Management of mechanical ventilation in patients with acute lung injury

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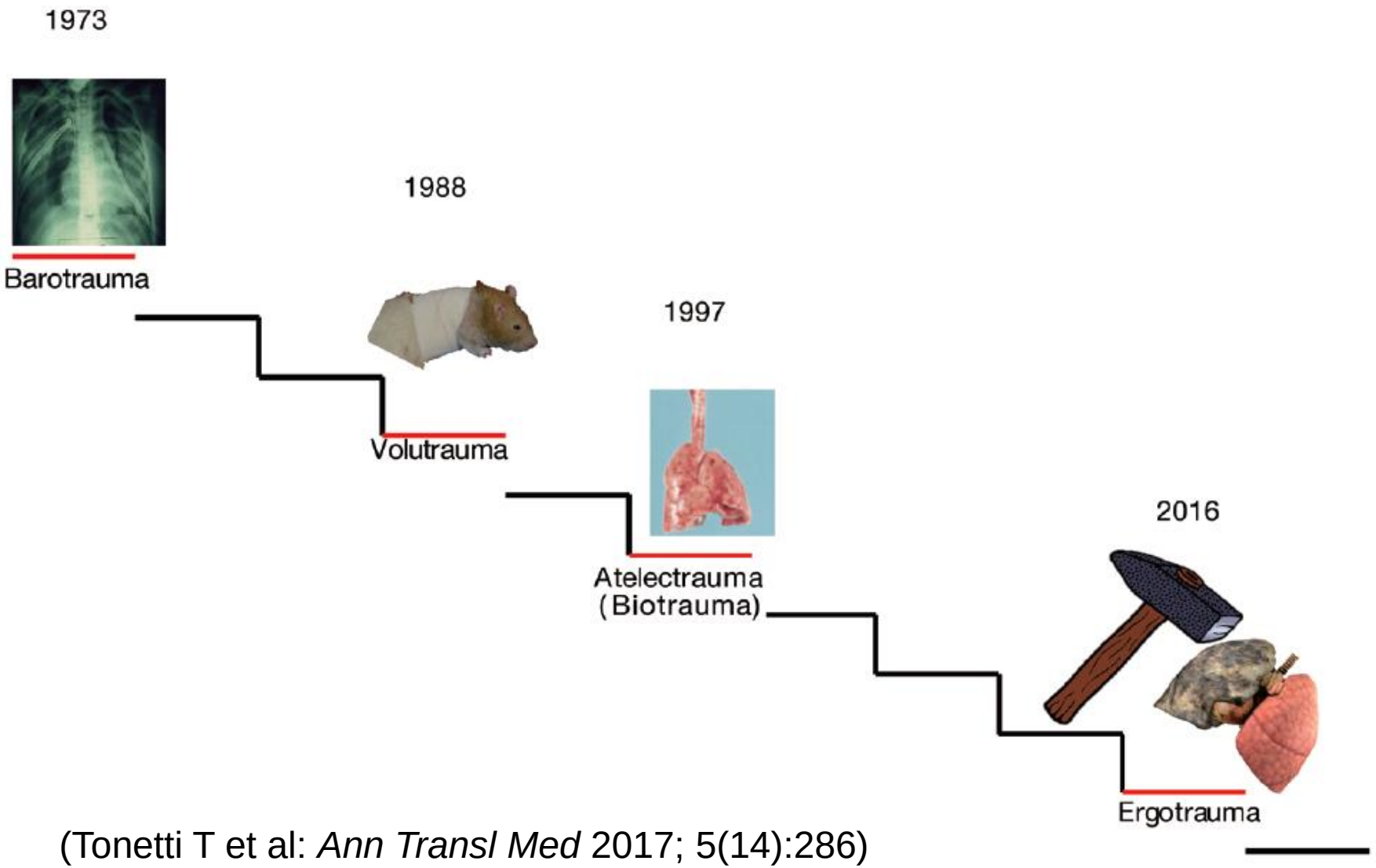
大綱

- Low tidal volume
- PEEP
- Prone
- Neuromuscular blocker
- Recruitment Maneuver
- ECMO
- Summary of treatment recommendation

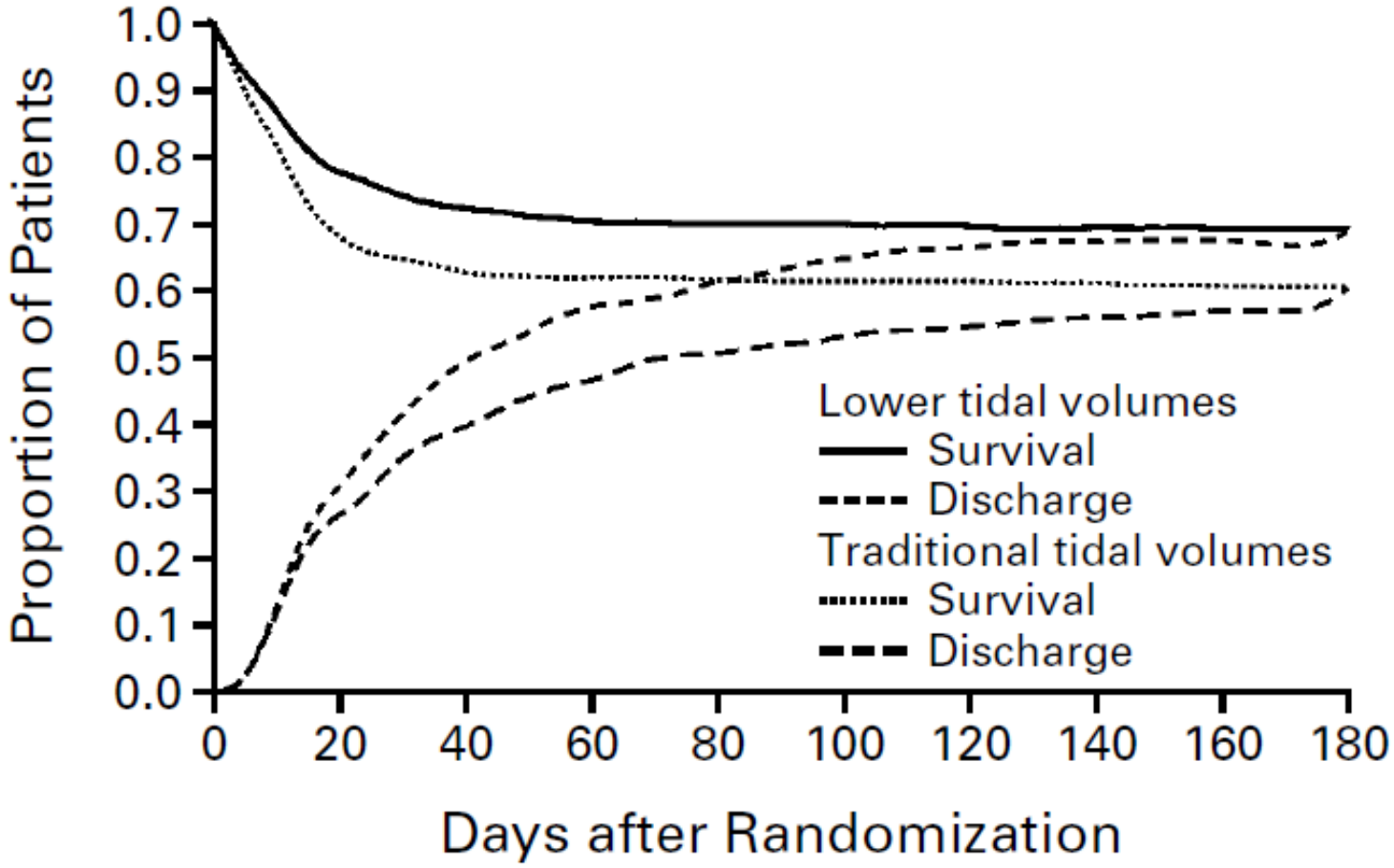
Low Tidal Volume

Ventilator-induced lung injury



(Tonetti T et al: *Ann Transl Med* 2017; 5(14):286)

小 tidal volume 的好處



(The ARDS Network. *N Engl J Med* 342:1301-1308, 2000.)

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 ARDS Network. *N Engl J Med* 342:1301-1308, 2000.)

Ventilator Mode

- Volume assist/control直到脫離呼吸器

(Vincent JL et al: *Textbook of Critical Care* , 6th ed,2011 Elsevier)

Tidal Volume (VT)

- 起初：VT: 8 mL/kg PBW
- 在1-3小時內漸次將VT調降至6 mL/kg
- PBW (Predicted body weight)
  - 男:50 + 0.91(身高[cm] − 152.4)
  - 女:45.5 + 0.91(身高 [cm] − 152.4).

(Vincent JL et al: *Textbook of Critical Care* , 6th ed,2011 Elsevier)

依Pplat調VT

- 測量 plateau pressure (Pplat) q4h 以及每當 PEEP 或 VT有更動時.
  - 若 Pplat > 30 cmH_2O, 將VT 降至4-5 mL/kg.
  - 若 Pplat < 25 cmH_2O 且VT < 6 mL/kg →將VT調高 1 ml/kg

(Vincent JL et al: *Textbook of Critical Care* , 6th ed,2011 Elsevier)

依pH調呼吸次數 (RR)

- 調整 RR以使 pH ＝7.30-7.45，直到RR已達上限 35/min
- 若RR＝35而仍舊pH ＜7.30，則給予bicarbonate.
- 當 pH＜7.15時, 可增加VT (Pplat也不受30 cmH_2O限制).

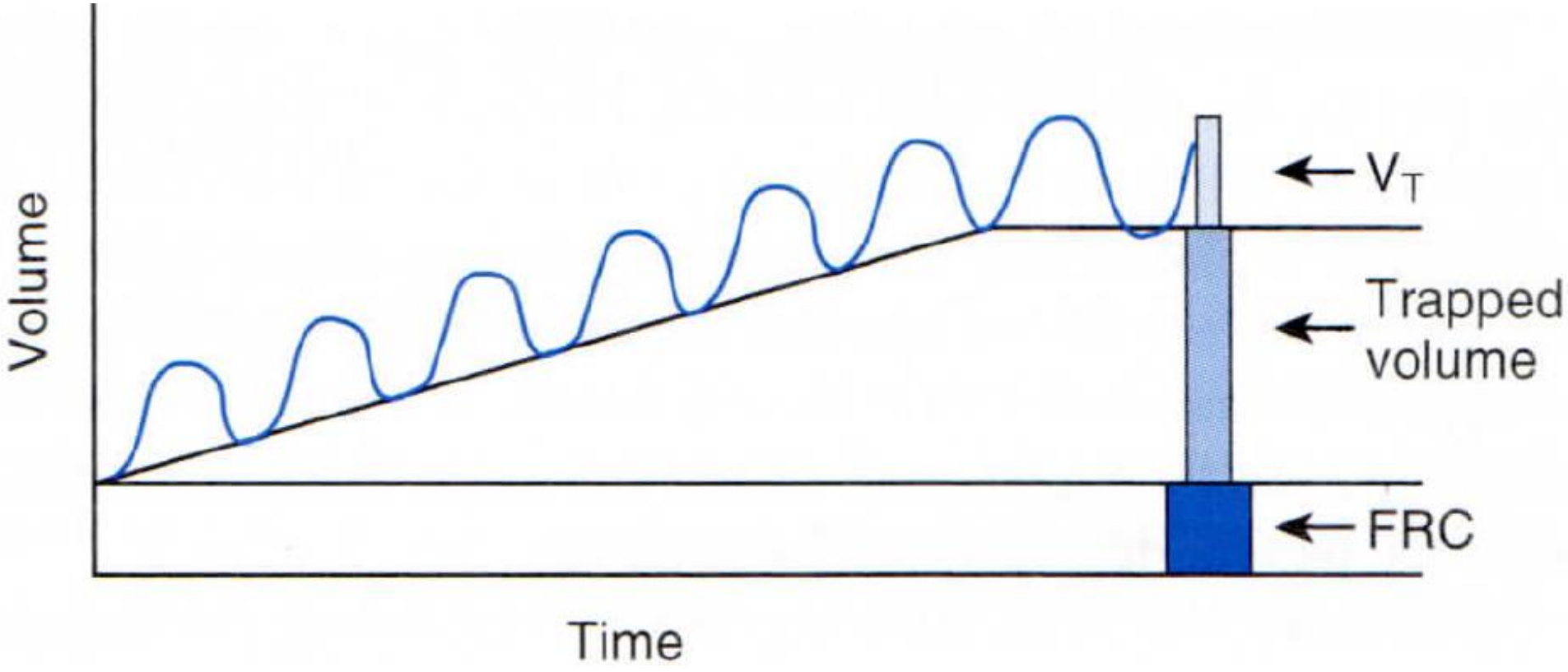
(Vincent JL et al: *Textbook of Critical Care* , 6th ed,2011 Elsevier)

I : E Ratio

- 目標 1 : 1 至1 : 3 (不宜I:E倒轉）

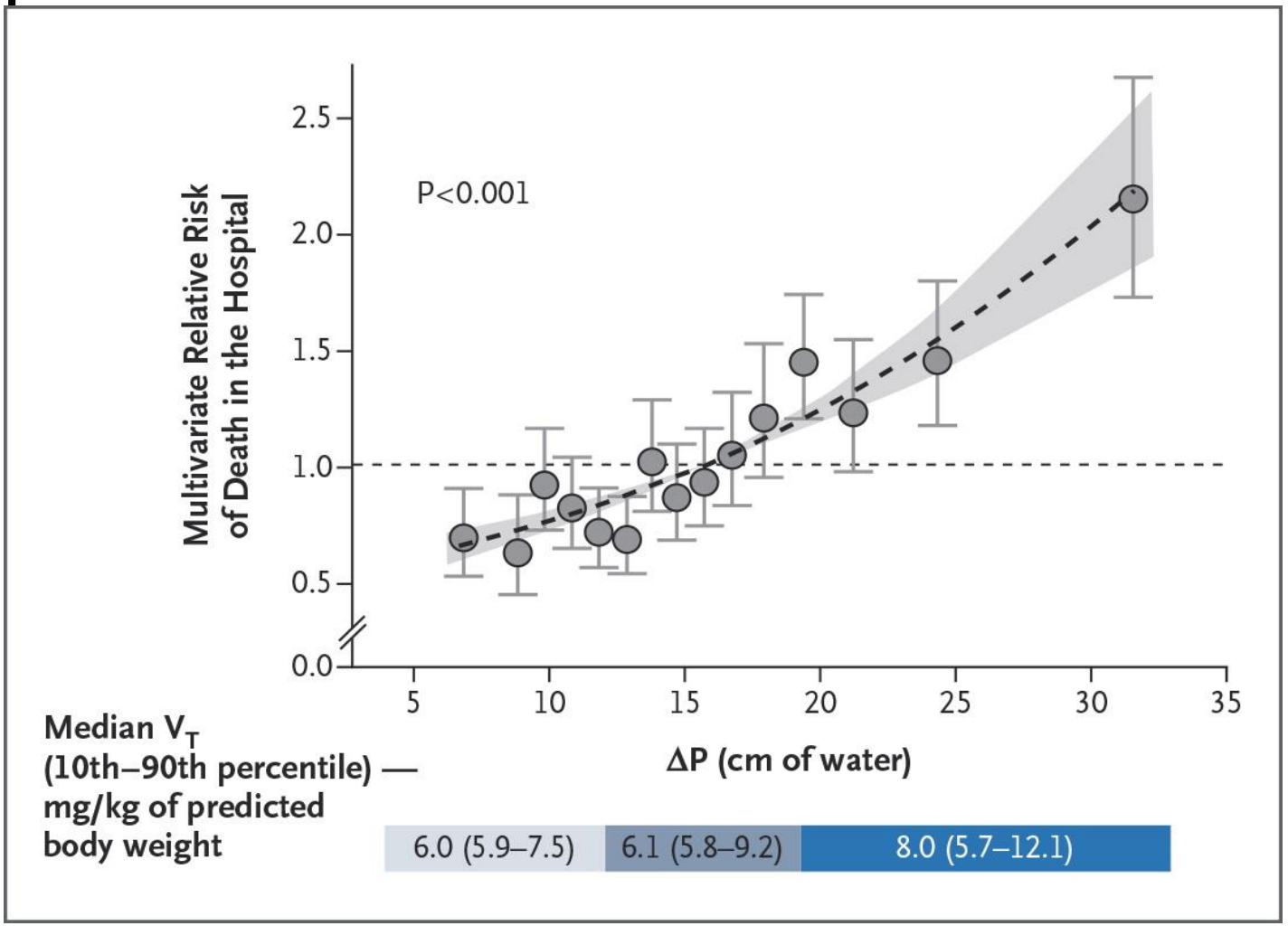
(Vincent JL et al: *Textbook of Critical Care* , 6th ed,2011 Elsevier)

Auto-PEEP



(Cairo JM: *Pilbeam's Mechanical Ventilation* 2012 Elsevier)

Driving pressure (= Pplat – PEEP = V_T/Crs) 宜小於15 cmH2O



Amato MB et al. N Engl J Med 2015;372:747-755.

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ARTICLE IN PRESS

Medicina Intensiva xxx (xxxx) xxx–xxx

ELSEVIER

medicina *intensiva*

http://www.medintensiva.org/

ORIGINAL ARTICLE

Intermediate tidal volume is an acceptable option for ventilated patients with acute respiratory distress syndrome

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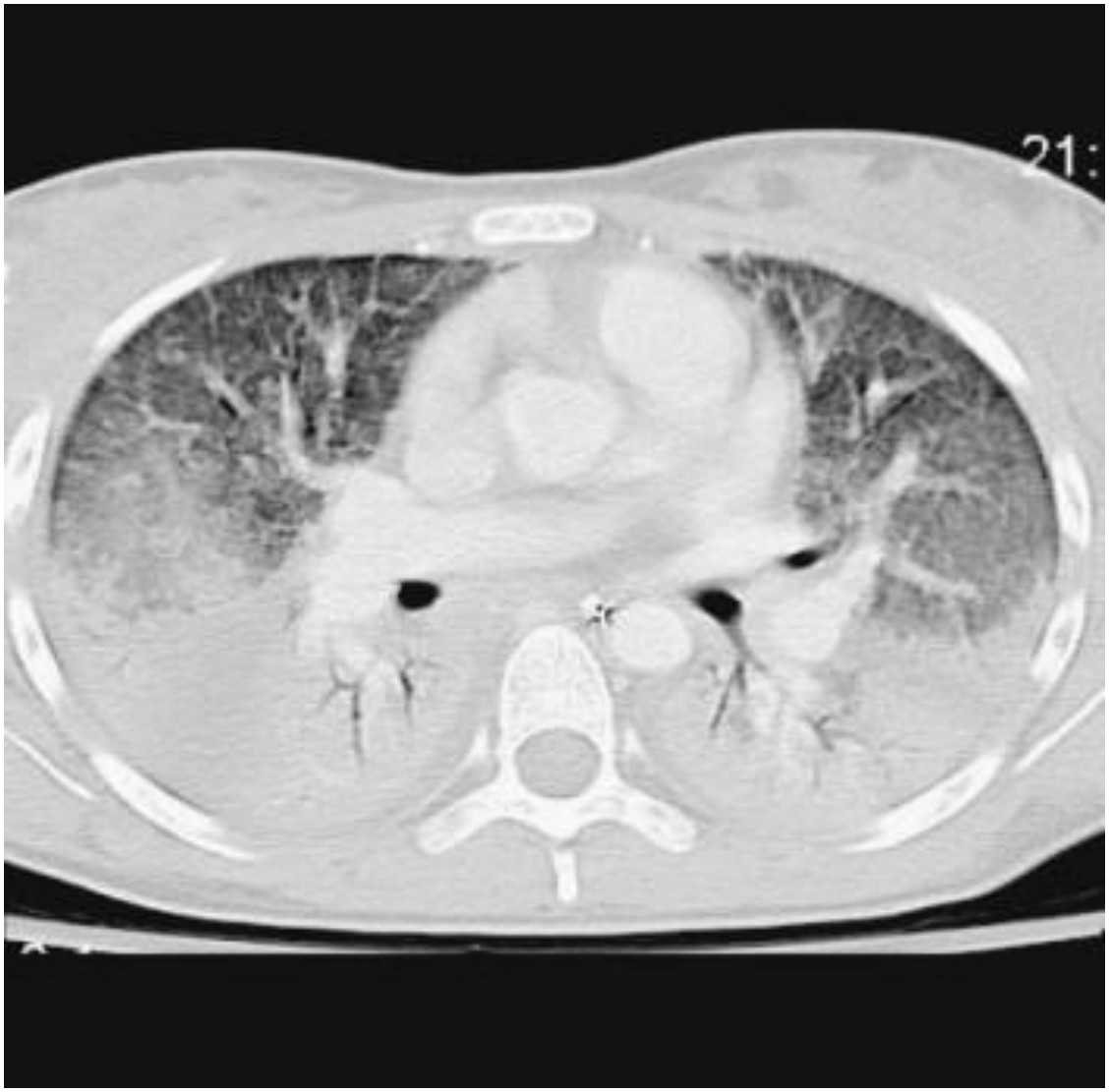
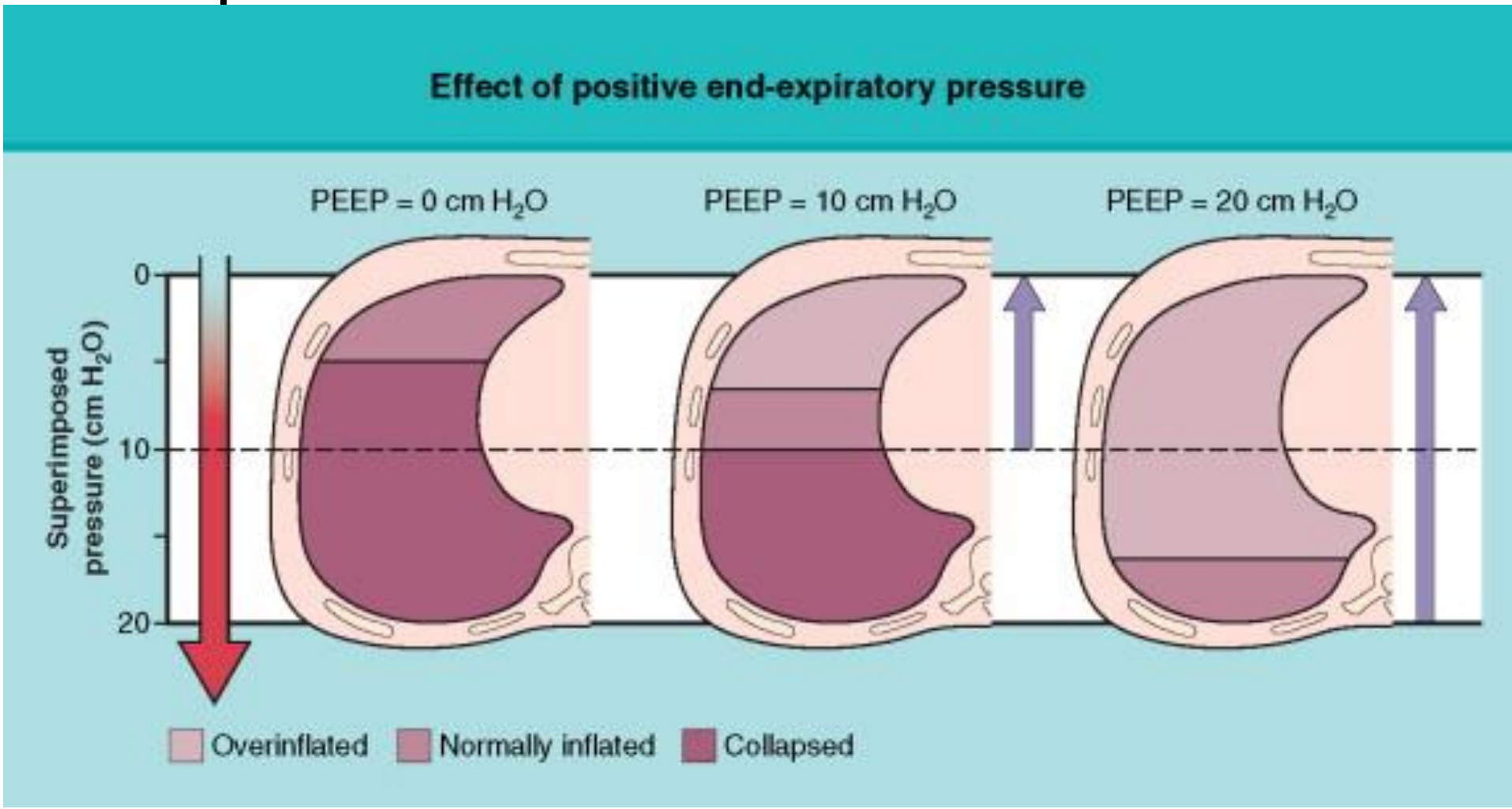
PEEP

ARDS dependent area 塌陷嚴重



(Dr. Thomas E. Stewart.)



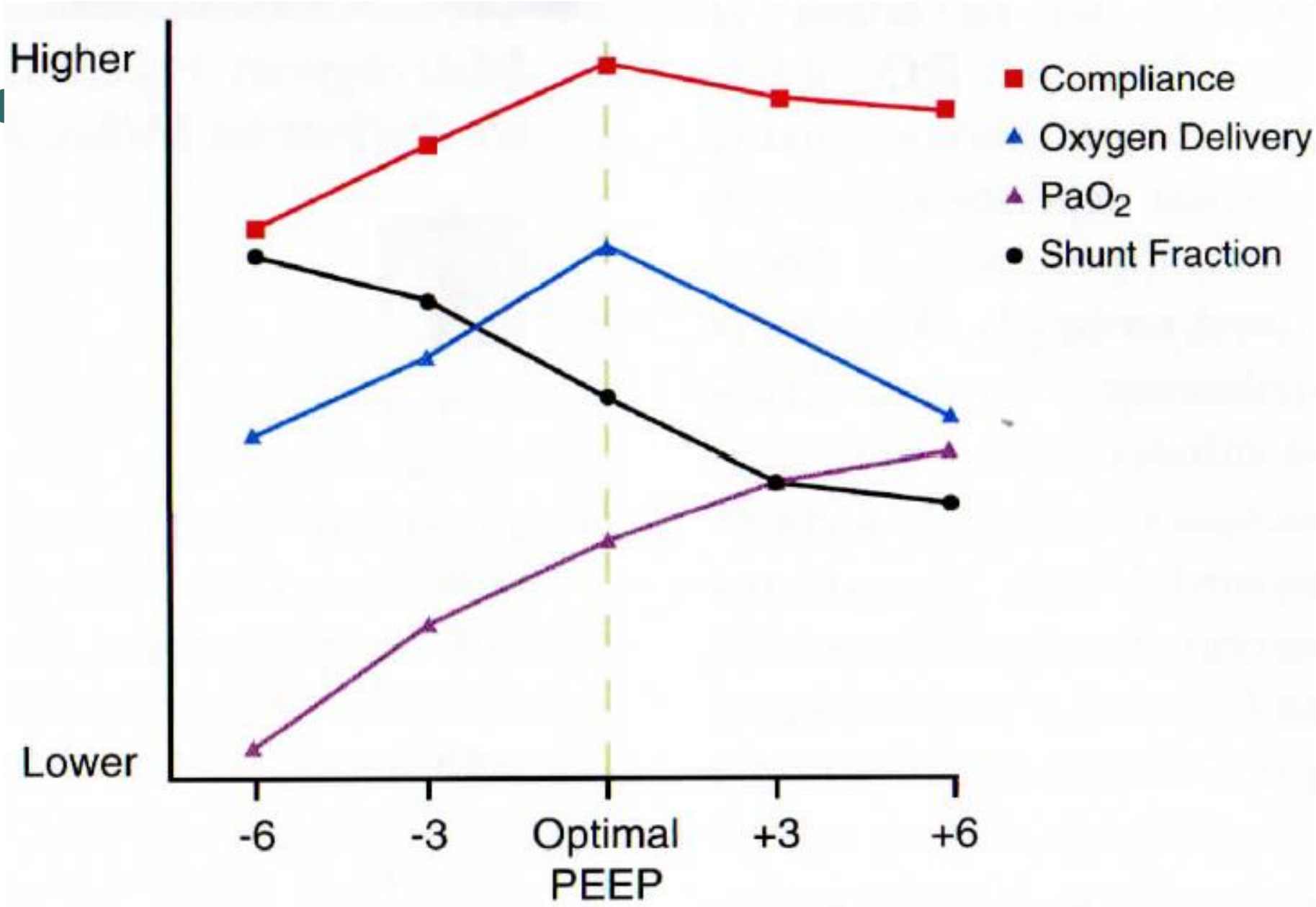
(Gattinoni et al: *Clinical Critical Care Medicine*, 237-252 © 2006 Mosby)

PEEP 的好處

- 藉著減少VQ mismatch 或分流(shunt)而達到增進氧合(oxygenation)的目的
- 增加肺順從性(compliance)
- 減少肺泡反覆開關造成的傷害(atelectrauma)

PEEP的壞處

- 減少cardiac output
- 降低BP



(Egan's Fundamentals of Respiratory Care 9th ed.2009, Mosby)

Oxygenation 目標

- Pao_2 55-80 mm Hg
- or Sao_2 88-95%

Lower PEEP chart

F_IO2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0
PEEP	5	5-8	8-10	10	10-14	14	14-18	18-24

(*N Engl J Med* 341(18) 2000)

(Siegel MD et al: *Uptodate* May 2014)

Higher PEEP chart

F_IO2	0.3	0.4	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* 351:(4) 2004)

(Siegel MD et al: *Uptodate* May 2014)

Mortality: High vs Low PEEP

Study or Subgroup	High Mortality Events	High Total Patients	Low Mortality Events	Low Total Patients	Weight	Risk Ratio M-H, Random, 95% CI	Y
Brower *et al.*, 2004	76	276	68	273	19.2%	1.11 [0.83, 1.46]	2004
Meade *et al.*, 2008	135	475	164	508	40.8%	0.88 [0.73, 1.06]	2008
Talmor *et al.*, 2008	5	30	12	31	1.9%	0.43 [0.17, 1.07]	2008
Mercat *et al.*, 2008	107	385	119	382	31.1%	0.89 [0.72, 1.11]	2008
Hodgson *et al.*, 2011	3	10	2	10	0.6%	1.50 [0.32, 7.14]	2011
Kacmarek *et al.*, 2016	22	99	27	101	6.4%	0.83 [0.51, 1.36]	2016
Total (95% CI)		**1275**		**1305**	**100.0%**	**0.91 [0.80, 1.03]**	
Total events	348		392				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.09$, df = 5 (P = 0.41); $I^2 = 2\%$

Test for overall effect: Z = 1.46 (P = 0.14)

(Walkey AJ: *Ann Am Thorac Soc* 2017; 14, Supplment 4)

P_aO_2/F_IO_2: High vs Low PEEP

	High PEEP			Low PEEP				Mean Difference	
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**	**Year**
Brower *et al.*, 2004	220	89	244	168	66	230	18.8%	52.00 [37.95, 66.05]	2004
Talmor *et al.*, 2008	280	126	29	191	71	29	6.1%	89.00 [36.36,141.64]	2008
Meade *et al.*, 2008	187.4	68.8	464	149.1	60.6	498	21.0%	38.30 [30.08, 46.52]	2008
Mercat *et al.*, 2008	218	97	378	150	69	371	19.6%	68.00 [55.96, 80.04]	2008
Hodgson *et al.*, 2011	220	20	10	140	20	10	17.3%	80.00 [62.47, 97.53]	2011
Kacmarek *et al.*, 2016	198.5	78.6	94	135.6	43.5	101	17.1%	62.90 [44.89, 80.91]	2016
Total (95% CI)			**1219**			**1239**	**100.0%**	**61.24 [45.92, 76.57]**	

Heterogeneity: $Tau^2 = 273.32$; $Chi^2 = 30.33$, df = 5 ($P < 0.0001$); $I^2 = 84\%$
Test for overall effect: $Z = 7.83$ ($P < 0.00001$)

(Walkey AJ: *Ann Am Thorac Soc* 2017; 14, Supplment 4)

ATS/ESICM/SCCM Recommendation 2017

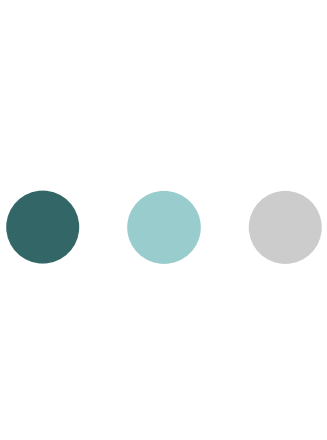
- *We suggest that adult patients with moderate or severe ARDS receive higher rather than lower levels of PEEP*
- *(conditional recommendation, moderate confidence in effect estimates).*

(Fan E: *Am J Respir Crit Care Med* 2017; 195(9))

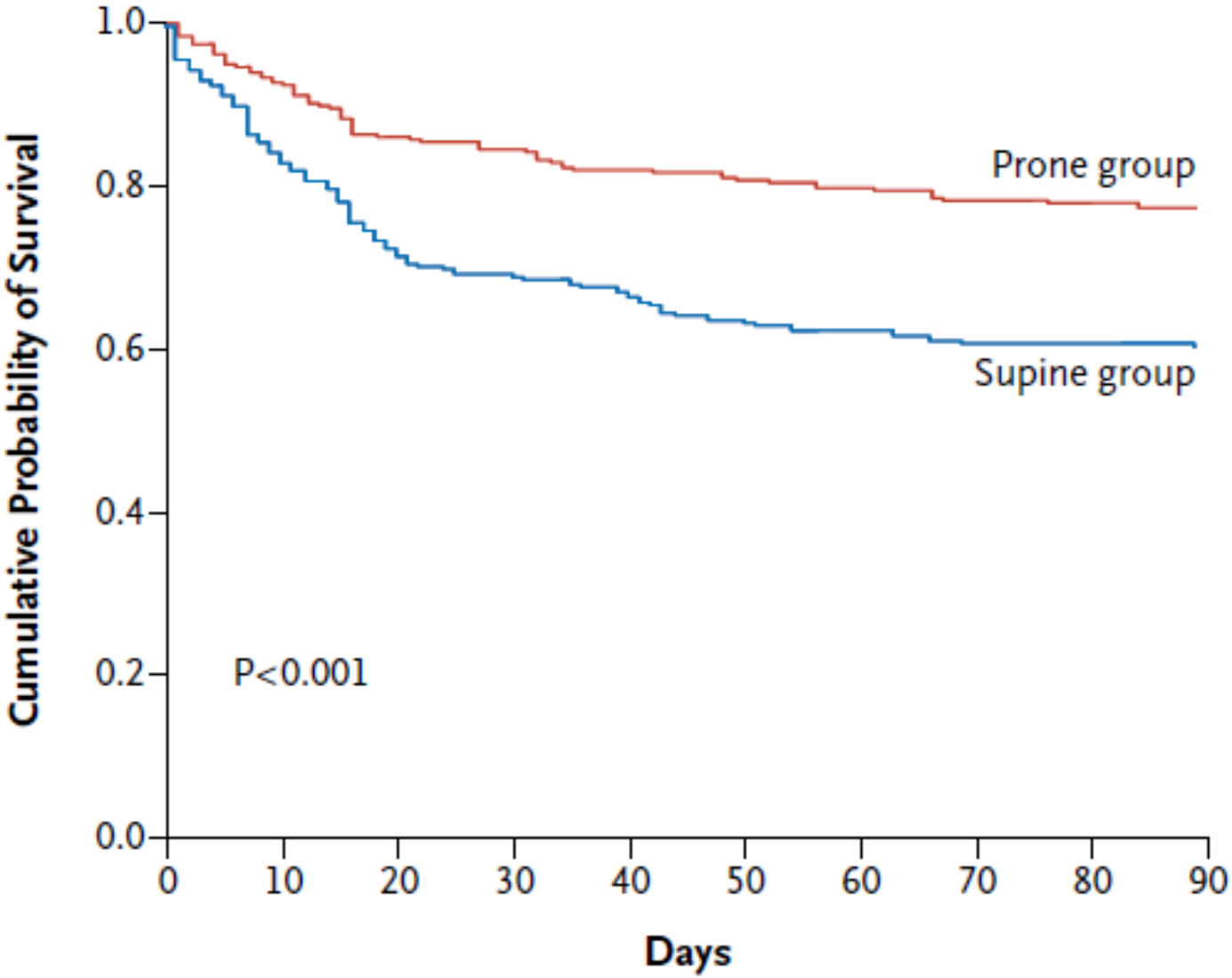
SRLF guideline 2019

- High PEEP should probably be used in patients with moderate or severe ARDS, but not in patients with mild ARDS. (GRADE 2 +, STRONG AGREEMENT)
- The experts suggest reserving high PEEP for patients in whom it improves oxygenation without marked deterioration of respiratory system compliance or hemodynamic status. PEEP settings should be individualized. (EXPERT OPINION)

(Papazian L. et al: *Ann Intensive Care* 2019; 9(1))



Prone



No. at Risk					
Prone group	237	202	191	186	182
Supine group	229	163	150	139	136

(Guérin Cet al: *N Engl J Med*. 2013 Jun 6;368(23)

Table 1 Summary of the five major trials on the prone position

Clinical Trials in the Prone Positioning					
Year	2001	2004	2006	2009	2013
	Gattinoni et al.	Guérin et al.	Mancebo et al.	Taccone et al.	Guérin et al.
Study period	1996–1999	1998–2002	1998–2002	2004–2008	2008–2011
Patients	304	802	142	344	466
Average PaO_2/FiO_2 at enrollment	127	152	105	113	100
PEEP at enrollment	10	8	7	10	10
SAPS II	40	46	41	41	46
Duration of prone position	7 h × 5 d	9 h × 4 d	17 h × 10 d	18 h × 8 d	17 h × 4 d
Protective ventilation	No	No	VT < 10 mL/kg	VT < 10 mL/kg	6 mL/kg
Follow-up	6 mo	90 d	Hospital discharge	6 mo	90 d
Mortality (%)					
Supine	58.3	42.2	60	52.9	41
Prone	62.2	43.3	50	47.6	23.6
p-Value	0.5	0.74	0.22	0.33	0.001

(Gattinoni, L et al: *Semin Respir Crit Care Med*; 2019; 40)

ATS/ESICM/SCCM Recommendation 2017

- *We recommend that adult patients with severe ARDS receive prone positioning for more than 12 hours per day*
- *(strong recommendation, moderate-high confidence in effect estimates).*

(Fan E: *Am J Respir Crit Care Med* 2017; 195(9))

SRLF guideline 2019

- *'Prone positioning should be used in ARDS patients with PaO2/FIO2 ratio < 150 mmHg to reduce mortality. Sessions of at least 16 consecutive hours should be performed.'*
- GRADE 1 +, STRONG AGREEMENT

(Papazian L. et al: *Ann Intensive Care* 2019; 9(1))

Neuromuscular blocker

SRLF guideline 2019

- *'A neuromuscular blocking agent should probably be considered in ARDS patients with a PaO2/FiO2 ratio < 150 mmHg to reduce mortality. The neuromuscular blocking agent should be administered by continuous infusion early (within 48 h after the start of ARDS), for no more than 48 h, with at least daily evaluation.'*
- GRADE 2 +, STRONG AGREEMENT

(Papazian L. et al: *Ann Intensive Care* 2019; 9(1))

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

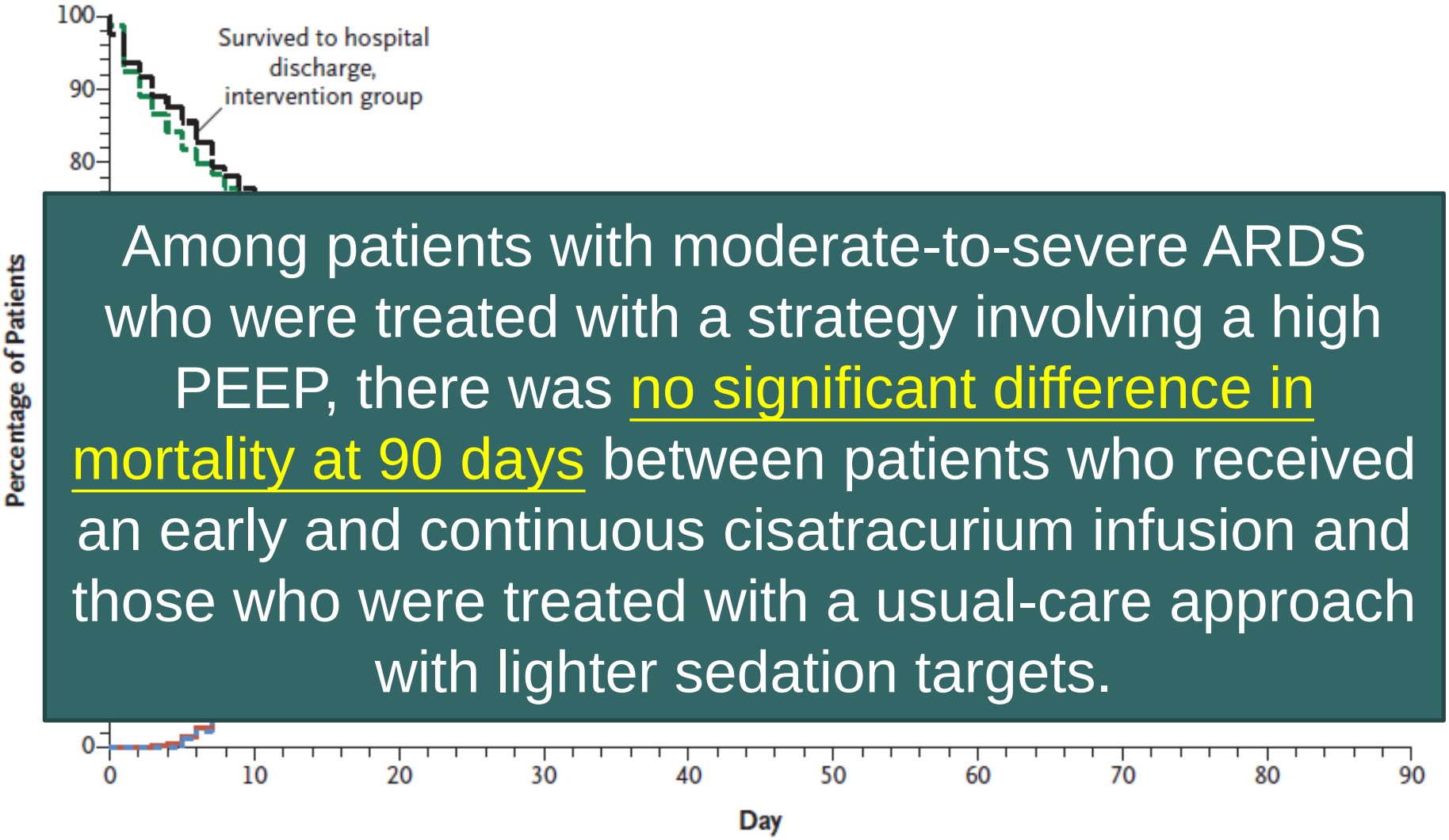
The National Heart, Lung, and Blood Institute PETAL Clinical Trials Network*

ABSTRACT

BACKGROUND

The benefits of early continuous neuromuscular blockade in patients with acute respiratory distress syndrome (ARDS) who are receiving mechanical ventilation remain unclear.

The members of the writing committee (Marc Moss, M.D., David T. Huang, M.D., M.P.H., Roy G. Brower, M.D., Niall D. Ferguson, M.D., Adit A. Ginde, M.D., M.P.H., M.N. Gong, M.D., Colin K. Gris-



Among patients with moderate-to-severe ARDS who were treated with a strategy involving a high PEEP, there was no significant difference in mortality at 90 days between patients who received an early and continuous cisatracurium infusion and those who were treated with a usual-care approach with lighter sedation targets.

(Moss, M., et al. (2019). *N Engl J Med* 380(21))

A

Study or Subgroup	NMBA Events	NMBA Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Forel 2006	5	18	10	18	8.3%	0.50 [0.21, 1.17]
Gainnier 2004	10	28	17	28	14.5%	0.59 [0.33, 1.05]
Guervilly 2017	5	13	3	11	4.8%	1.41 [0.43, 4.61]
Lyu 2014	9	48	18	48	11.4%	0.50 [0.25, 1.00]
Moss 2019	184	501	187	505	35.0%	0.99 [0.84, 1.17]
Papazian 2010	42	177	54	162	24.7%	0.71 [0.51, 1.00]
Rao 2016	1	24	2	17	1.4%	0.35 [0.03, 3.60]
Total (95% CI)		**809**		**789**	**100.0%**	**0.74 [0.56, 0.98]**
Total events	256		291			

Heterogeneity: Tau² = 0.05; Chi² = 10.90, df = 6 (P = 0.09); I² = 45%

Test for overall effect: Z = 2.11 (P = 0.03)

Risk of bias legend

(**A**) Random sequence generation (selection bias)

(**B**) Allocation concealment (selection bias)

(**C**) Blinding of participants and personnel (performance bias)

(**D**) Blinding of outcome assessment (detection bias)

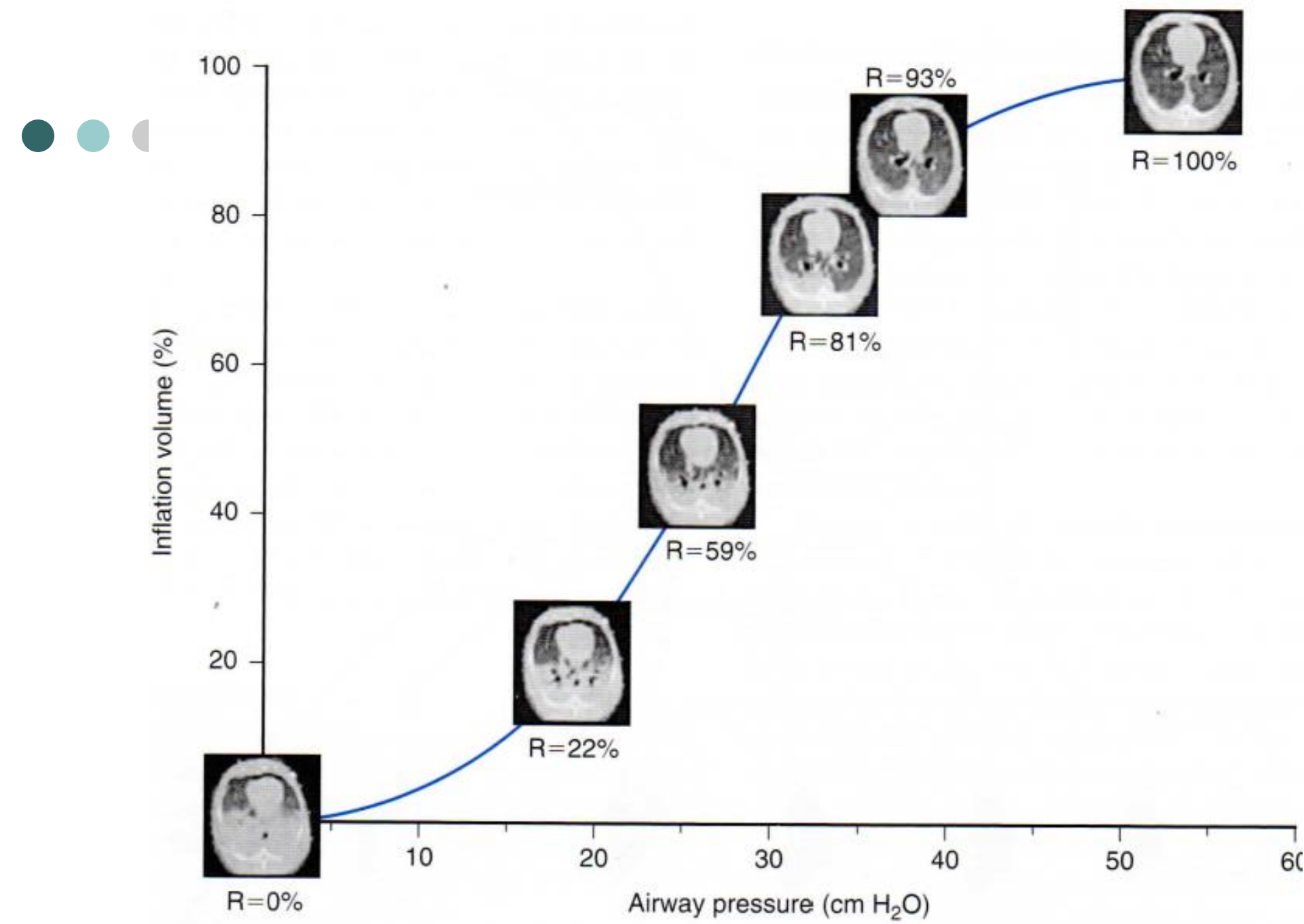
(**E**) Incomplete outcome data (attrition bias)

(**F**) Selective reporting (reporting bias)

(**G**) Other bias

(Chang, W., et al. (2020). *Crit Care* 24(1))

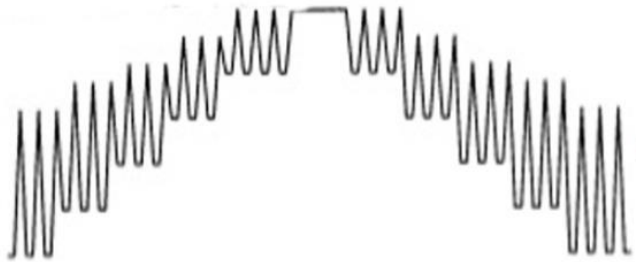
Recruitment Maneuvers



(Cairo JM: *Pilbeam's Mechanical Ventilation* 2012 Elsevier)

幾種達成recruitment maneuvers常見的作法

Sustained inflation
20–40 s/35–40 cmH_2O



eSigh pressure control

2 to 4 minutes

eSigh volume control

5 to 10 minutes

(Constantin JM et al: *Ann Transl Med* 2017; 5 (14))

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of particip (studies)
	Assumed risk	Corresponding risk		
	Control	Intervention		
28-Day mortality	Risk for the population		RR 0.86 (0.74 to 1.01)	1450 (5 studies)
	347 per 1000	294 per 1000		
ICU mortality	Risk for the population		RR 0.83 (0.72 to 0.97)	1370 (5 studies)
	362 per 1000	303 per 1000		
In-hospital mortality	Risk for the population		RR 0.88 (0.77 to 1.01)	1313 (4 studies)
	405 per 1000	356 per 1000		
Rate of barotrauma	Risk for the population		RR 1.09 (0.78 to 1.51)	1508 (7 studies)
	90 per 1000	86 per 1000		

(Hodgson C: *Cochrane Database Syst Rev*. 2016, 11:CD006667)

ATS/ESICM/SCCM Recommendation 2017

- *We suggest that adult patients with ARDS receive recruitment maneuver.*
- *(conditional recommendation, low–moderate confidence in the effect estimates).*

(Fan E: *Am J Respir Crit Care Med* 2017; 195(9))

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Lung Recruitment and Titrated Positive End-Expiratory Pressure (PEEP) vs Low PEEP on Mortality in Patients With Acute Respiratory Distress Syndrome
A Randomized Clinical Trial

Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART) Investigators

IMPORTANCE The effects of recruitment maneuvers and positive end-expiratory pressure (PEEP) titration on clinical outcomes in patients with acute respiratory distress syndrome (ARDS) remain uncertain.

OBJECTIVE To determine if lung recruitment associated with PEEP titration according to the best respiratory-system compliance decreases 28-day mortality of patients with moderate to severe ARDS compared with a conventional low-PEEP strategy.

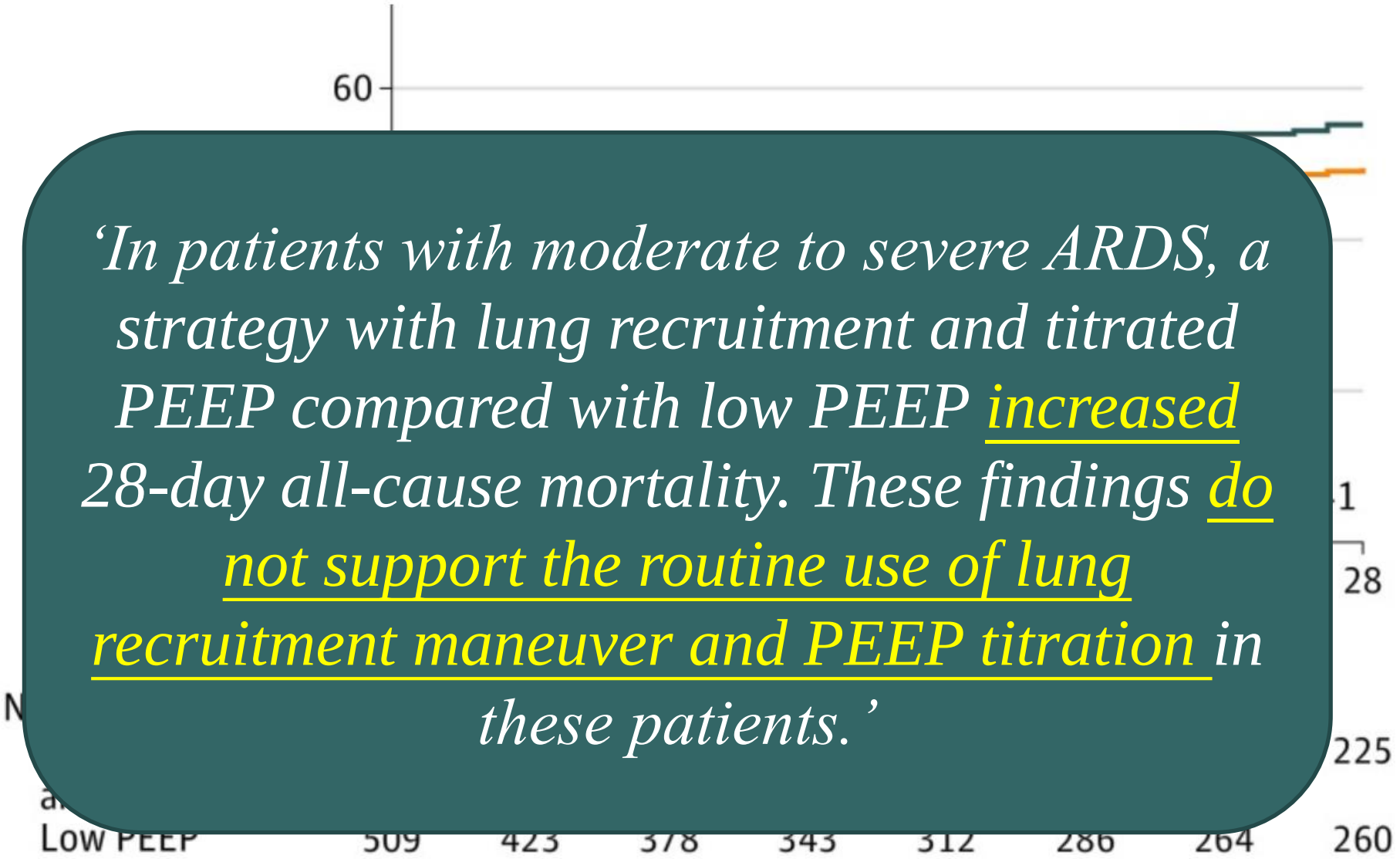
DESIGN, SETTING, AND PARTICIPANTS Multicenter, randomized trial conducted at 120 intensive care units (ICUs) from 9 countries from November 17, 2011, through April 25, 2017, enrolling adults with moderate to severe ARDS.

Editorial page 1327

Supplemental content

CME Quiz at jamanetwork.com/learning and CME Questions page 1389

(Cavalcanti, A. B.:*JAMA* 2017; 318(14))



'In patients with moderate to severe ARDS, a strategy with lung recruitment and titrated PEEP compared with low PEEP increased 28-day all-cause mortality. These findings do not support the routine use of lung recruitment maneuver and PEEP titration in these patients.'

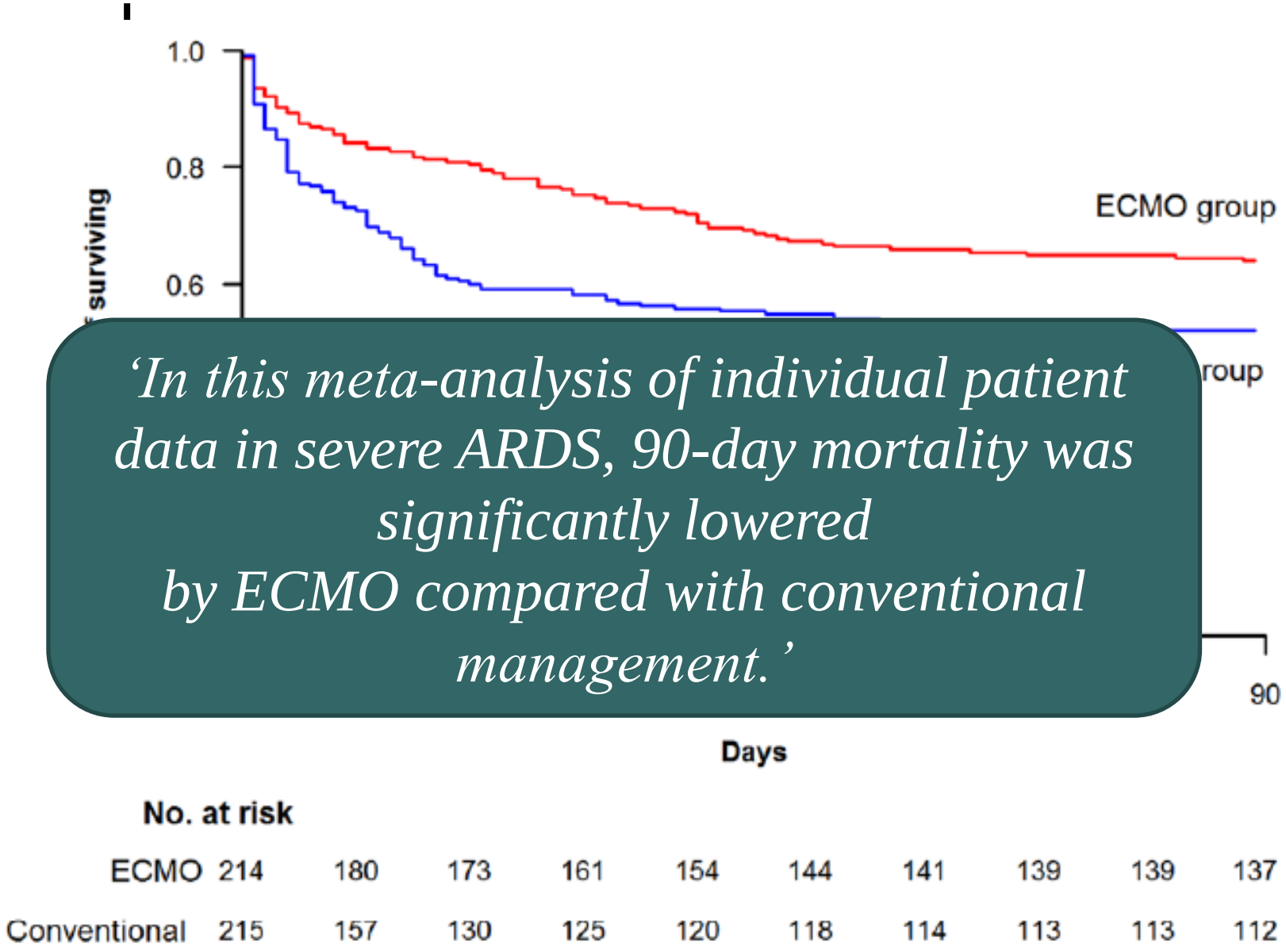
(Cavalcanti, A. B.:*JAMA* 2017; 318(14))

SRLF guideline 2019

- *'Recruitment maneuvers should probably not be used routinely in ARDS patients.'*
- GRADE 2 −, STRONG AGREEMENT

(Papazian L. et al: *Ann Intensive Care* 2019; 9(1))

ECMO



'In this meta-analysis of individual patient data in severe ARDS, 90-day mortality was significantly lowered by ECMO compared with conventional management.'

(Combes, A., et al. (2020). *Intensive Care Med* 46(11))

Table 1 Mechanical ventilation in VV ECMO according to the opinion of

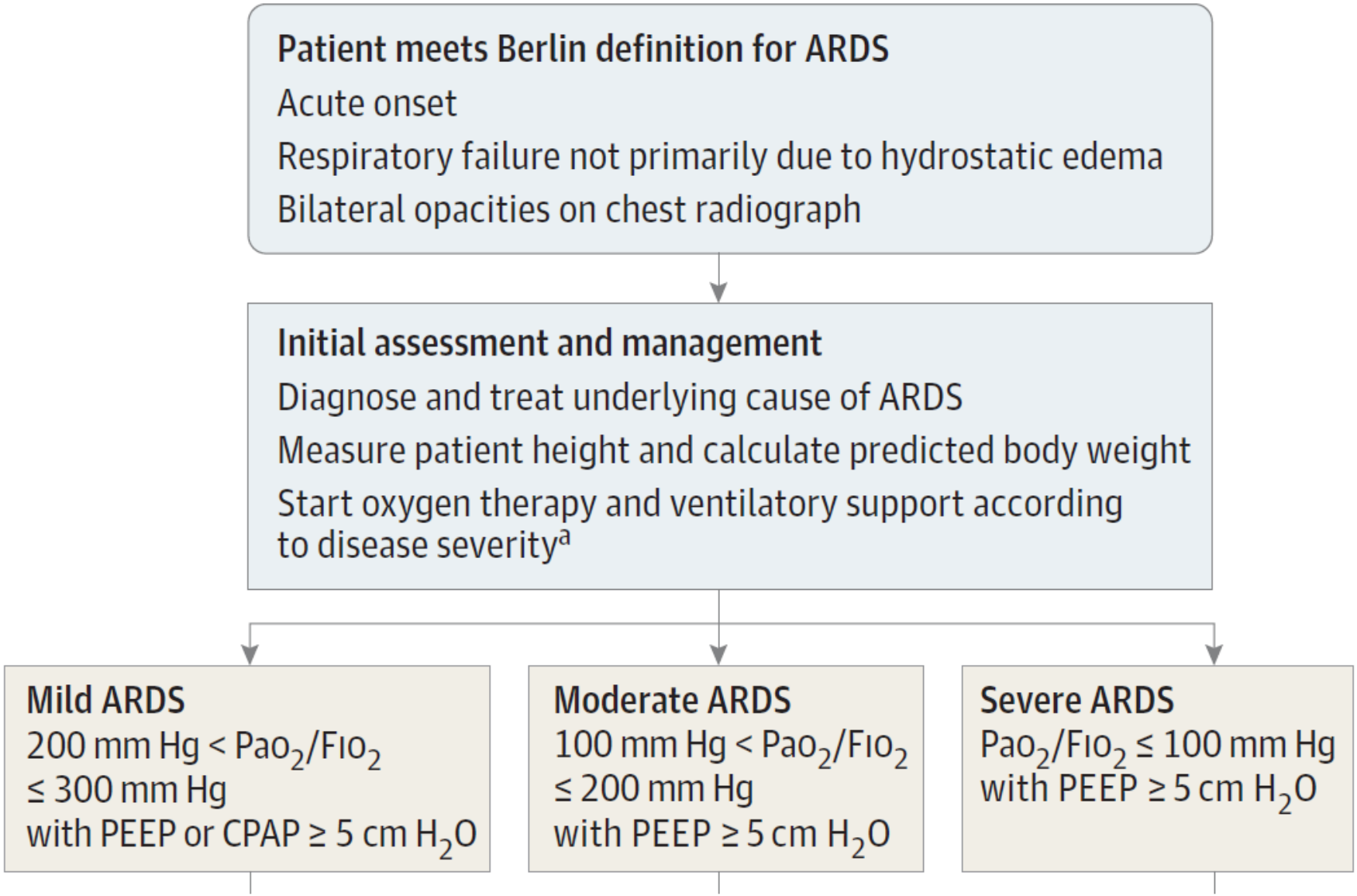
Source	MV objective	MV mode	Vt
ELSO guides 2013[35]	Lung rest	PCV	–
European Network of MV (REVA)[37]	Lung rest	VCV	–
Consensus Conference ECMO[36]	Lung rest	–	–

PEEP: positive end-expiratory pressure; Pp: plateau pressure; FiO_2: inspired f
Europeen de Recherche en Ventilation Artificielle; PCV: pressure control ver
ventilation; Vt: tidal volume.

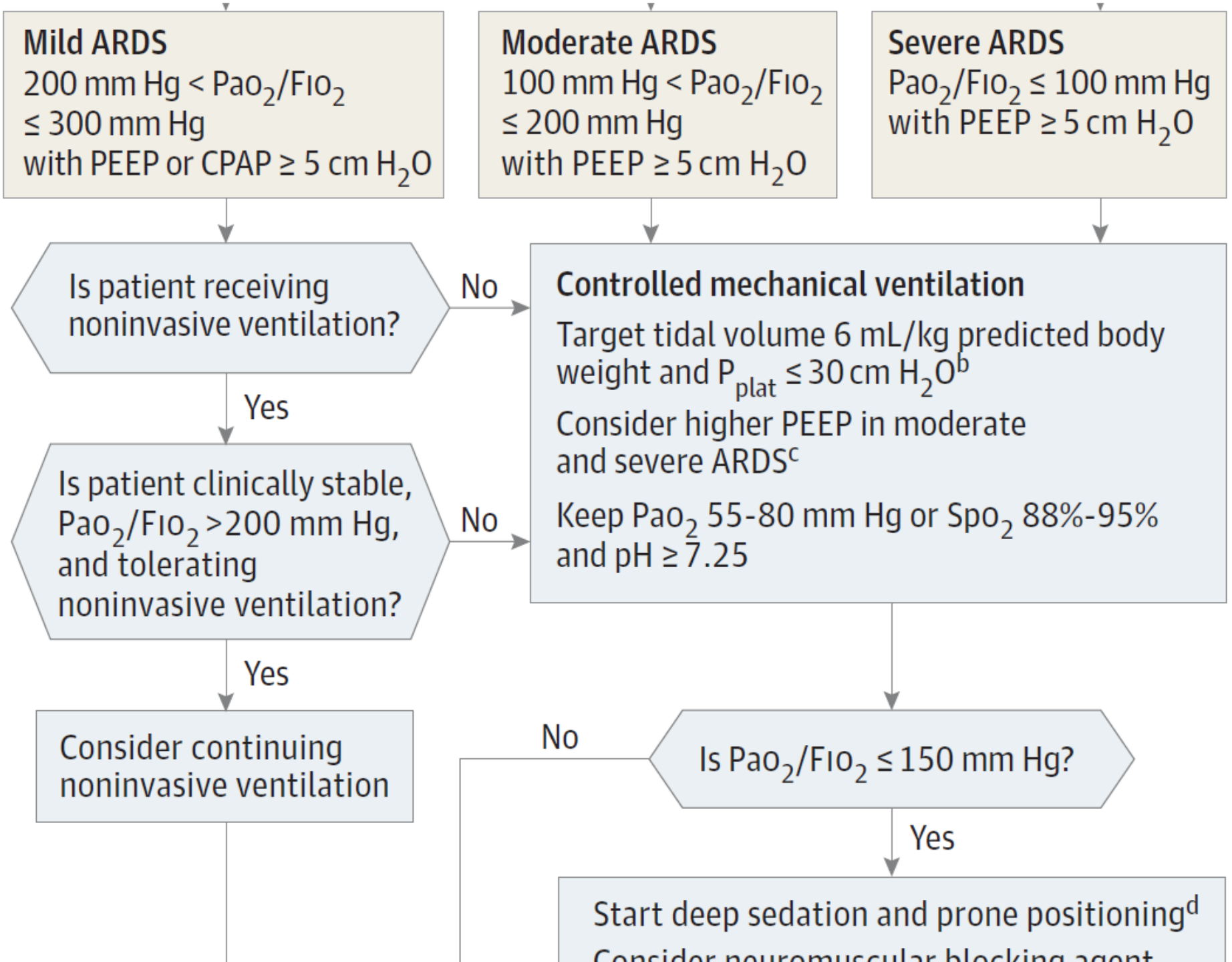
(López Sanchez, M. (2017). *Med Intensiva* 41(8))

Summary of Treatment Recommendations

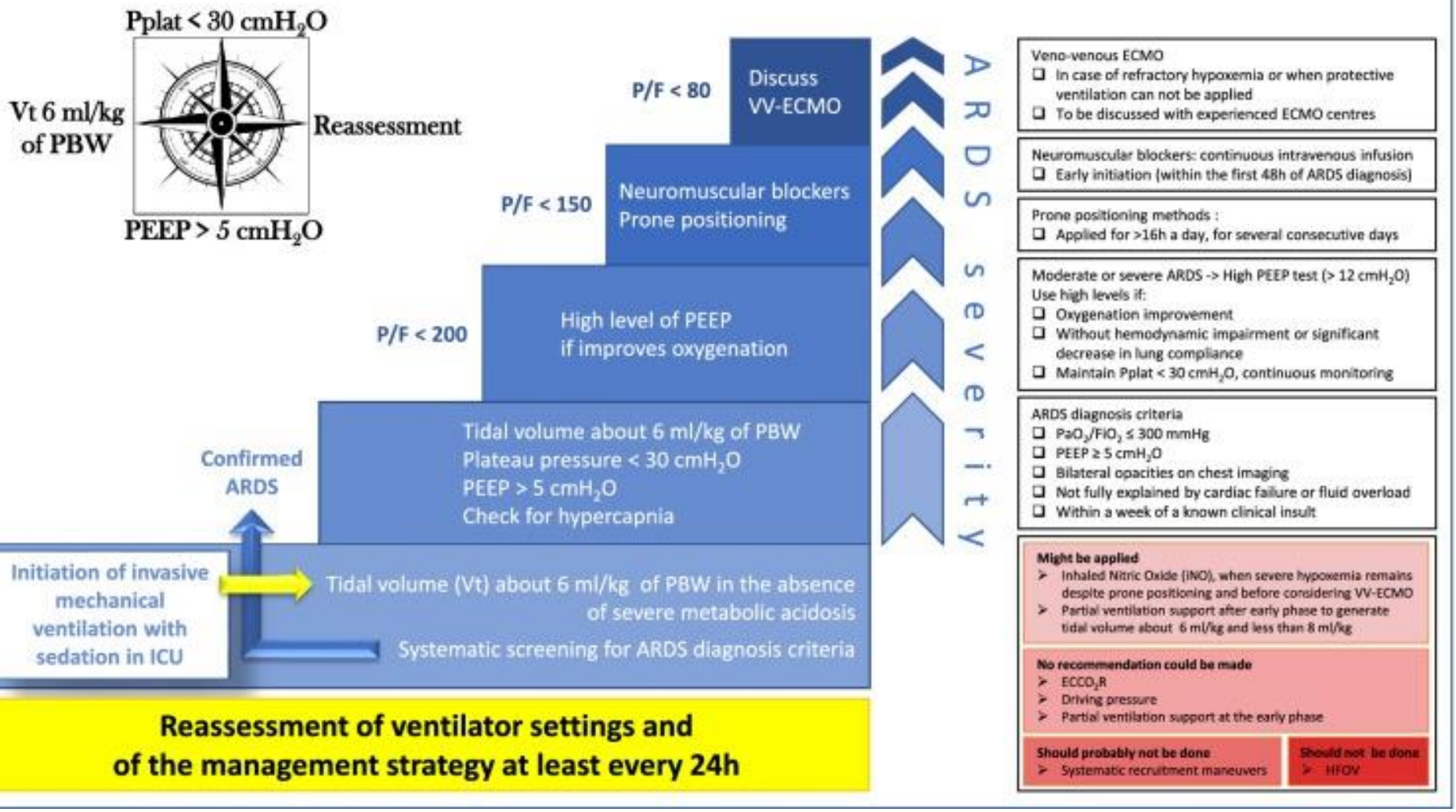
Figure 2. A Sample Treatment Algorithm for Patients With ARDS



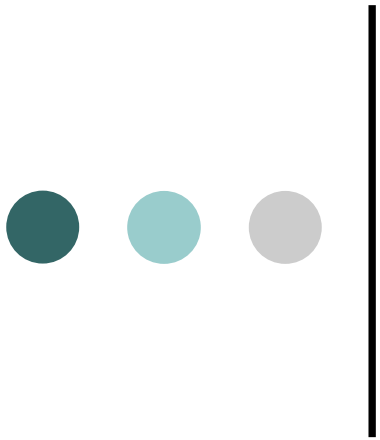
(Fan E. et al: *JAMA* 2018, 319)


Mild ARDS
200 mm Hg < Pao_2/Fio_2 ≤ 300 mm Hg with PEEP or CPAP ≥ 5 cm H_2O
Moderate ARDS
100 mm Hg < Pao_2/Fio_2 ≤ 200 mm Hg with PEEP ≥ 5 cm H_2O
Severe ARDS
Pao_2/Fio_2 ≤ 100 mm Hg with PEEP ≥ 5 cm H_2O
Is patient receiving noninvasive ventilation?
No
Yes
Controlled mechanical ventilation
Target tidal volume 6 mL/kg predicted body weight and P_{plat} ≤ 30 cm H_2O[b]
Consider higher PEEP in moderate and severe ARDS[c]
Keep Pao_2 55-80 mm Hg or Spo_2 88%-95% and pH ≥ 7.25
Is patient clinically stable, Pao_2/Fio_2 >200 mm Hg, and tolerating noninvasive ventilation?
No
Yes
Consider continuing noninvasive ventilation
No
Is Pao_2/Fio_2 ≤ 150 mm Hg?
Yes
Start deep sedation and prone positioning[d]

Early management of ARDS in 2019



(Papazian L. et al: *Ann Intensive Care* 2019; 9(1))



Thank You!