg PBW in initial tidal volume was associated with a 23% increase in ICU mortality risk (adjusted HR 1.23; 95% CI, 1.06-1.44, P=0.008).

Conclusions:

Higher tidal volumes shortly after ARDS onset were associated with a greater risk of ICU mortality compared with subsequent tidal volumes.

Am J Respir Crit Care Med Vol 191, Iss 2, pp 177–185, Jan 15, 2015

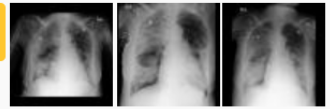
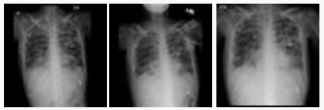
Table 3 Cox proportional hazard regression for 30-day mortality.

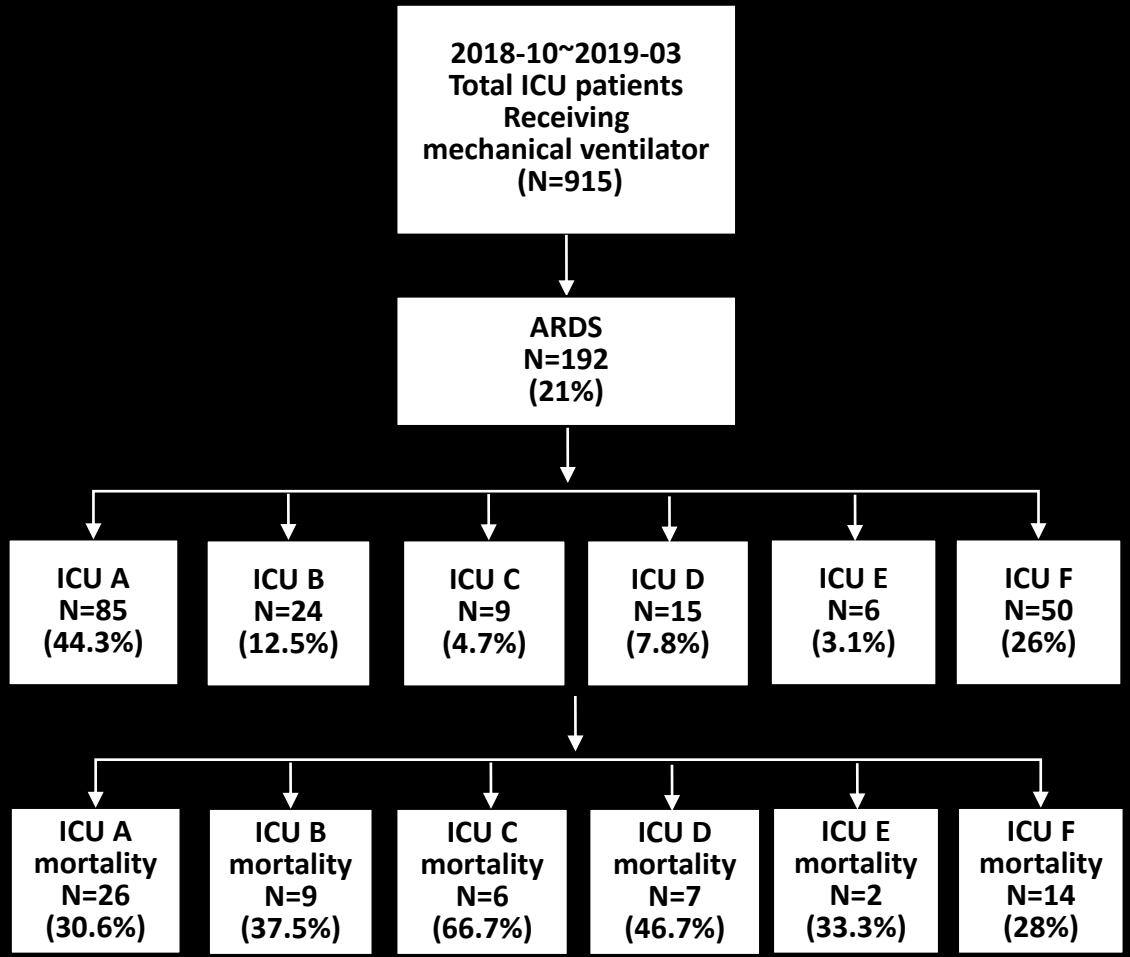
Characteristics	Univariate		Multivariate	
	HR (95% C.I.)	P value	HR (95% C.I.)	P value
Age, per 1 year increment	1.009 (0.991–1.027)	0.33	1.016 (0.992–1.041)	0.19
Sex				
Female	1 [Reference]		1 [Reference]	
Male	1.072 (0.663–1.819)	0.80	0.845 (0.452–1.581)	0.60
BMI, per 1 kg/m^2 increment	0.940 (0.889–0.994)	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

請選擇病房(可多選) | 20190220 | Go | POR | ARDS | ARDS screen | 病歷號或就診號 | Go | DailyScreen

ARDS 的病人清單，總共： 15 人 ☑ 僅顯示有呼吸器病人

床號 姓名	呼吸器及其記錄 ☐ 病情摘要	GCS	I/O	連結 功能
CCU 16 [redacted] 002146219B	840RT-48 9 ARDS day5 137 102 112  5天前 4天前 1天前			請選擇…
✔0030 ✖1600 入院資訊 61.02 病摘	I 0100 6.6 cc/kg　I 0152 6.4 cc/kg　I 0622 6.4 cc/kg　I 0800 6.4 cc/kg			
ICU 03 [redacted] 001754878G	840RT-87 6 ARDS day5 108 81 103  4天前 2天前 2天前			請選擇…
✔0030 ✖1600 入院資訊 42.82 病摘	I 0028 6.1 cc/kg　I 0800 6.2 cc/kg　I 0824 6.3 cc/kg			
ICU 05 [redacted] 002008396J	840RT-41 10 ARDS day9 122 186 90 			請選擇…


2018-10~2019-03
Total ICU patients
Receiving
mechanical ventilator
(N=915)
ARDS
N=192
(21%)
ICU A
N=85
(44.3%)
ICU B
N=24
(12.5%)
ICU C
N=9
(4.7%)
ICU D
N=15
(7.8%)
ICU E
N=6
(3.1%)
ICU F
N=50
(26%)
ICU A
mortality
N=26
(30.6%)
ICU B
mortality
N=9
(37.5%)
ICU C
mortality
N=6
(66.7%)
ICU D
mortality
N=7
(46.7%)
ICU E
mortality
N=2
(33.3%)
ICU F
mortality
N=14
(28%)

ARDS 分析圖表

歡迎您 楊惠喬 *2019/02/20 08:43:07*

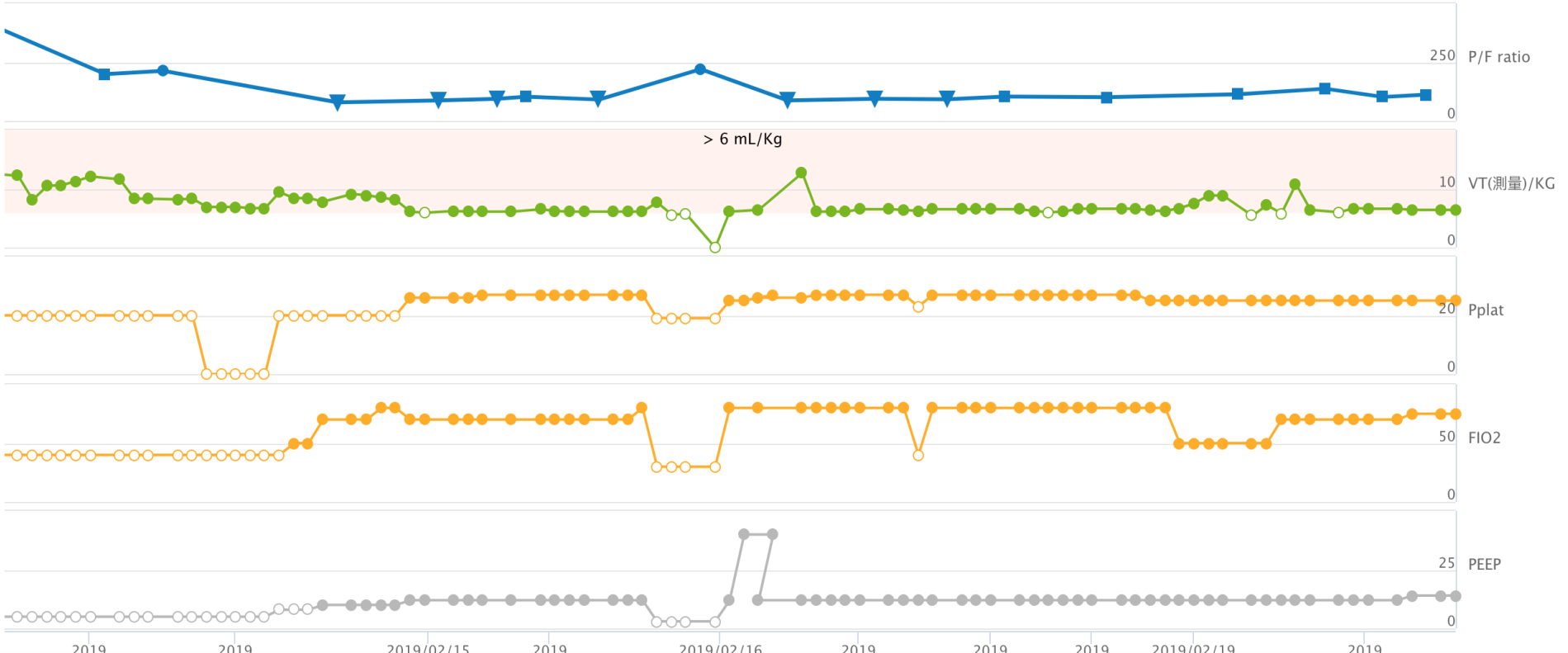
P/F ratio | VT(設定)/KG | VT(測量)/KG | Pplat | PIP | RR(設定) | RR(測量) | MV | FIO2 | PEEP

更新資料

預測體重：61.02 Kg

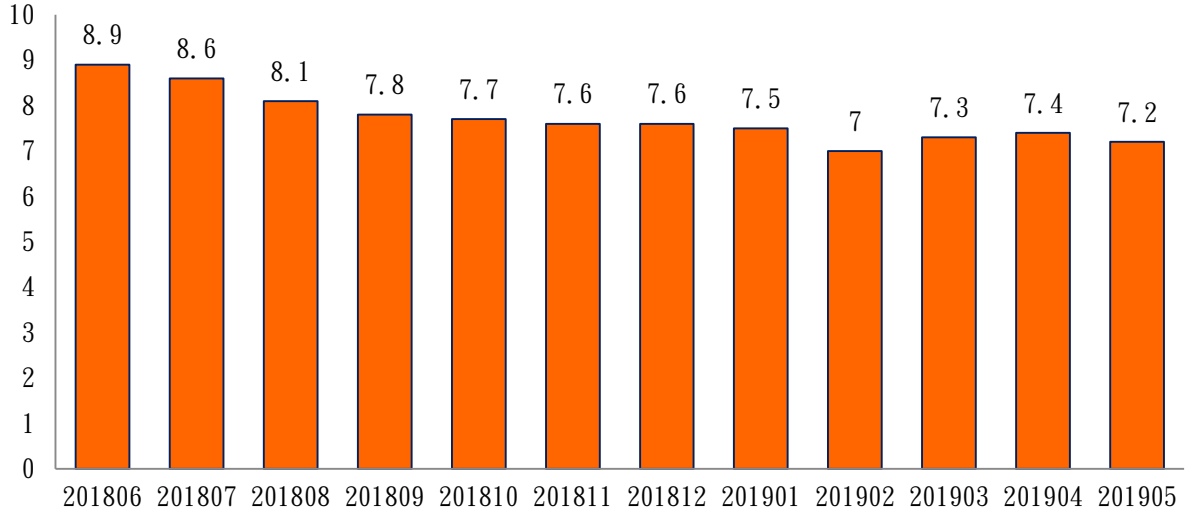
Zoom 3d **7d** 14d 3m All

From 2019-02-13 To 2019-02-20



Tidal volume 平均值(201806-201905)

Day -0



指標/月份	201806	201807	201808	201809	201810	201811	201812	201901	201902	201903	201904	201905
Tv mean± SD	8.9±0.9	8.6±1.5	8.1±1.5	7.8±1.7	7.7±1.3	7.6±1	7.6±1.5	7.5±1.5	7±1.8	7.3±1.6	7.4±1.7	7.2±1.5

Higher versus Lower Positive End-Expiratory Pressures in Patients with the Acute Respiratory Distress Syndrome

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

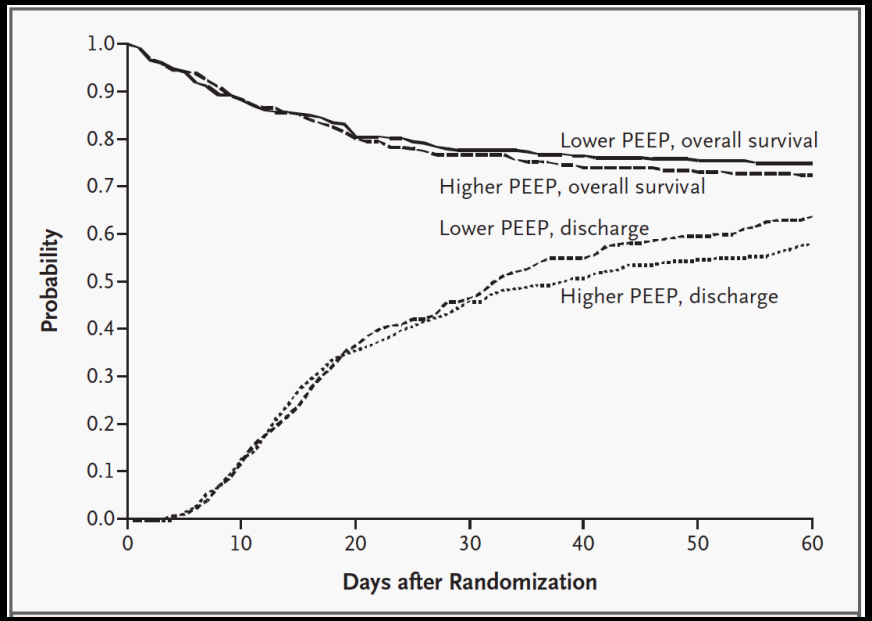


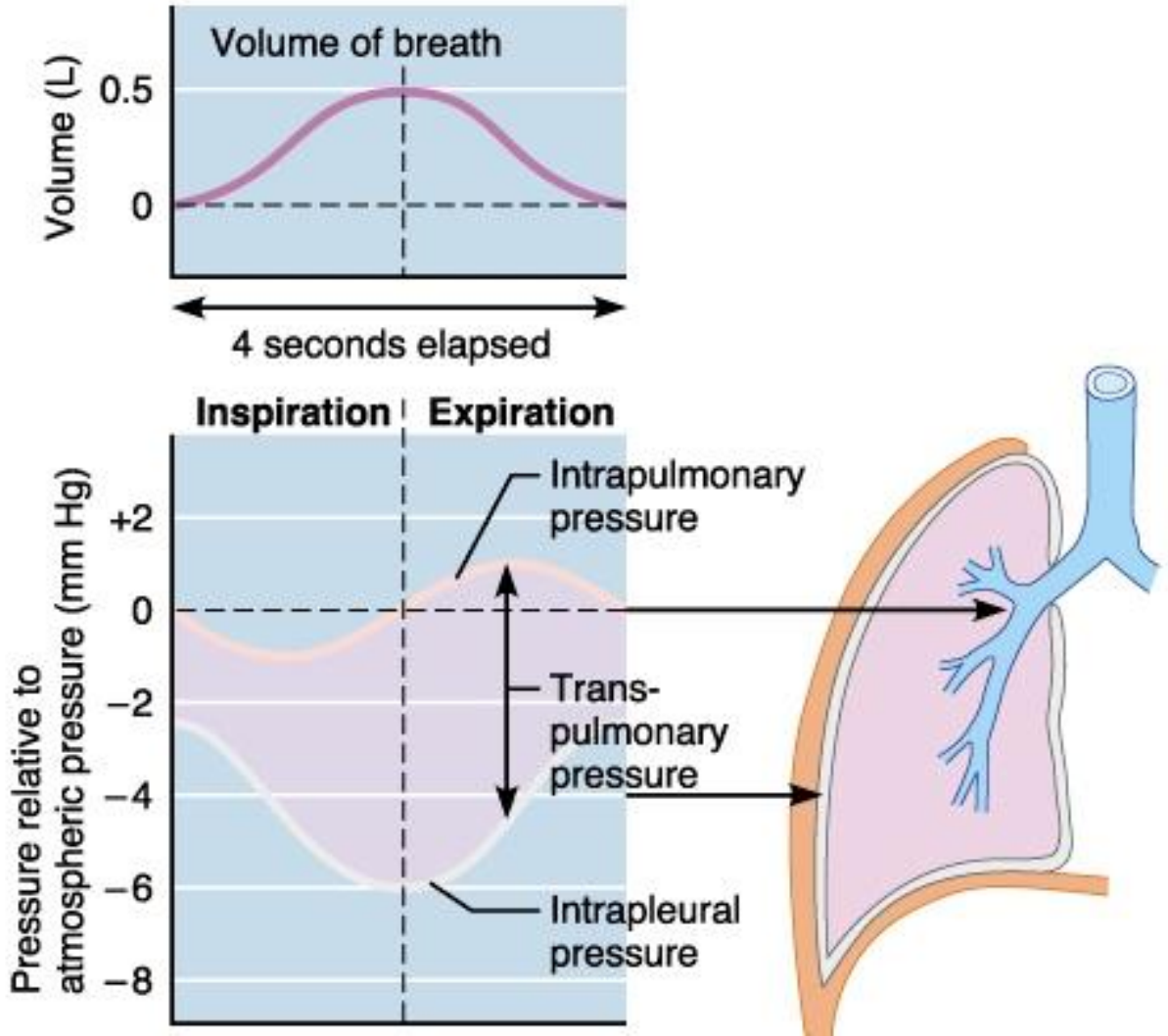
Table 1. Summary of Ventilator Procedures in the Lower- and Higher-PEEP Groups.*

Procedure	Value
Ventilator mode	Volume assist/control
Tidal-volume goal	6 ml/kg of predicted body weight
Plateau-pressure goal	≤30 cm of water
Ventilator rate and pH goal	6–35, adjusted to achieve arterial pH ≥7.30 if possible
Inspiration:expiration time	1:1–1:3
Oxygenation goal	
PaO_2	55–80 mm Hg
SpO_2	88–95%
Weaning	Weaning attempted by means of pressure support when level of arterial oxygenation acceptable with PEEP ≤8 cm of water and FiO_2 ≤0.40

Allowable combinations of PEEP and FiO_2†

Lower-PEEP group														
FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	18–24
Higher-PEEP group (before protocol changed to use higher levels of PEEP)														
FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.5–0.8	0.8	0.9	1.0	
PEEP	5	8	10	12	14	14	16	16	18	20	22	22	22–24	
Higher-PEEP group (after protocol changed to use higher levels of PEEP)														
FiO_2	0.3	0.3	0.4	0.4	0.5	0.5	0.5–0.8	0.8	0.9	1.0				
PEEP	12	14	14	16	16	18	20	22	22	22–24				

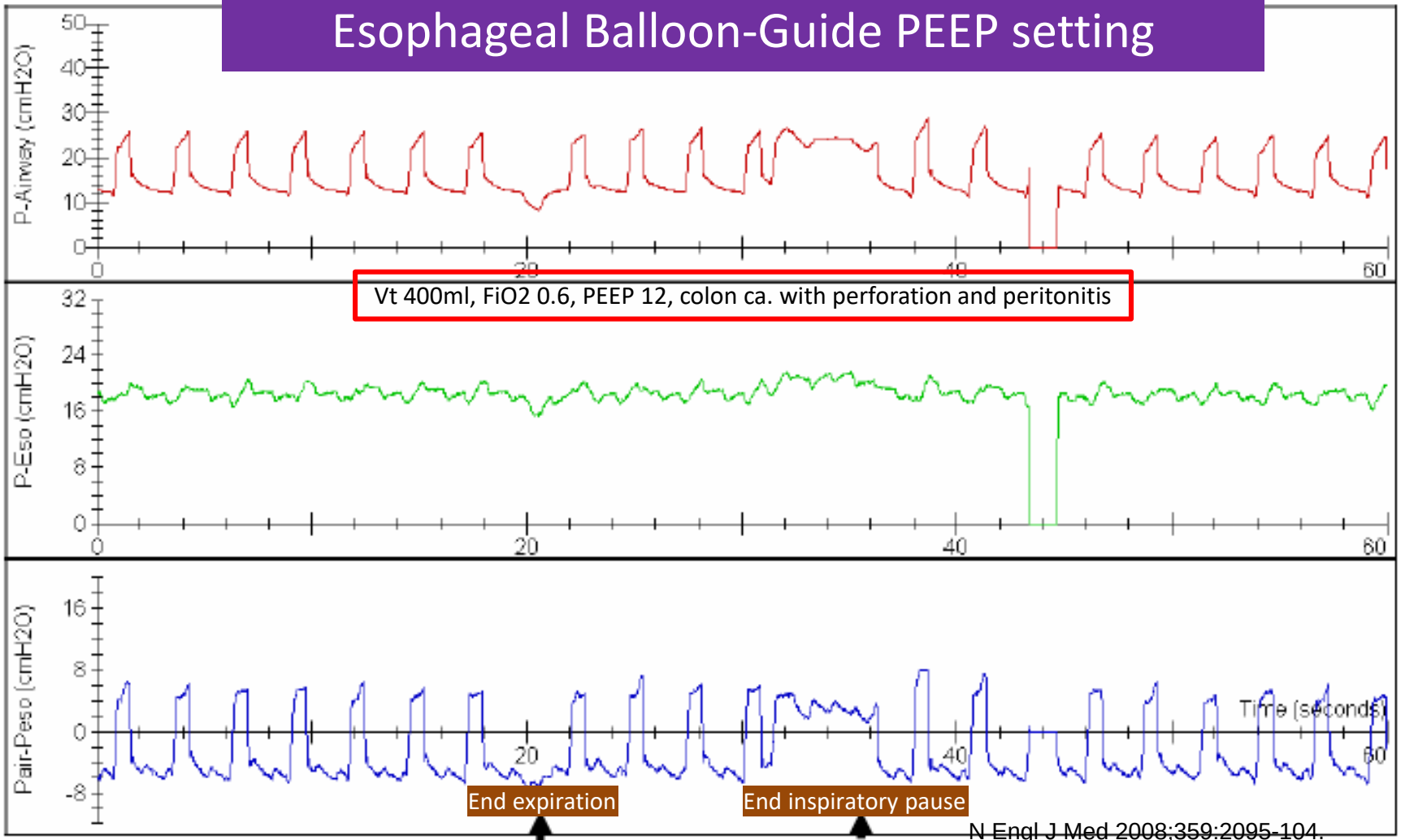
N Engl J Med 2004;351:327-36.



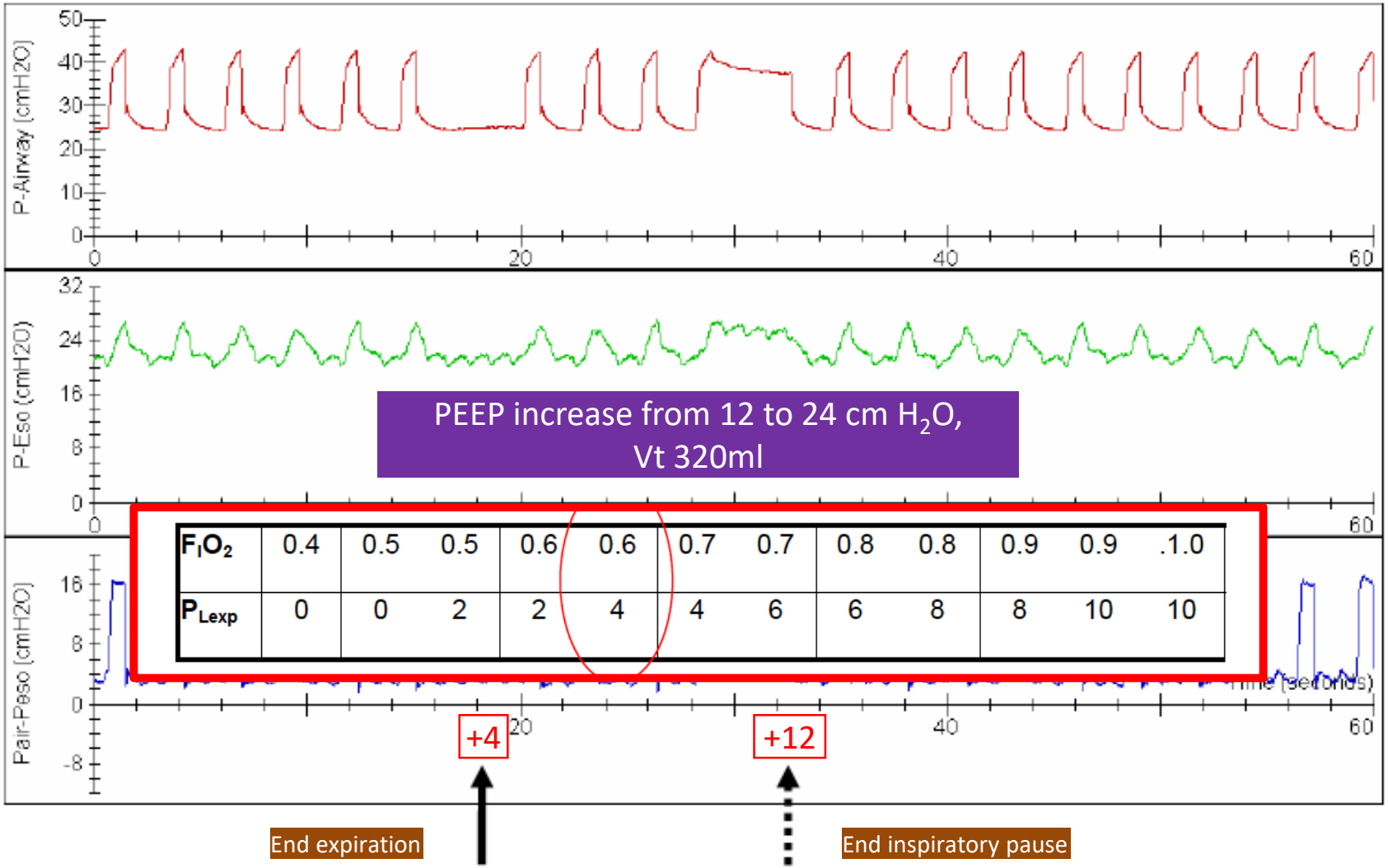
PEEP Guided by Esophageal Balloon

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})

Esophageal Balloon-Guide PEEP setting

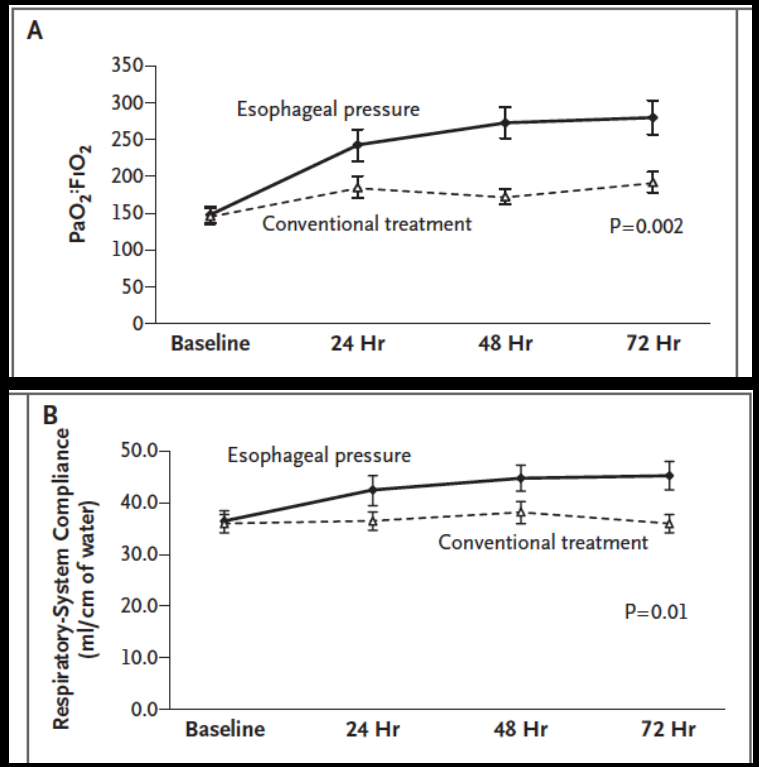


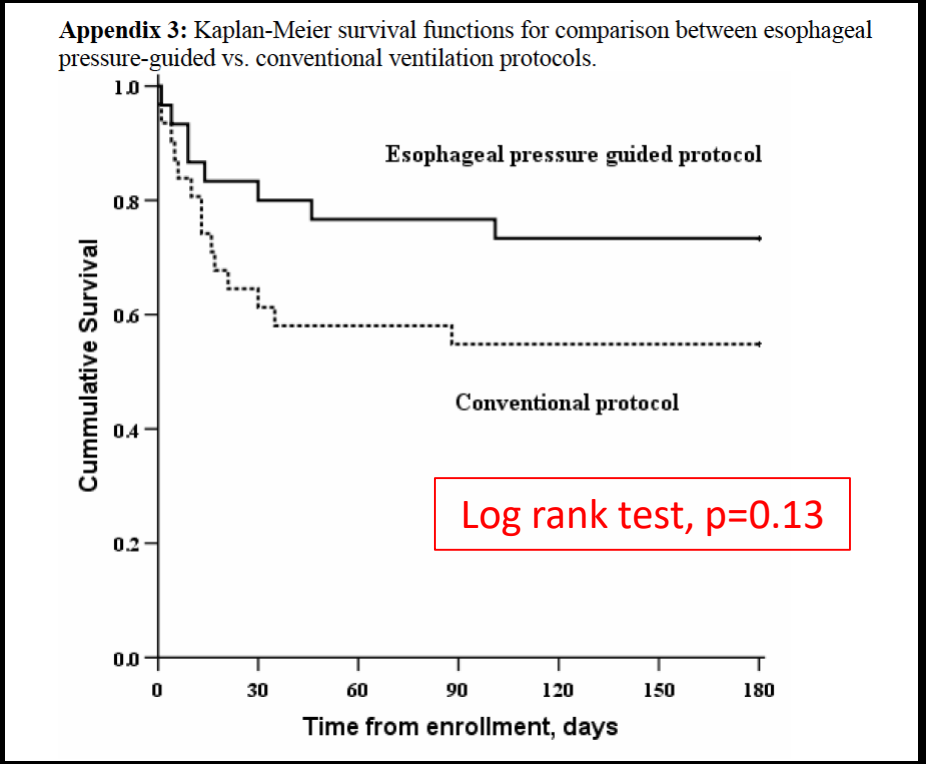
N Engl J Med 2008;359:2095-104.



F_IO_2	0.4	0.5	0.5	0.6	0.6	0.7	0.7	0.8	0.8	0.9	0.9	.1.0
P_{Lexp}	0	0	2	2	4	4	6	6	8	8	10	10

Esophageal P. vs Conventional Tx

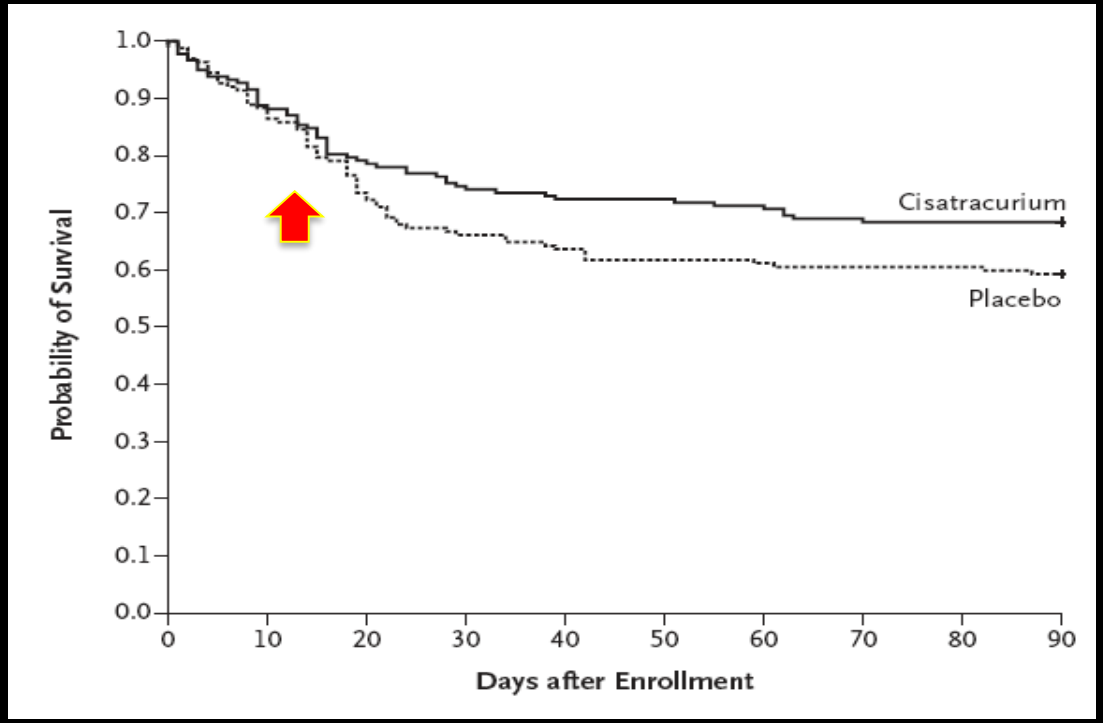




N Engl J Med 2008;359:2095-104.

Neuromuscular Blockade in Early ARDS

ACURASYS study

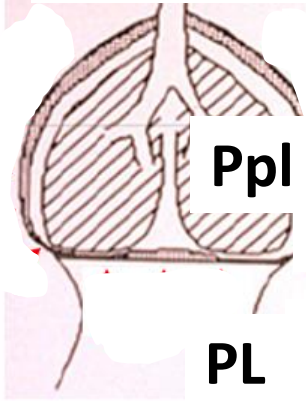


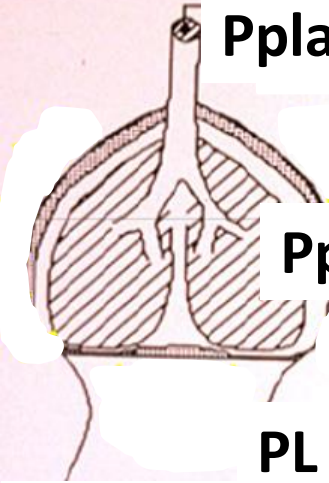
- Multi-center, double-blind, randomized controlled trial
- 340 patients with ARDS admitted to ICU within 48 hours
- Cisatracurium besylate v.s. placebl
- Hazard ratio of 90 days death in the cisatracurium v.s. placebo is 0.68 (95% CI, 0.48 to 0.98; P = 0.04),

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

High P_L & Strong Effort

Paralysis		Strong Effort
Pplat 30 cmH_2O	=	Pplat 30 cmH_2O
Ppl 10 cmH_2O (Pleural)	≠	Ppl −20 cmH_2O (Pleural)
PL 20 cmH_2O (Transpulmonary)	≪	PL 50 cmH_2O (Transpulmonary)



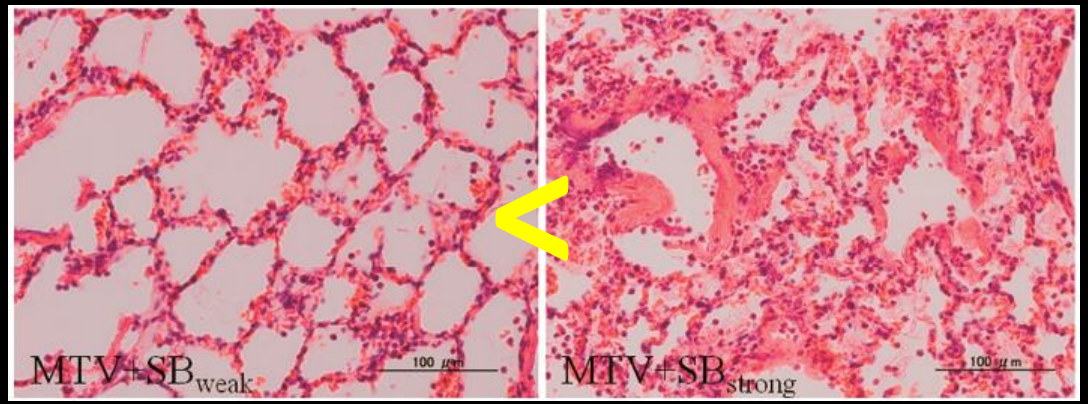


Spontaneous breathing during lung-protective ventilation in an experimental acute lung injury model: High transpulmonary pressure associated with strong spontaneous breathing effort may worsen lung injury*

Takeshi Yoshida, MD; Akinori Uchiyama, MD, PhD; Nariaki Matsuura, MD, PhD;
Takashi Mashimo, MD, PhD; Yuji Fujino, MD, PhD

(Crit Care Med 2012; 40:1578–1585)

Weak Effort Strong Effort



Progression of Lung Injury

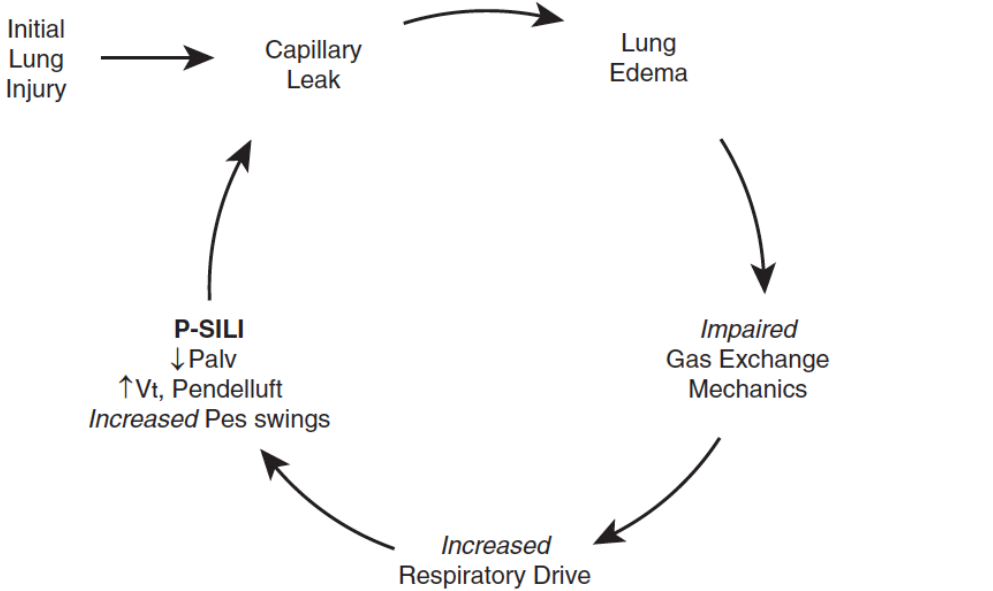


Figure 2. Illustration of the vicious cycle of injury present in patients with acute respiratory failure. Palv = alveolar pressure; Pes = esophageal pressure swings; P-SILI = patient self-inflicted lung injury.

Am J Respir Crit Care Med Vol 195, Iss 4, pp 438–442

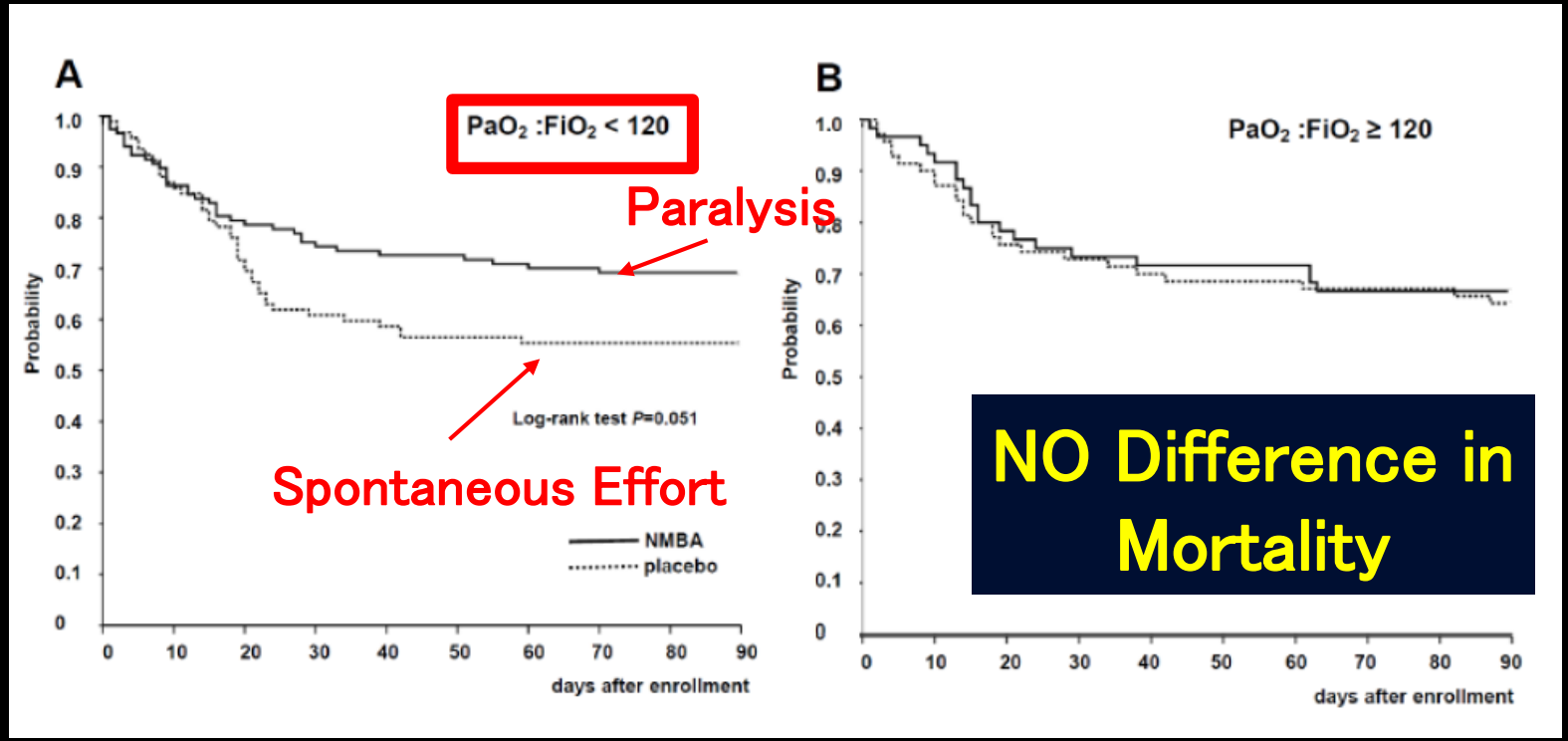
Severe Lung Injury

Papazian L et al. *New Engl J Med* 2010

More Severe

Less Severe

Survival



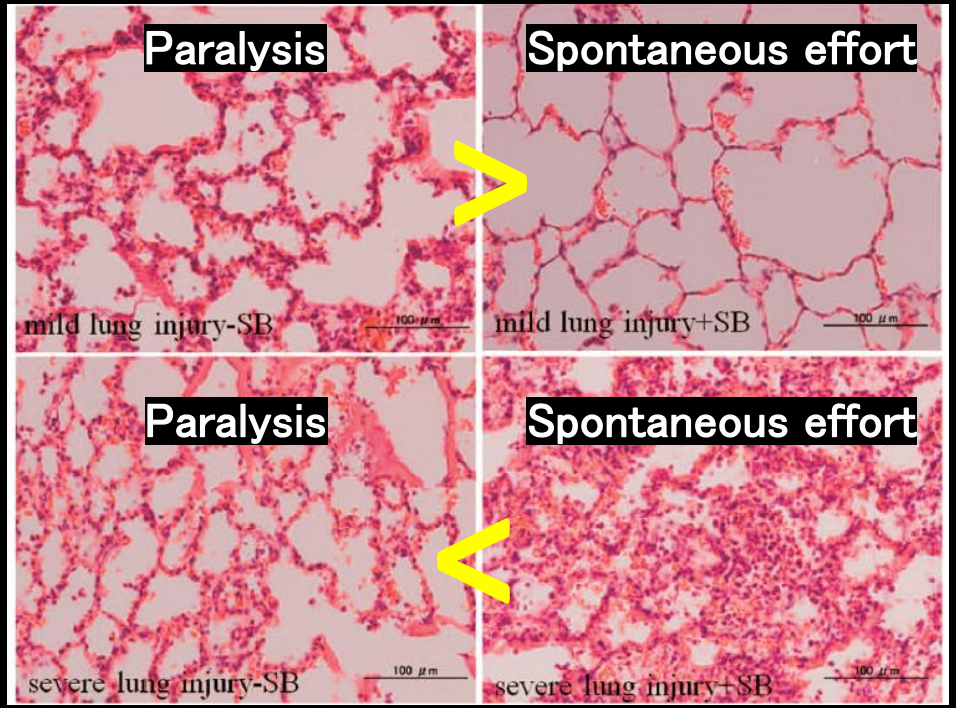
The Comparison of Spontaneous Breathing and Muscle Paralysis in Two Different Severities of Experimental Lung Injury*

Takeshi Yoshida, MD[1,2]; Akinori Uchiyama, MD, PhD[2]; Nariaki Matsuura, MD, PhD[3]; Takashi Mashimo, MD, PhD[2]; Yuji Fujino, MD, PhD[2]

(*Crit Care Med* 2013; 41:536–545)

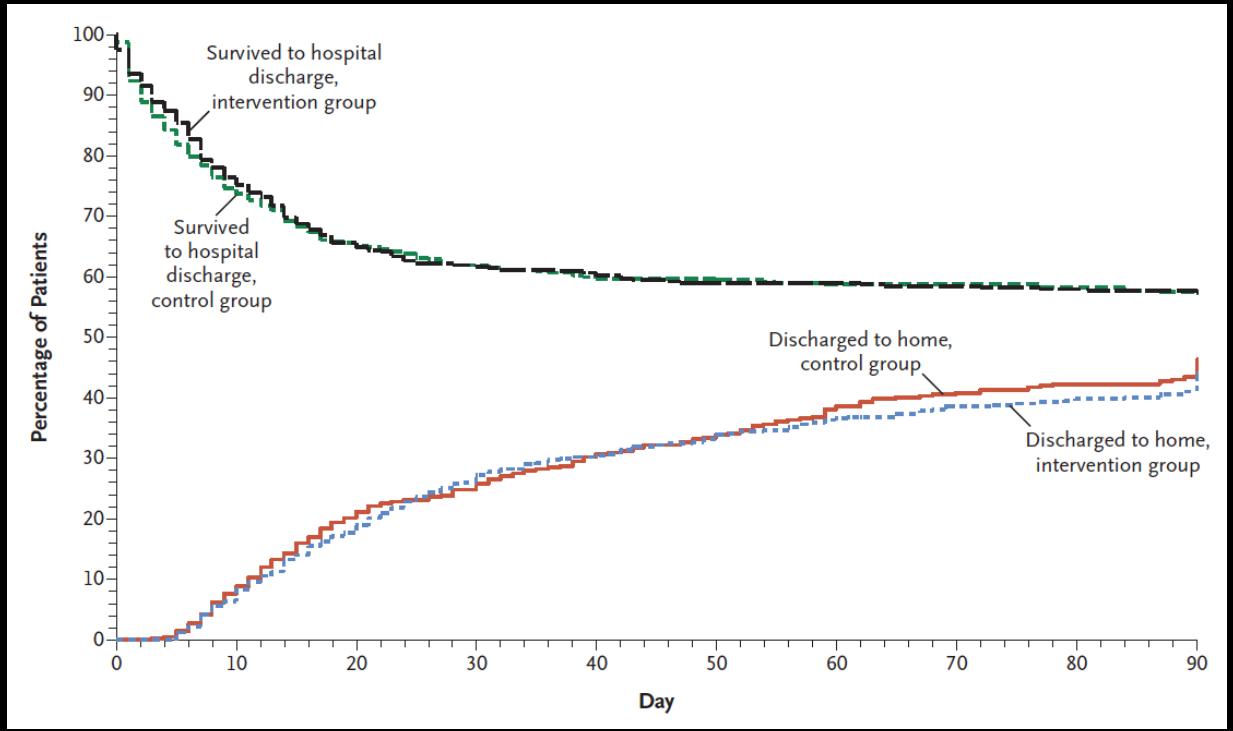
MILD ARDS

SEVERE ARDS



Early Neuromuscular Blockade in ARDS

ROSE trial, PETAL network



NEJM May 19, 2019

Table 1. Comparisons of the ACURASYS and ROSE Trials.*

Variable	ACURASYS Trial	ROSE Trial	Commentary
No. of centers (location)	20 ICUs (Europe)	48 hospitals (United States)	It is unlikely that different practices across the Atlantic would explain the different results of the two trials.
No. of patients (intervention group vs. control group)	340 (178 vs. 162)	1006 (501 vs. 505)	Estimates for sample-size calculations were different.
Trial design for group assignment	Double blind	Unblinded	Potential effect should be minimal.
ARDS definition	American–European consensus	Berlin criteria	It is unlikely that this difference had a major effect on the characteristics of patients enrolled in the trials.
Criteria for moderate-to-severe ARDS	Pao_2:FIO_2 <150 mm Hg with PEEP ≥5 cm of water	Pao_2:FIO_2 <150 mm Hg with PEEP ≥8 cm of water	ROSE allowed enrollment of patients with Pao_2:FIO_2 of 150–200 mm Hg after initial assessment but before randomization.
Median time from ARDS diagnosis to trial inclusion (IQR) — hr	16 (6–29)	8 (4–16)	Earlier inclusion time in ROSE may have resulted in enrollment of some patients who might have died before they could have been enrolled in ACURASYS.
Intervention vs. control strategies	Cisatracurium infusion plus deep sedation vs. deep sedation	Cisatracurium infusion plus deep sedation vs. light sedation	No routine neuromuscular blocking agents were allowed in the control groups.
Mechanical-ventilation approach	Lung-protective ventilation with low PEEP	Lung-protective ventilation with high PEEP	In the first 7 days, PEEP levels were higher by about 2–3 cm of water in ROSE than in ACURASYS.
Monitoring of patient–ventilator dyssynchrony	Not reported	Not reported	Ideally, future studies should assess dyssynchronies.
ICU-acquired paresis and long-term outcomes	No difference between groups	No difference between groups	Patients in the control group in ROSE had higher mean levels of activity to day 6 than patients in the intervention group.
Serious adverse events	Pneumothorax more frequent in the control group (11.7% vs. 4%)	Rates of overall barotrauma did not differ between groups	There were more acute cardiovascular events in the intervention group in ROSE than in the control group.

* Shown are comparisons between the ARDS et Curarisation Systematique (ACURASYS)[2] and Reevaluation of Systemic Early Neuromuscular Blockade (ROSE)[5] trials, which assessed the use of neuromuscular blocking agents in patients with moderate-to-severe acute respiratory distress syndrome (ARDS). ICU denotes intensive care unit, IQR interquartile range, Pao_2:FIO_2 the ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen, and PEEP positive end-expiratory pressure.

Arthur S. Slutsky et al NEJM 2019

Reverse Triggering

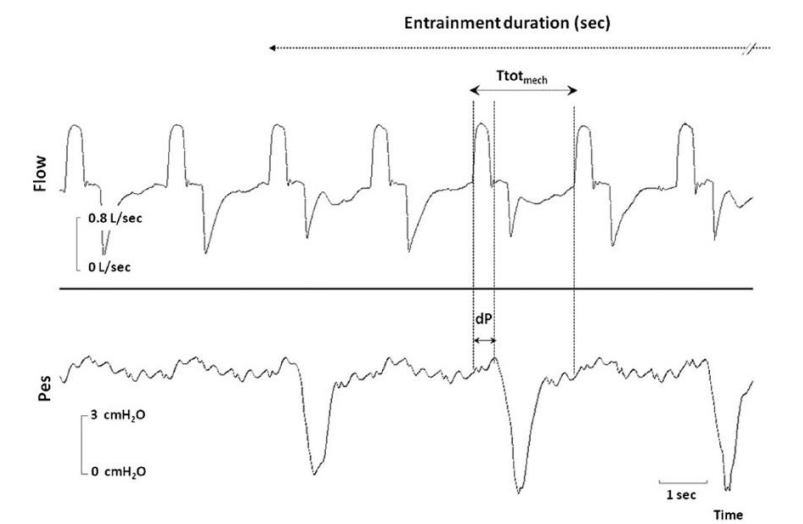


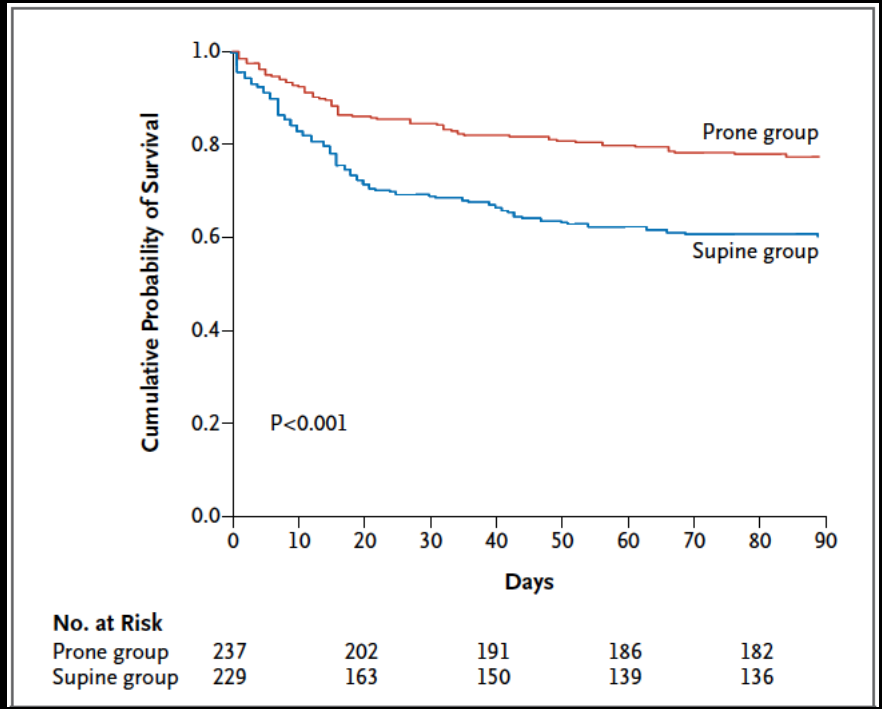
FIGURE 1. Definition of variables based on flow and Pes tracings. The entrainment duration in this patient was 32.17 s, and the entrainment ratio was 1:2 (one neural cycle every two mechanical cycles). Dotted lines denote the commencement of the mechanical and neural cycles. $Ttot_{mech}$ is the duration, in seconds, of the mechanical cycle, and dP is defined as the interval between the commencement of the mechanical and the neural inspiration. In this example, dP was 0.66 s and $Ttot_{mech}$ was 2.29 s. The phase angle (θ) was calculated as $\theta = dP/ Ttot_{mech} \times 360°$, resulting in a value of 104°. dP = phase difference; Pes = esophageal pressure; $Ttot_{mech}$ = ventilator cycle duration.

- Reverse triggering is a type of dyssynchrony that occurs when a patient effort occurs after (‘is triggered by’) the initiation of a ventilator (non-patient triggered) breath.
- Frequently recognized, in patients heavily sedated.
- Can be injurious, including breath stacking, pendelluft, excessive regional stress.

CHEST 2013; 143(4):927–938

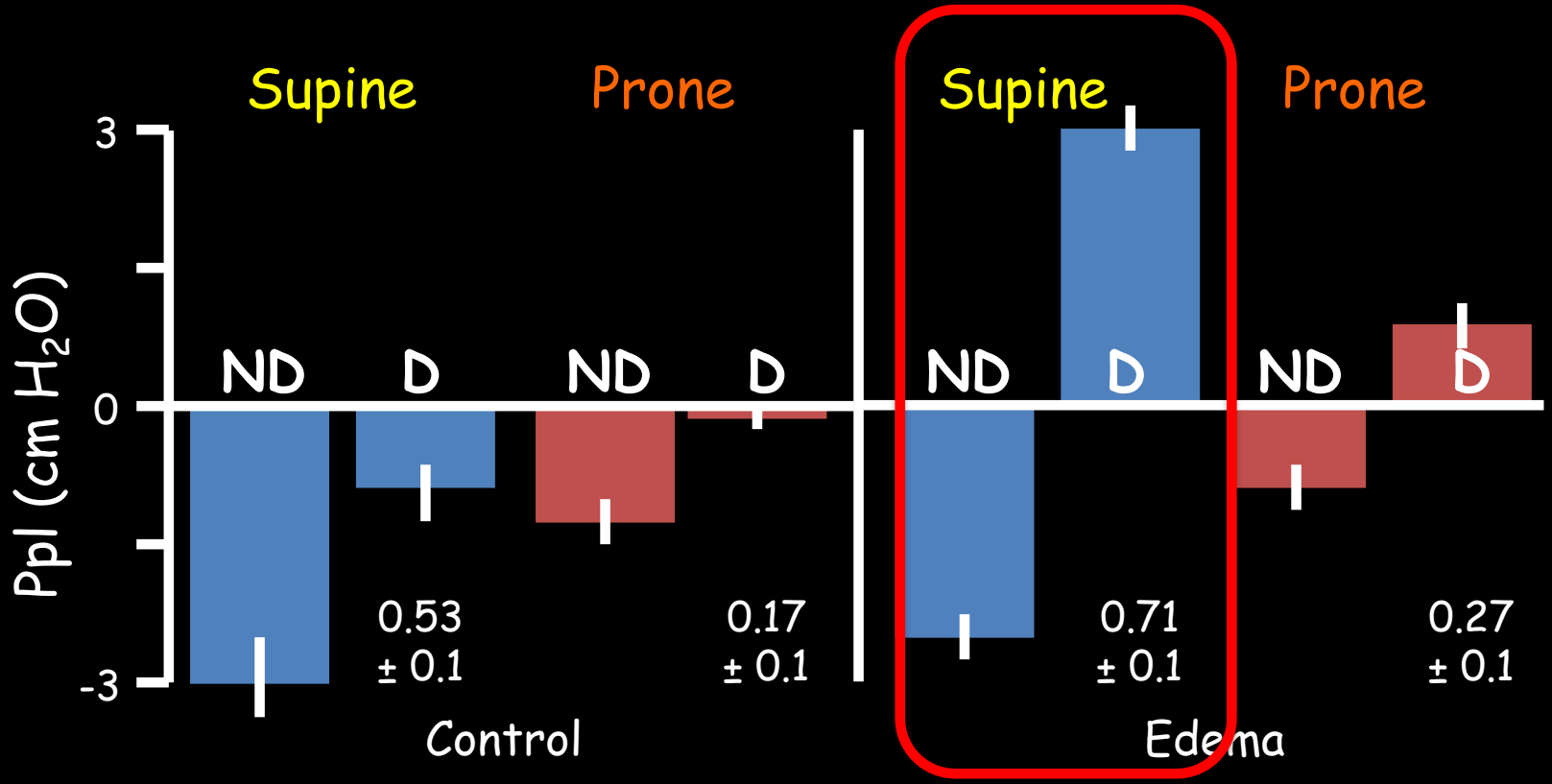
Prone positioning in severe ARDS

- 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.

Dual Effect of Prone Position on Ppl Gradient in Acute Lung Injury



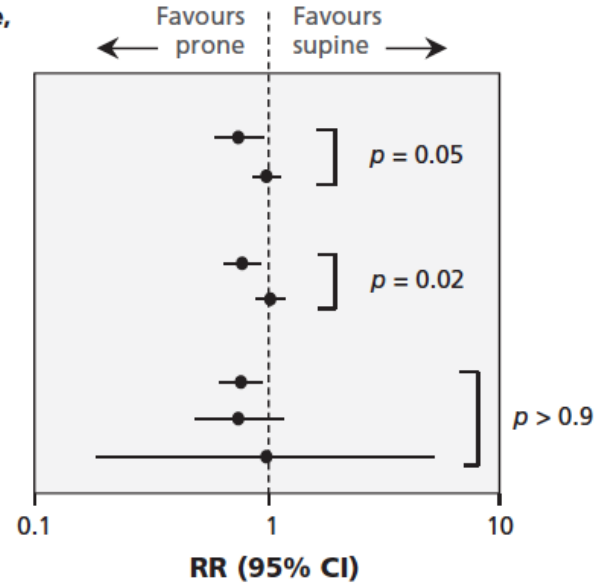
Mutoh, JAP 1992

CMAJ RESEARCH

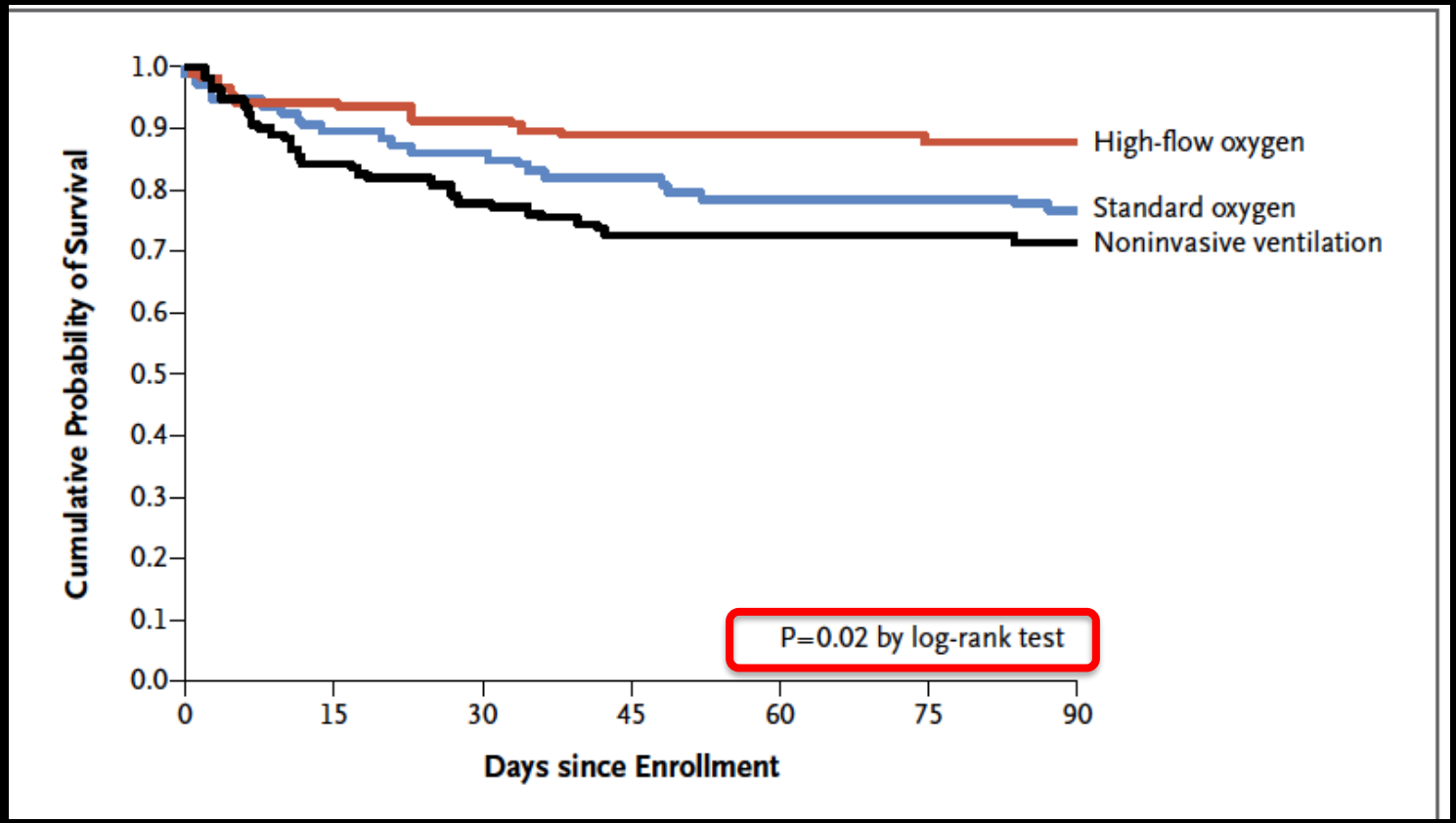
CMAJ 2014. DOI:10.1503/cmaj.140081

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



Nasal High Flow for Acute Hypoxemia



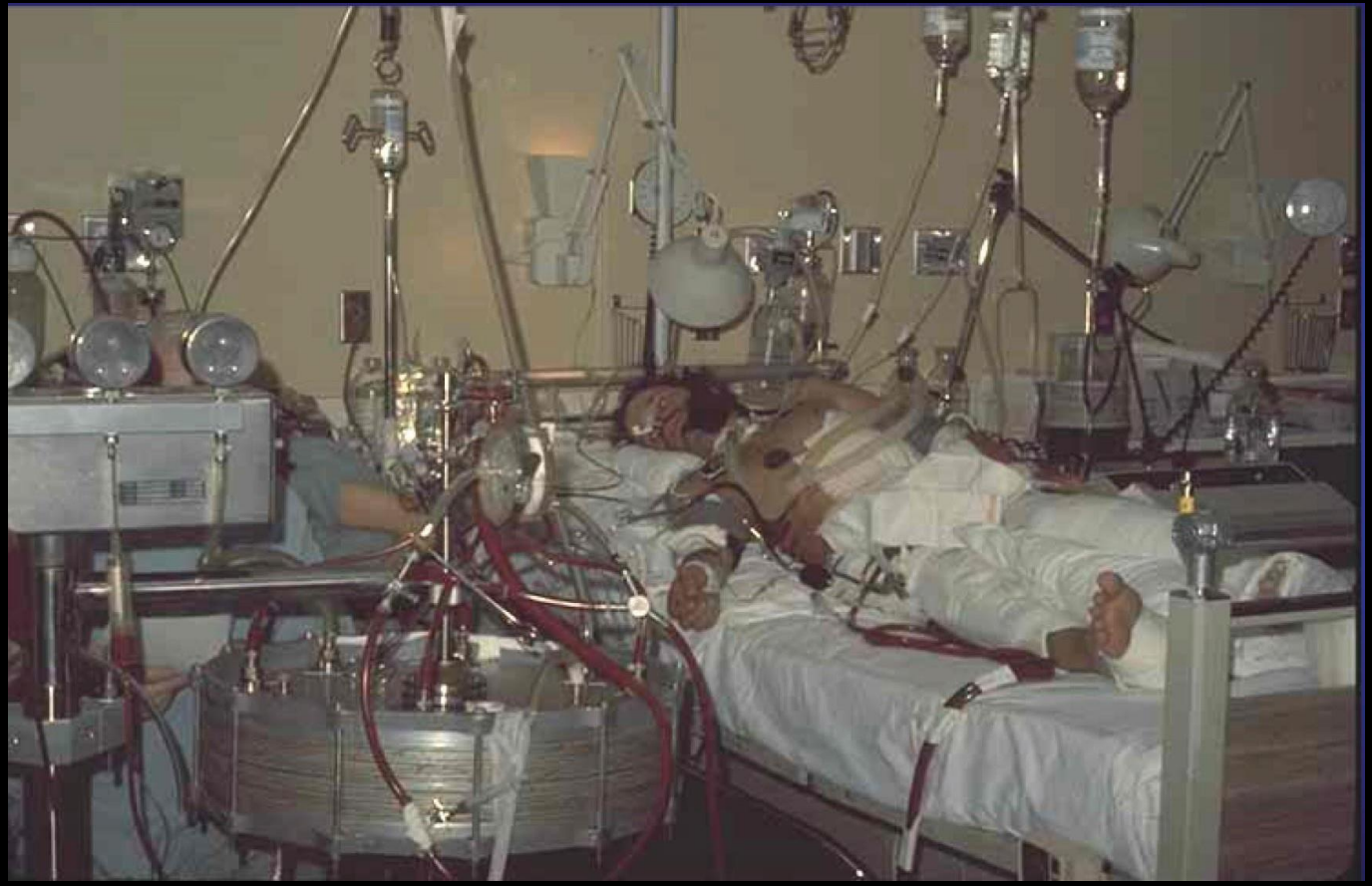
N Engl J Med 2015;372:2185-96.

ExtraCorporeal Life Support (ECLS)

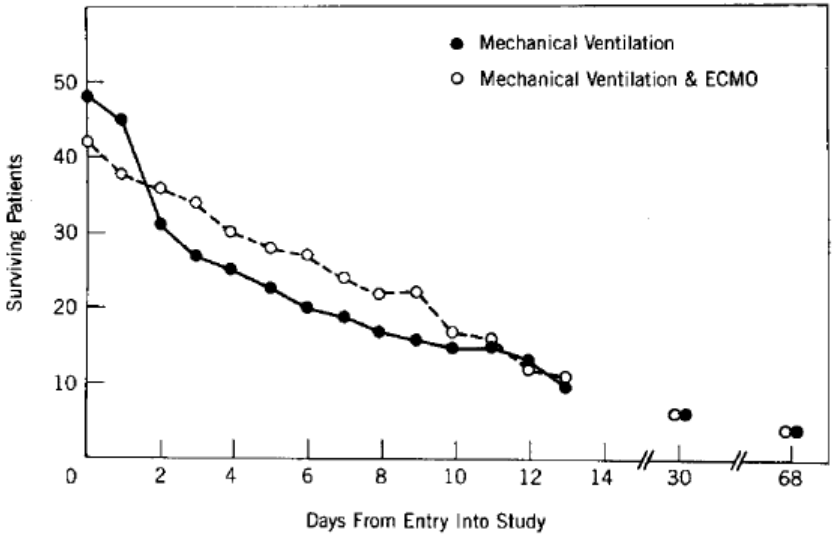
ExtraCorporeal Membrane Oxygenation (ECMO)

ExtraCorporeal CO_2 Removal (ECCO2R)

ECMO in 1971



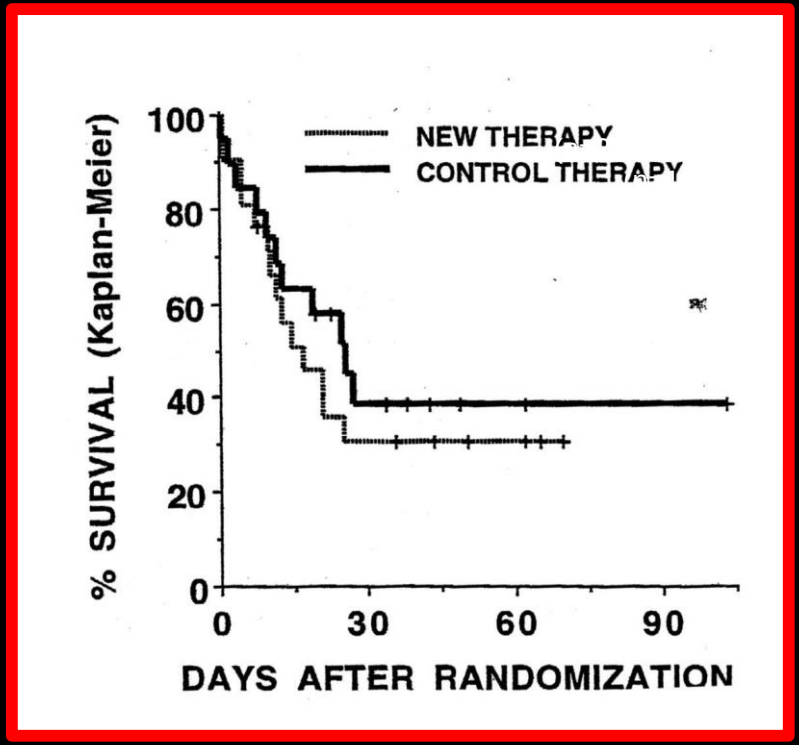
Patient Outcome			
Therapy*	Dead—Respiratory Improvement Never Occurred	Dead After Respiratory Improvement	Survived After Respiratory Improvement
ECMO and MV	34	4	4
MV (control)	41	3	4



Zapol W. JAMA 1979:242:2193-6

Salt Lake City study

PCIRV + $ECCO_2R$



Morris A.H. AJRCCM 1994, ***149:295–305***

ECMO volumes and indications

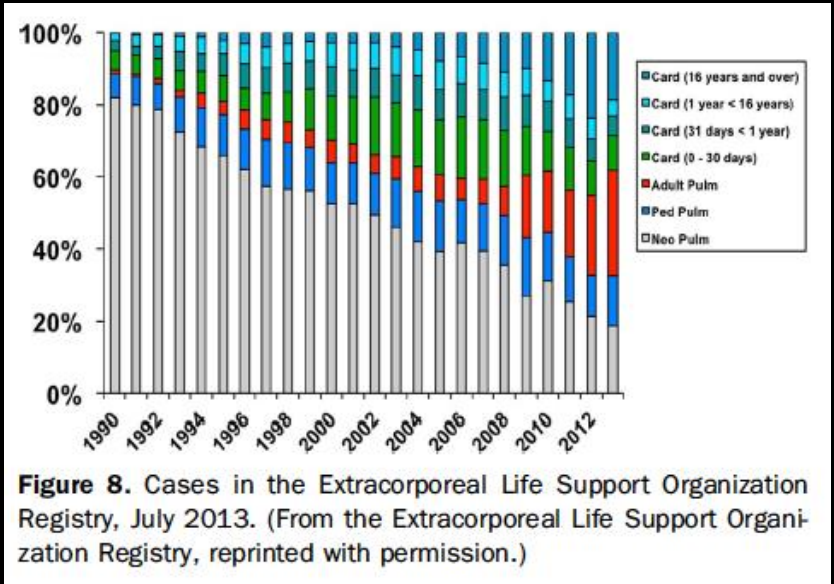


Figure 8. Cases in the Extracorporeal Life Support Organization Registry, July 2013. (From the Extracorporeal Life Support Organization Registry, reprinted with permission.)

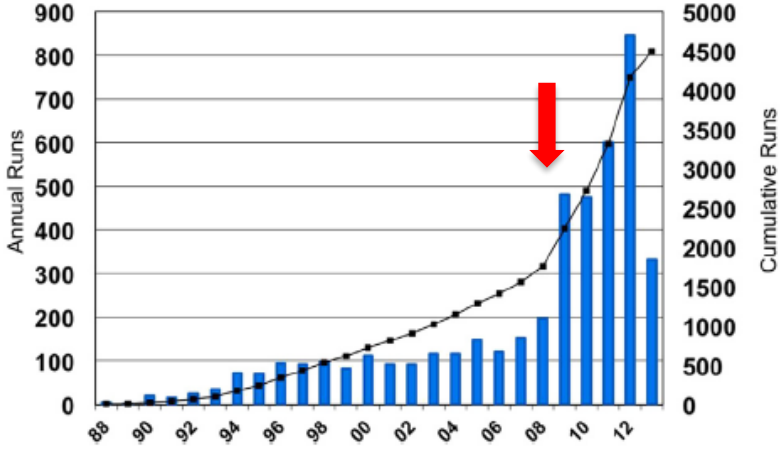


Figure 9. Adult respiratory cases, Extracorporeal Life Support Organization Registry July 2013. (From the Extracorporeal Life Support Organization Registry, reprinted with permission.)

Bartlett RH, J Am Coll Surg, 2014

The explosion (2009-today)

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

Lancet 2009; 374: 1351–63

Extracorporeal Membrane Oxygenation for 2009 Influenza A(H1N1) Acute Respiratory Distress Syndrome

The Australia and New Zealand Extracorporeal Membrane Oxygenation (ANZ ECMO) Influenza Investigators*

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

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)

Position paper for the organization of ECMO for ARDS (ECMONet)

- Because ECMO is a complex, high-risk, and costly modality, at present it should be conducted in centers with sufficient experience, volume, and expertise to ensure it is used safely.

- The aim of this paper is to provide a description of the optimal approach to organizing ECMO programs for ARF in adult patients.

- Given the need for further evidence, we encourage restraint in the widespread use of ECMO until we have a better appreciation for both the potential clinical applications and the optimal techniques for performing ECMO.

Am J Respir Crit Care Med Vol 190, Iss 5, pp 488–496

“In God we trust;
All others must bring data”

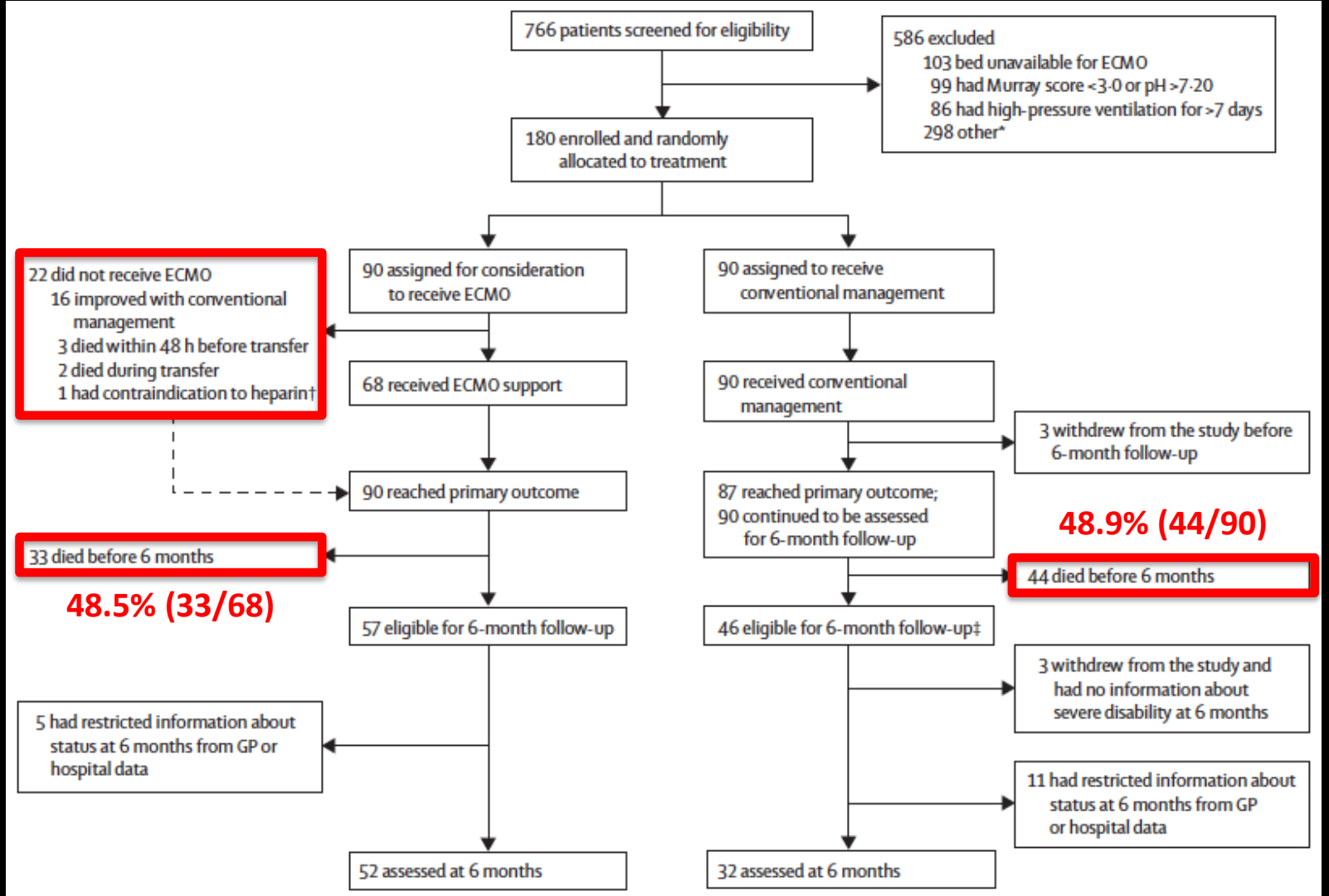
E. Edwards Deming
1900-1993

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

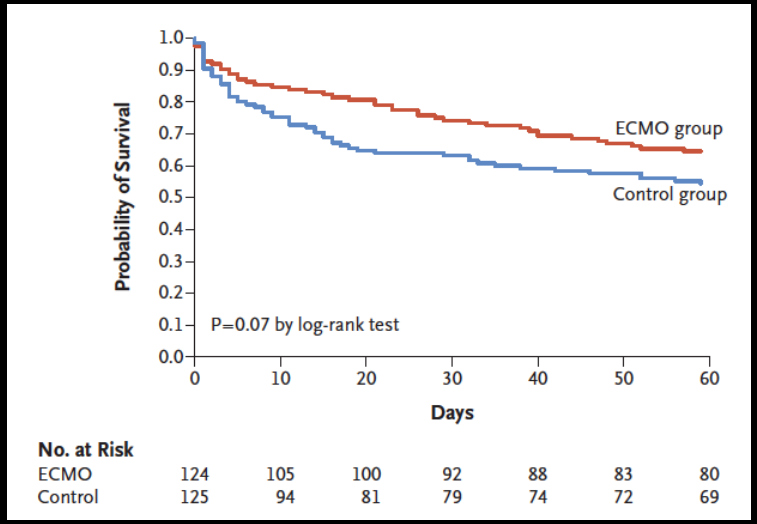

766 patients screened for eligibility
586 excluded
103 bed unavailable for ECMO
99 had Murray score <3·0 or pH >7·20
86 had high-pressure ventilation for >7 days
298 other*
180 enrolled and randomly allocated to treatment
90 assigned for consideration to receive ECMO
90 assigned to receive conventional management
22 did not receive ECMO
16 improved with conventional management
3 died within 48 h before transfer
2 died during transfer
1 had contraindication to heparin†
68 received ECMO support
90 received conventional management
3 withdrew from the study before 6-month follow-up
90 reached primary outcome
87 reached primary outcome; 90 continued to be assessed for 6-month follow-up
48.9% (44/90)
33 died before 6 months
48.5% (33/68)
44 died before 6 months
57 eligible for 6-month follow-up
46 eligible for 6-month follow-up‡
3 withdrew from the study and had no information about severe disability at 6 months
5 had restricted information about status at 6 months from GP or hospital data
11 had restricted information about status at 6 months from GP or hospital data
52 assessed at 6 months
32 assessed at 6 months

Adherence to protective ventilation strategy

	ECMO	Conventional	
Treatment by low-volume low-pressure ventilation strategy at any time	84 (93%)	63 (70%)	<0·0001
Time under strategy (days)	23·9 (20·4)	15·0 (21·1)	<0·0001

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*



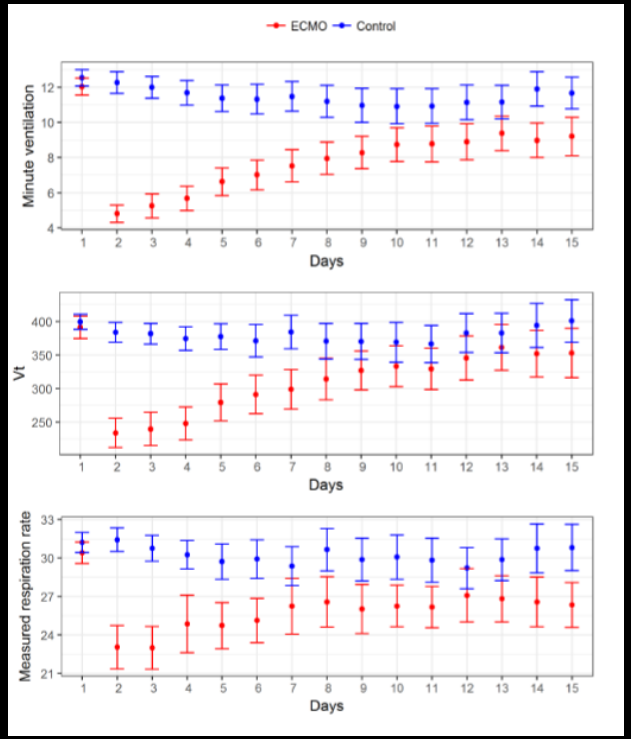
1. Very sick patients
   - P/F ratio < 80 mmHg
   - C_{RS} < 30 cmH_2O
   - Driving pressure > 16 cmH_2O
   - SOFA > 10
2. Strict study design
   - 100% ECMO in study group
   - Optimal care in control group
     - Low tidal volume, 90% prone, 100% NM blockade

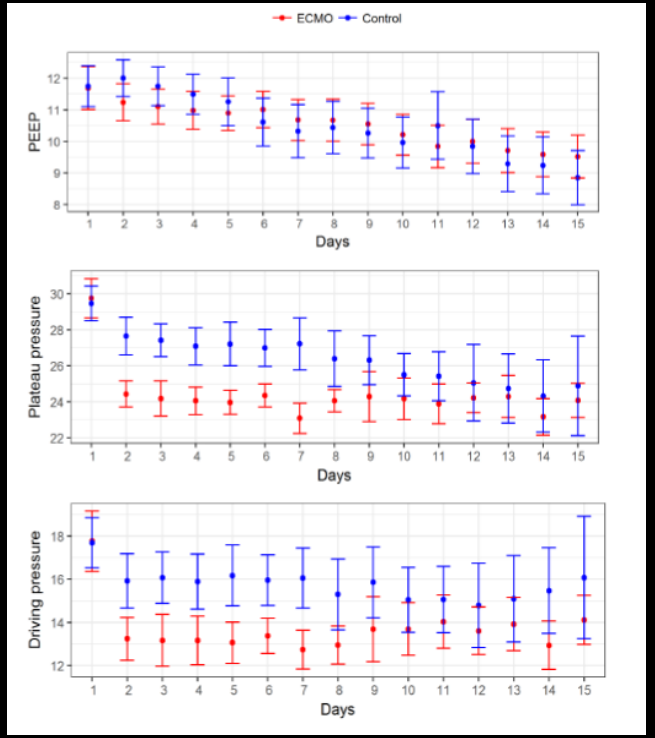
The routine use of ECMO in patients with severe ARDS is not superior to the use of ECMO as a rescue maneuver in patients whose condition has deteriorated further.

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

ECMO vs Control

ultraprotective strategy

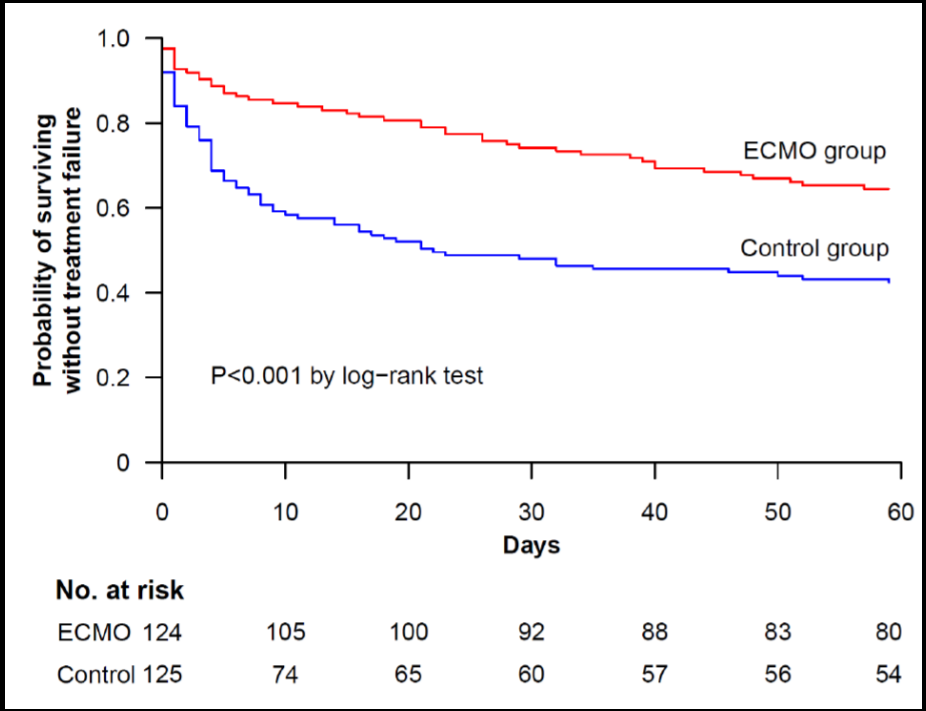




N Engl J Med 2018; 378: 1965-75.

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.

Meta-analysis of ECMO for ARDS

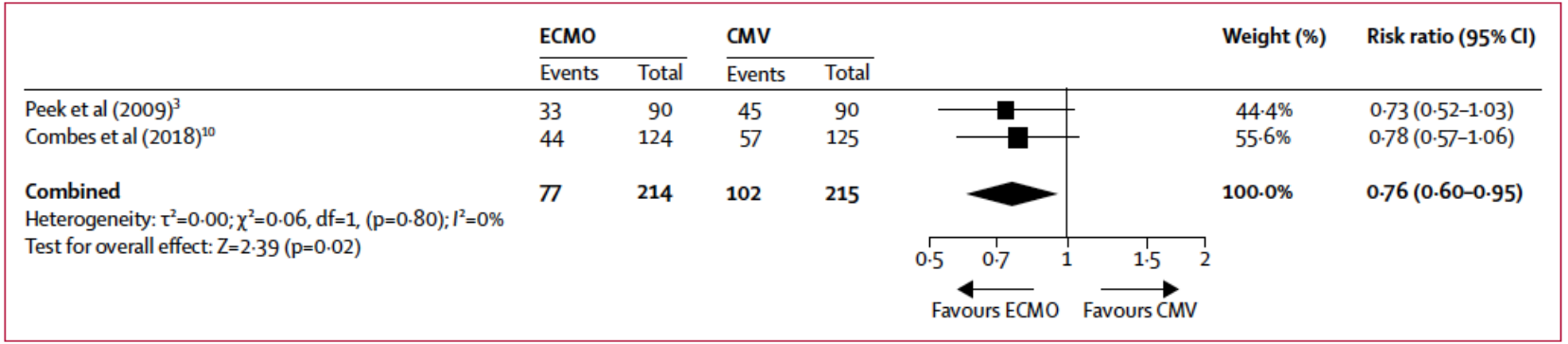
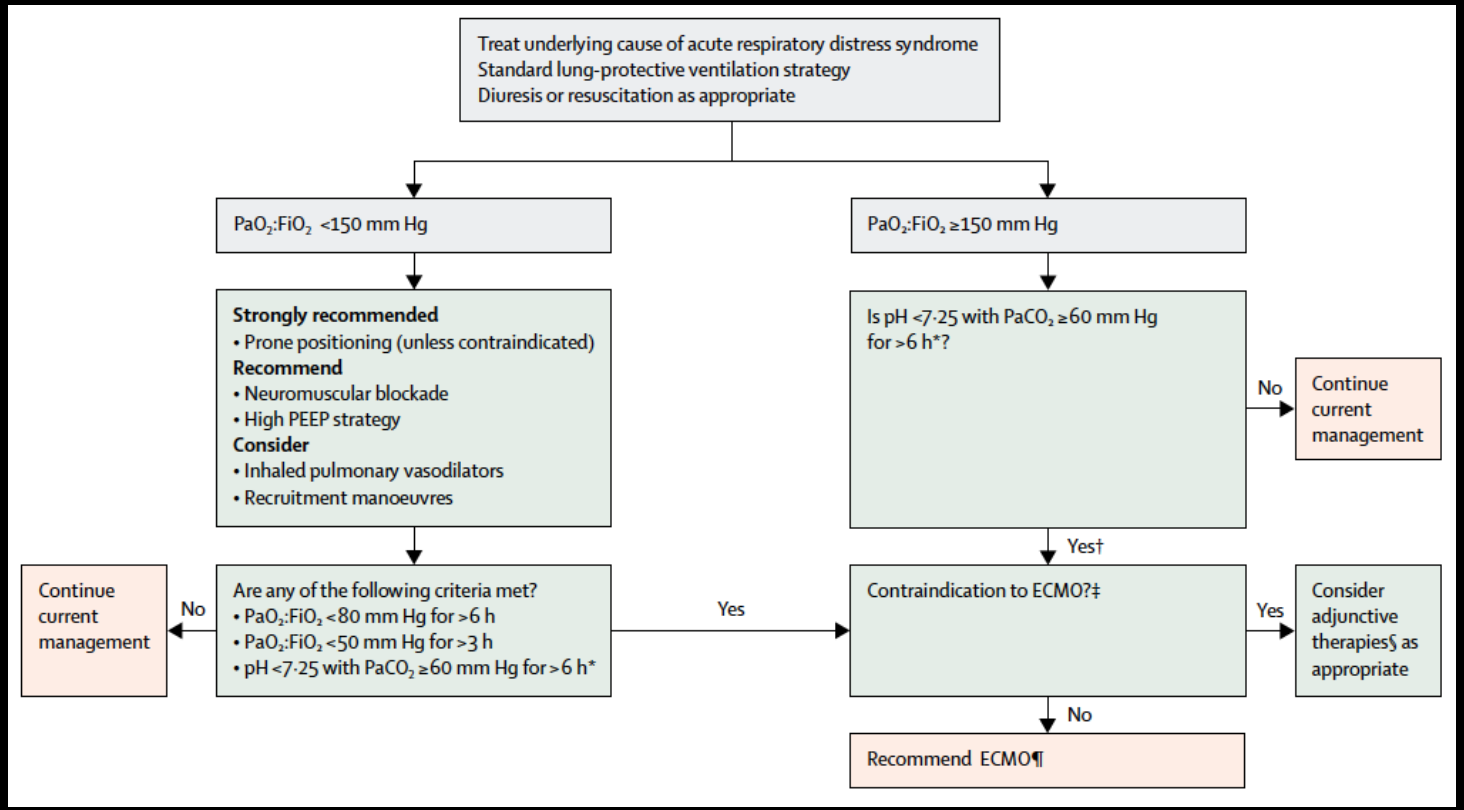


Figure 3: **Forest plot of mortality at latest follow-up in randomised controlled trials of ECMO *vs* CMV in adults with severe acute respiratory distress syndrome**
6-month mortality or death before discharge was the latest follow-up timepoint in Peek et al's trial, whereas 60-day mortality was the latest timepoint in Combes et al's trial. Risk ratios were calculated with a random-effects model. ECMO=extracorporeal membrane oxygenation. CMV=conventional mechanical ventilation. df=degree of freedom.

Interpretation: Compared with conventional mechanical ventilation, use of venovenous ECMO in adults with severe acute respiratory distress syndrome was associated with reduced 60-day mortality. However, venovenous ECMO was also associated with a moderate risk of major bleeding.

Lancet Respir Med 2019;7: 163–72

Management Algorithm of ECMO for ARDS



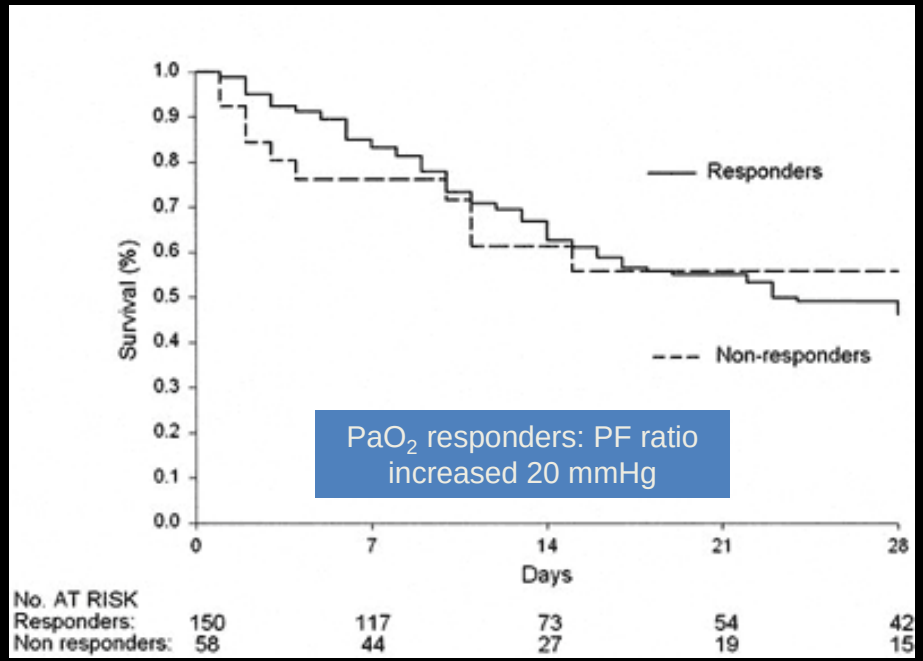
The Lancet Respiratory Medicine 2019/01

“Prediction is very difficult, especially about the future”

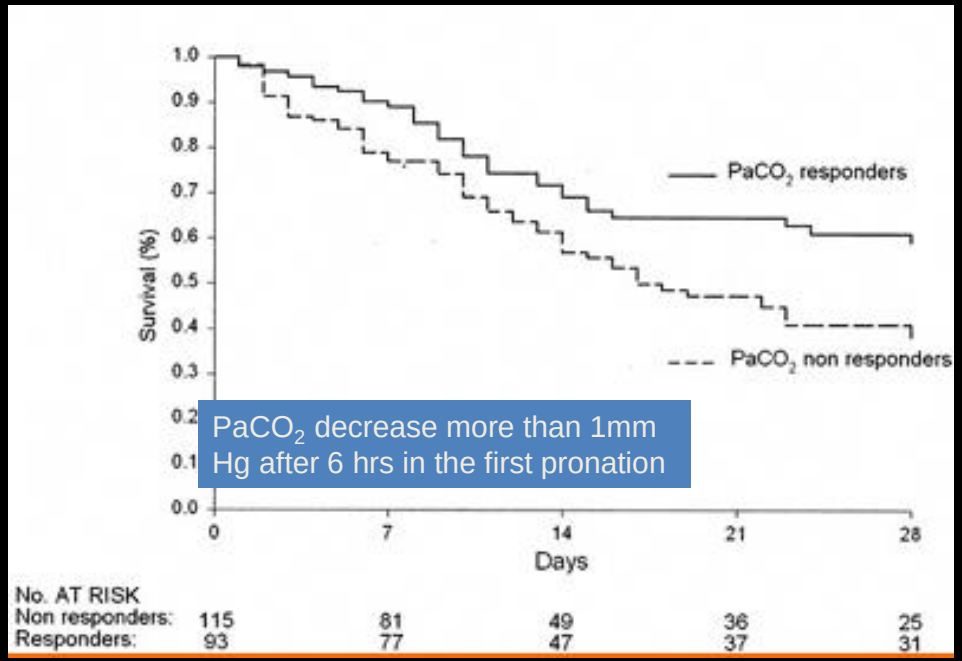
Niels Bohr 1885-1962

Physics Nobel Price - 1922

PaO_2 v.s. $PaCO_2$ Responders



PaO_2 responders: PF ratio increased 20 mmHg



$PaCO_2$ decrease more than 1mm Hg after 6 hrs in the first pronation

Gattinoni et al, Crit Care Med 2003; 31:2727–2733

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

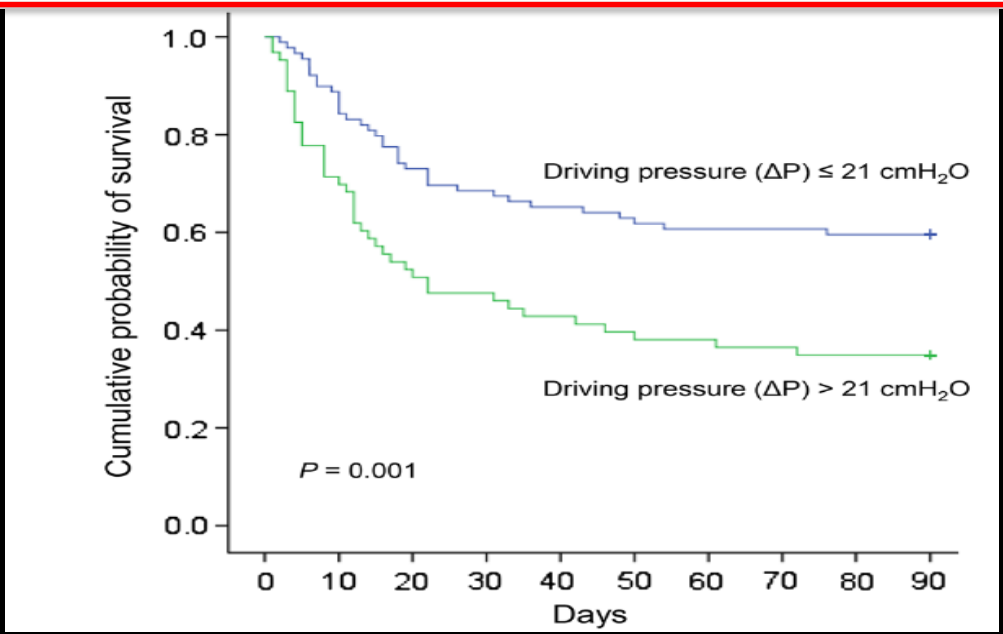
*$p < 0.05$

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

Dynamic Driving Pressure for ARDS with ECMO

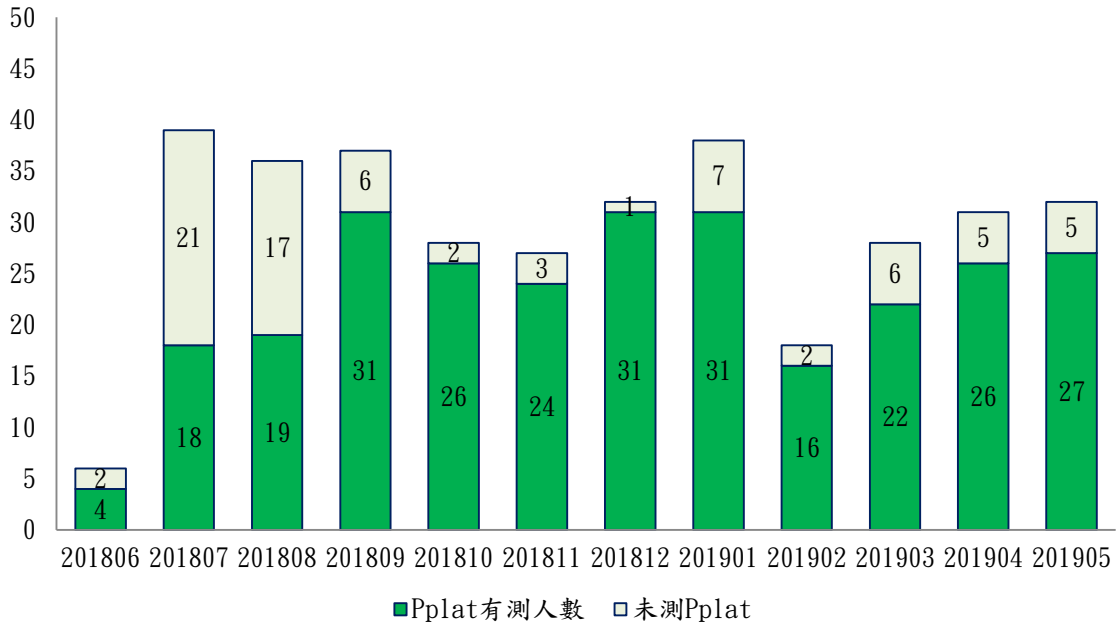
Table 2 Cox proportional hazards regression model with ICU mortality as outcome

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

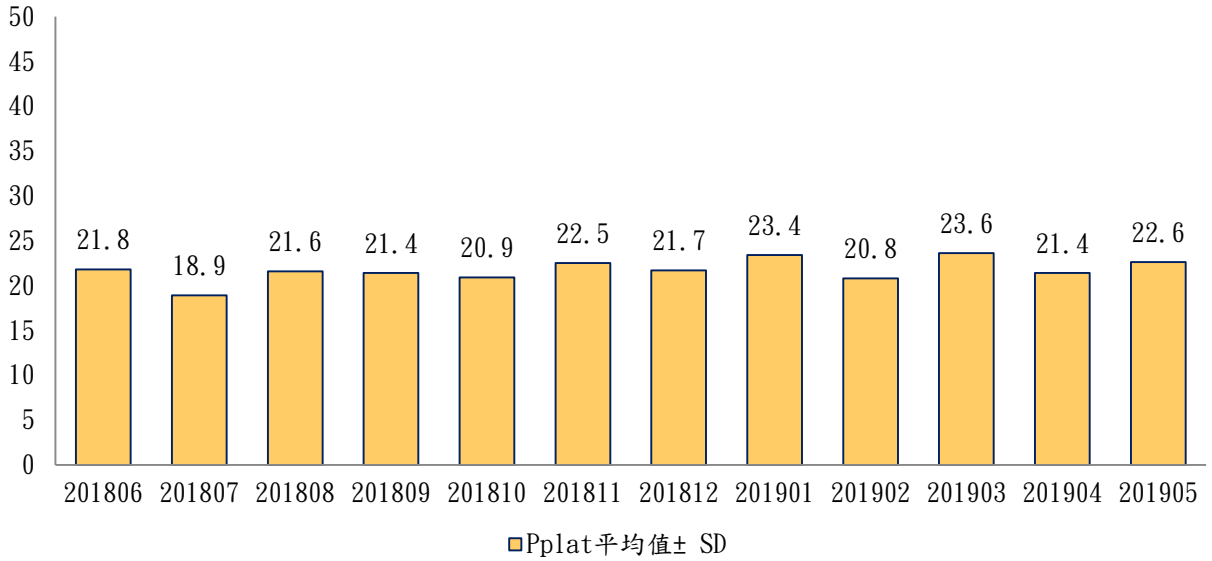


Chiu *et al. Ann. Intensive Care* (2017) 7:12

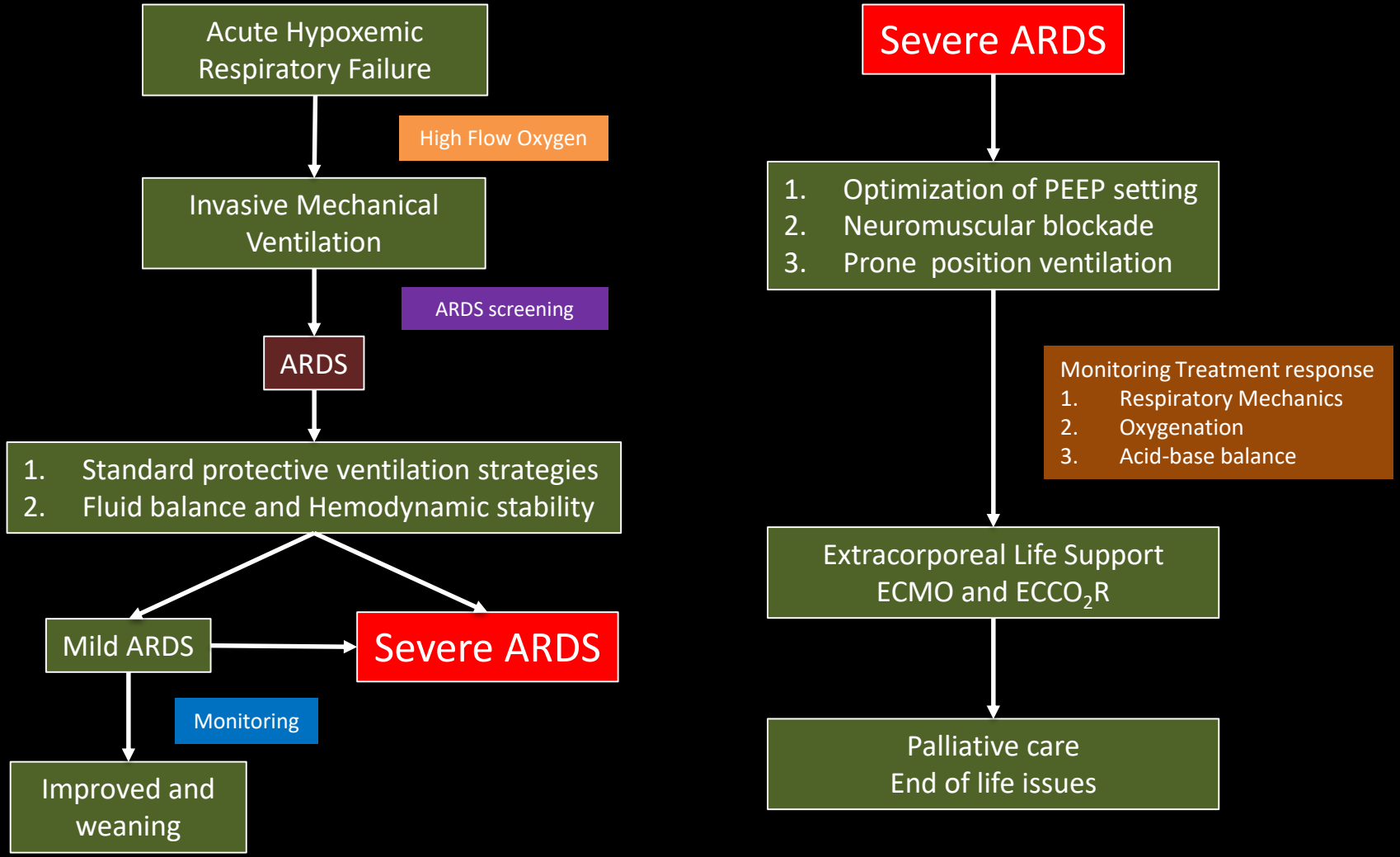
Plateau pressure測量人數(201806~201905)

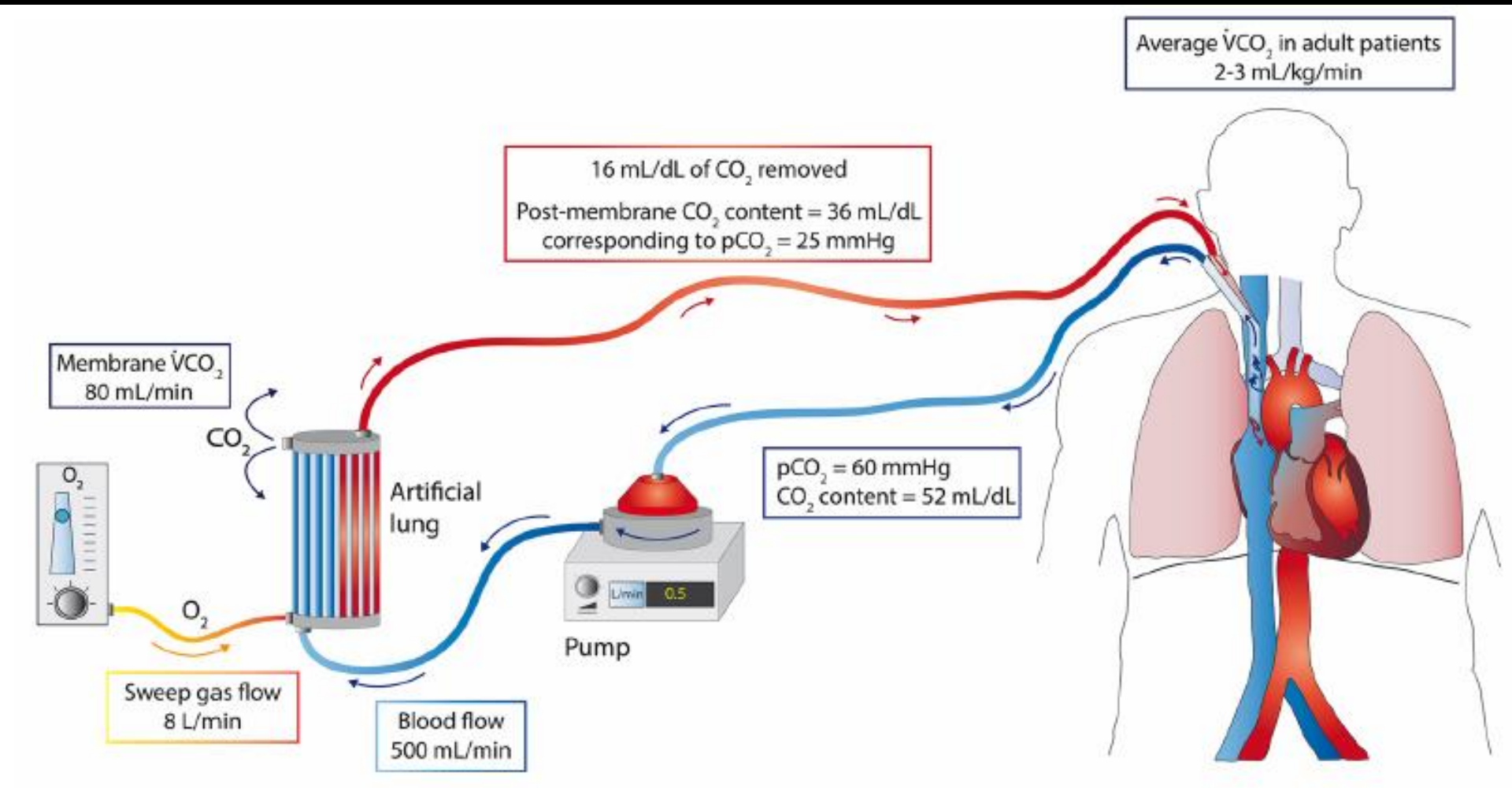


Plateau pressure 平均值m (201806~201905)



指標/月份	201806	201807	201808	201809	201810	201811	201812	201901	201902	201903	201904	201905
Pplat平均值±SD	21.8±6.6	18.9±3.4	21.6±3.9	21.4±5.2	20.9±5.1	22.5±5.4	21.7±4.9	23.4±5.7	20.8±4	23.6±3.9	21.4±3.9	22.6±6.1


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 $ECCO_2R$
Palliative care
End of life issues



VENO-VENOUS ECCO$_2$R

Feasibility and safety of extracorporeal CO_2 removal to enhance protective ventilation in ARDS: the SUPERNOVA study

- Prospective multicenter international phase 2 study
- Primary endpoint was the proportion of patients achieving ultra-protective ventilation (VT 4 mL/kg and $P_{PLAT} \leq 25$ cmH_2O)with $PaCO_2$ not increasing more than 20% from baseline, and arterial pH > 7.30
- Results
  - Ninety-five patients were enrolled
  - 78% and 82% of patients achieved ultra-protective settings by 8 h and 24 h respectively
  - ECCO2R was maintained for 5 [3–8] days
- Use of $ECCO_2R$ to facilitate ultra-protective ventilation was feasible. A randomized clinical trial is required to assess the overall benefits and harms.

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Conclusions

- ARDS remains a common and important issue in critically ill patients needing mechanical ventilation, but often under-recognized and under-treated.
- Mortality of ARDS remains high, even in mild ARDS.
- Routine screening ARDS management should be individualized based on physiological management.
- ECLS for severe ARDS are evolving, should be reserved and centralized in skilled and well-organized units and teams.

Thank you!