Ventilation protectrice au cours du SDRA

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Médecine Intensive-Réanimation

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Excluded from the talk

- Ventilatory modes
  - APRV
  - HFO
- Drugs
  - Surfactant
  - PLV
  - Steroids
  - Almitrine
- Other adjuvants
  - RV performance
  - Nutrition
  - Fluid balance
  - Physical therapy
  - Prevention and treatment of VAP…

Objectives

Hypoxemia

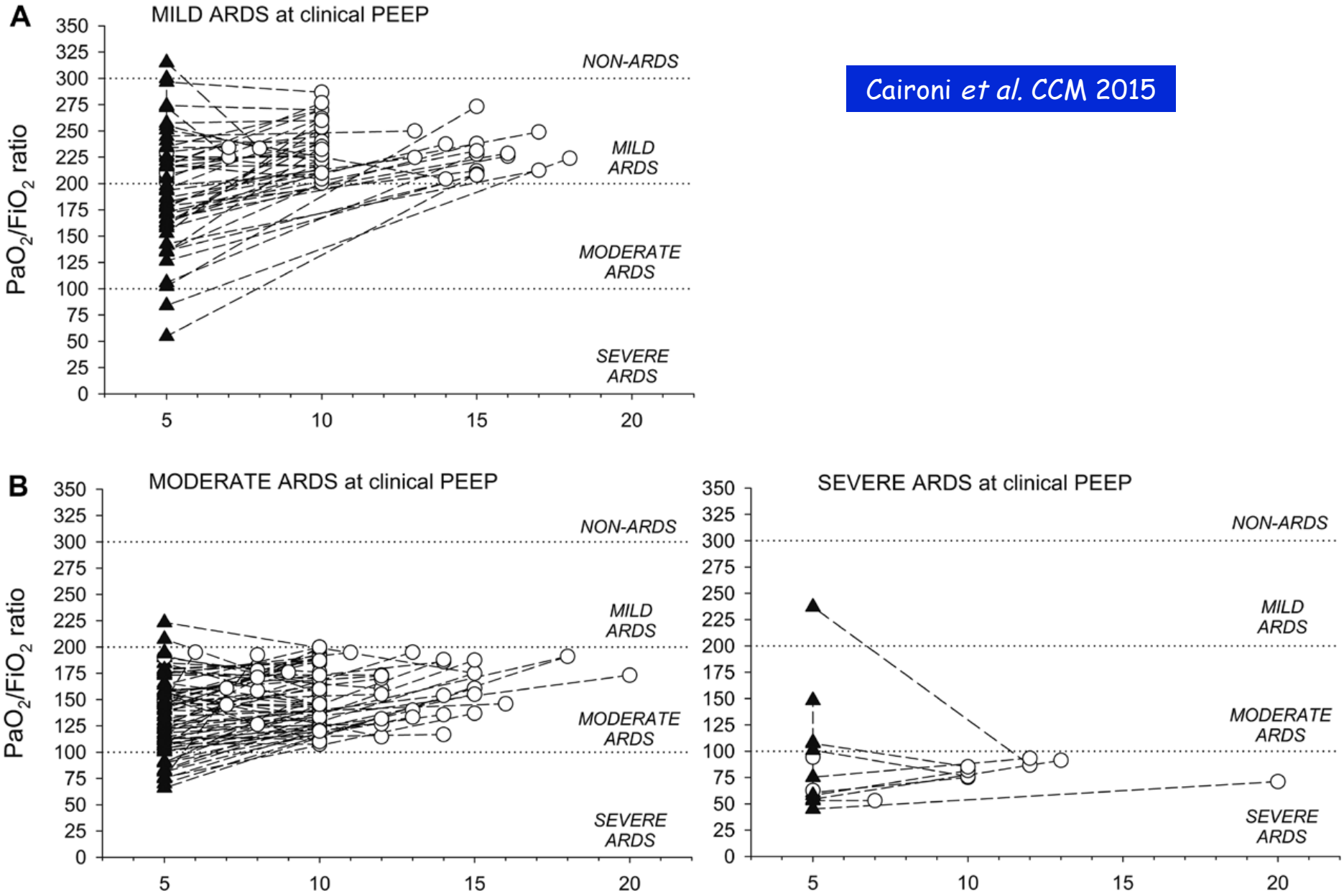
VILI prevention

Berlin definition

	Acute respiratory distress syndrome		
Timing	Within 1 week of a known clinical insult or new/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 (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present		
	Mild	Moderate	Severe
Oxygenation[b]	$200 < PaO_2/FiO_2 \leq 300$ with PEEP or CPAP ≥ 5 cmH_2O[c]	$100 < PaO_2/FiO_2 \leq 200$ with PEEP ≥ 5 cmH_2O	$PaO_2/FiO2 \leq 100$ with PEEP ≥ 5 cmH_2O

Ferguson *et al.* Intensive Care Med 2012

PEEP 5 cmH2O ?



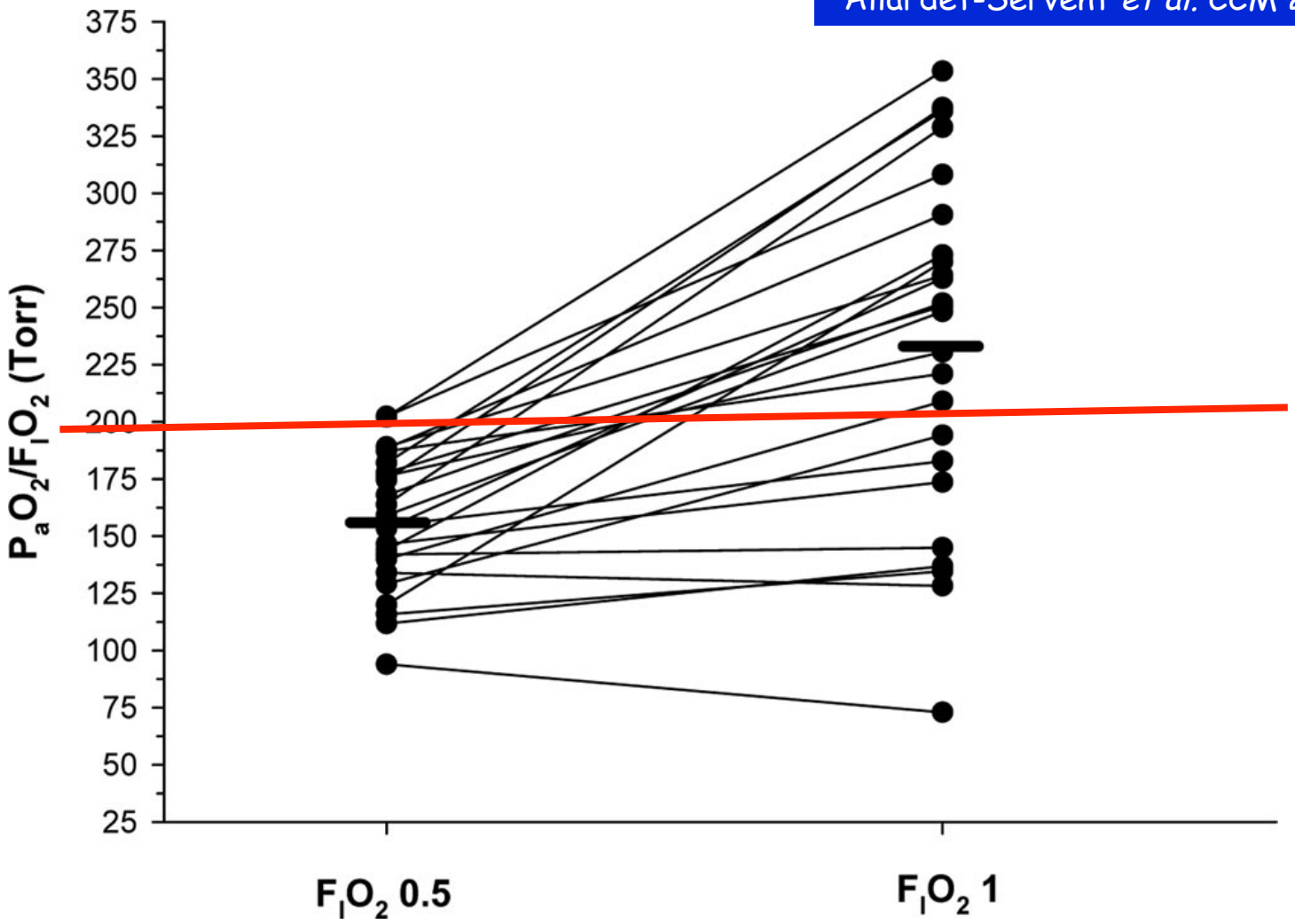
Caironi *et al.* CCM 2015

Characteristics	Classification	Acute Respiratory Distress Syndrome Severity			p^a
		Mild	Moderate	Severe	
Patients, *n* (%)	Clinical	52 (37)	76 (55)	11 (8)	–
	5 cm H_2O	27 (19)	92 (67)	20 (14)	–
	15 cm H_2O	52 (42)	68 (54)	5 (4.0)	–
Normally aerated lung tissue, g	Clinical	400 [297–522]	338 [244–475][b]	232 [124–503][b]	0.006
	5 cm H_2O	455 [334–566]	349 [252–497][b]	249 [188–420][b]	0.002
	15 cm H_2O	366 [288–492]	326 [244–506]	232 [187–253]	0.11
Poorly aerated lung tissue, g	Clinical	389 [302–474]	377 [276–643]	524 [327–853]	0.10
	5 cm H_2O	336 [241–423]	418 [284–569]	685 [337–868][b,c]	0.002
	15 cm H_2O	392 [315–485]	399 [264–699]	347 [327–769]	0.76
Nonaerated lung tissue, g	Clinical	445 [350–580]	511 [360–849]	1,153 [661–1,293][b,c]	< 0.001
	5 cm H_2O	405 [336–503]	502 [348–701]	961 [579–1,376][b,c]	< 0.001
	15 cm H_2O	431 [336–633]	576 [388–863]	1,217 [1,031–1,282]	0.004
ICU Mortality, *n* (%)	Clinical	12 (23)	31 (41)	7 (64)	0.02
	5 cm H_2O	7 (26)	29 (32)	14 (70)	0.002
	15 cm H_2O	16 (31)	27 (40)	4 (80)	0.08

Caironi *et al.* CCM 2015

Is it really a moderate-to-severe ARDS?

Allardet-Servent *et al.* CCM 2009

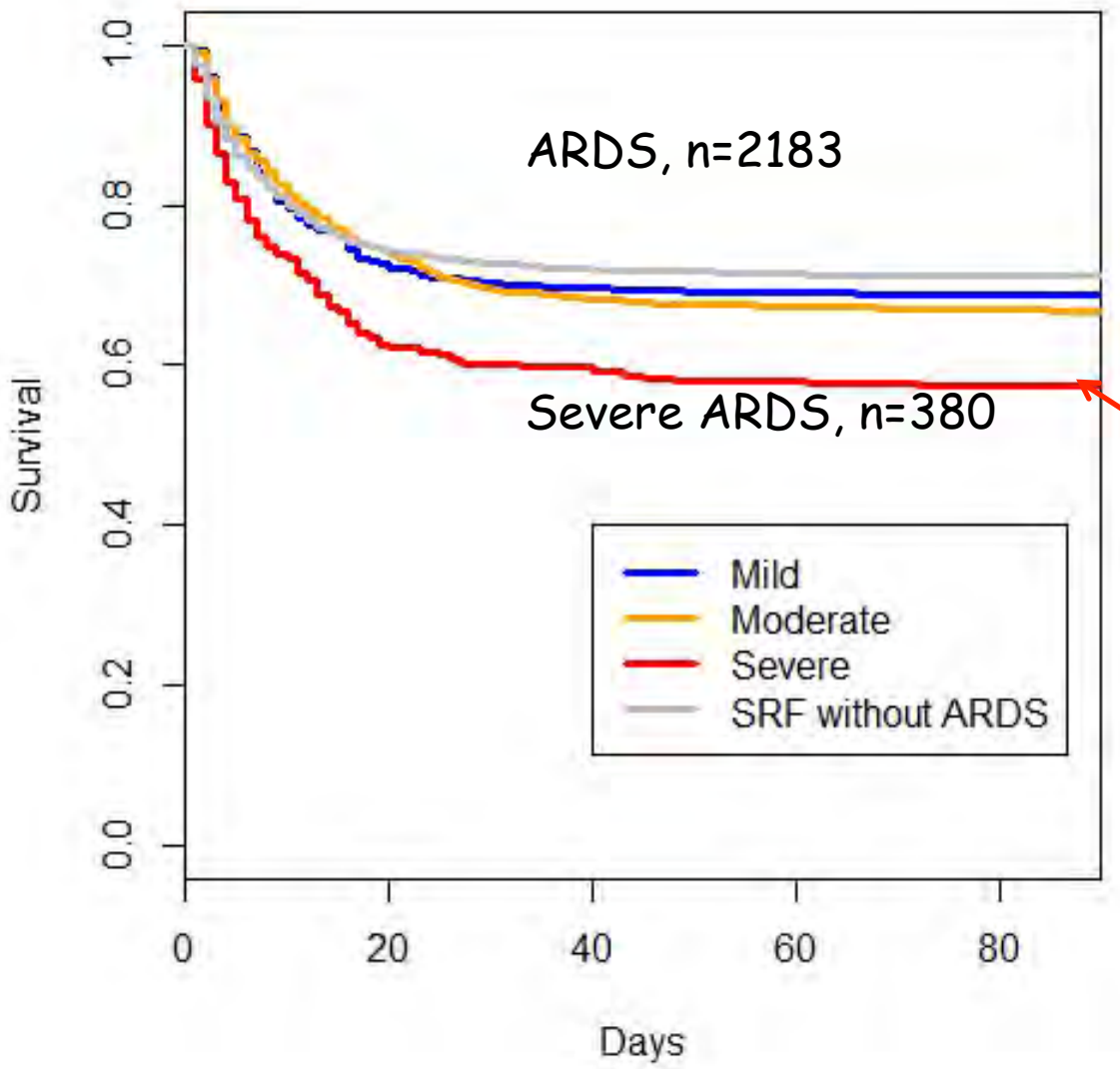


Mortality and hypoxemia

	Modified AECC Definition[a]		Berlin Definition ARDS[a]		
	ALI Non-ARDS	ARDS	Mild	Moderate	Severe
No. (%) [95% CI] of patients	1001 (24) [23-25]	3187 (76) [75-77]	819 (22) [21-24]	1820 (50) [48-51]	1031 (28) [27-30]
Progression in 7 d from mild, No. (%) [95% CI]		336 (34) [31-37]		234 (29) [26-32]	33 (4) [3-6]
Progression in 7 d from moderate, No. (%) [95% CI]					230 (13) [11-14]
Mortality, No. (%) [95% CI][b]	263 (26) [23-29]	1173 (37) [35-38]	220 (27) [24-30]	575 (32) [29-34]	461 (45) [42-48]
Ventilator-free days, median (IQR)[b]	20 (2-25)	12 (0-22)	20 (1-25)	16 (0-23)	1 (0-20)
Duration of mechanical ventilation in survivors, median (IQR), d[b]	5 (2-10)	7 (4-14)	5 (2-11)	7 (4-14)	9 (5-17)

JAMA 2012

Patient Survival to Day 90



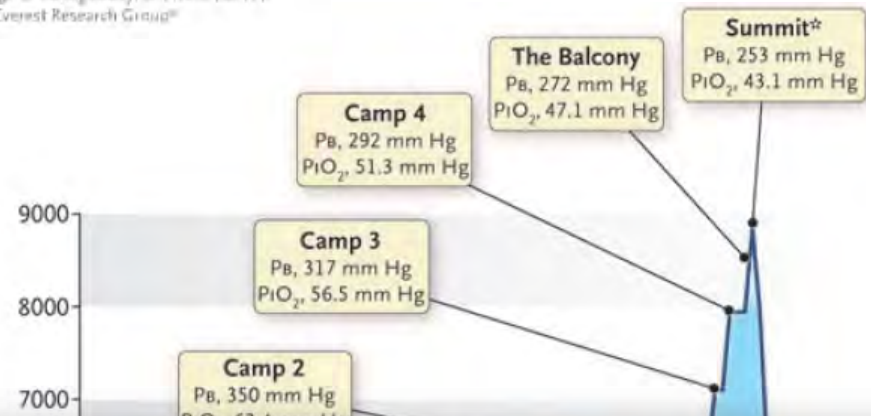
46% Mortality

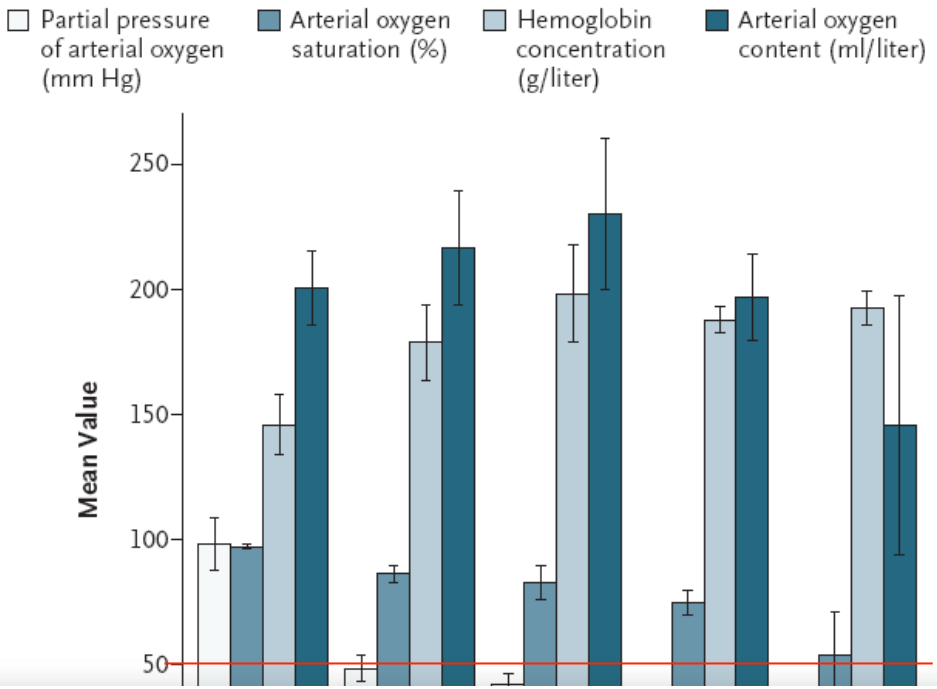
THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

ial Blood Gases and Oxygen Content in Climbers on Mount Everest

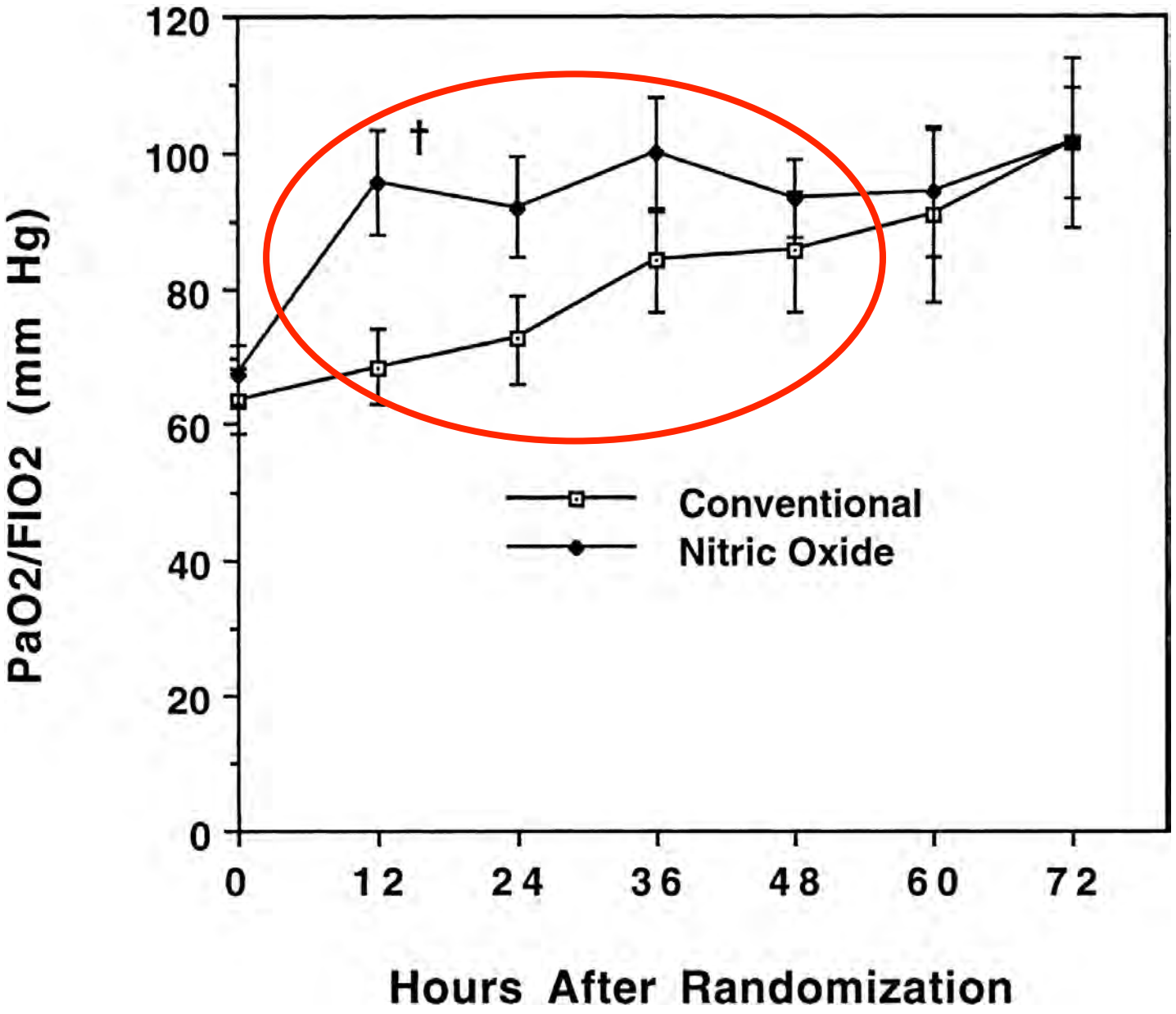
chael P.W. Grocott, M.B., B.S., Daniel S. Martin, M.B., Ch.B., rny Z.H. Levett, B.M., B.Ch., Roger McMorrow, M.B., B.Ch., Windsor, M.B., Ch.B., and Hugh E. Montgomery, M.B., B.S., M.D., for the Caudwell Xtreme Everest Research Group*





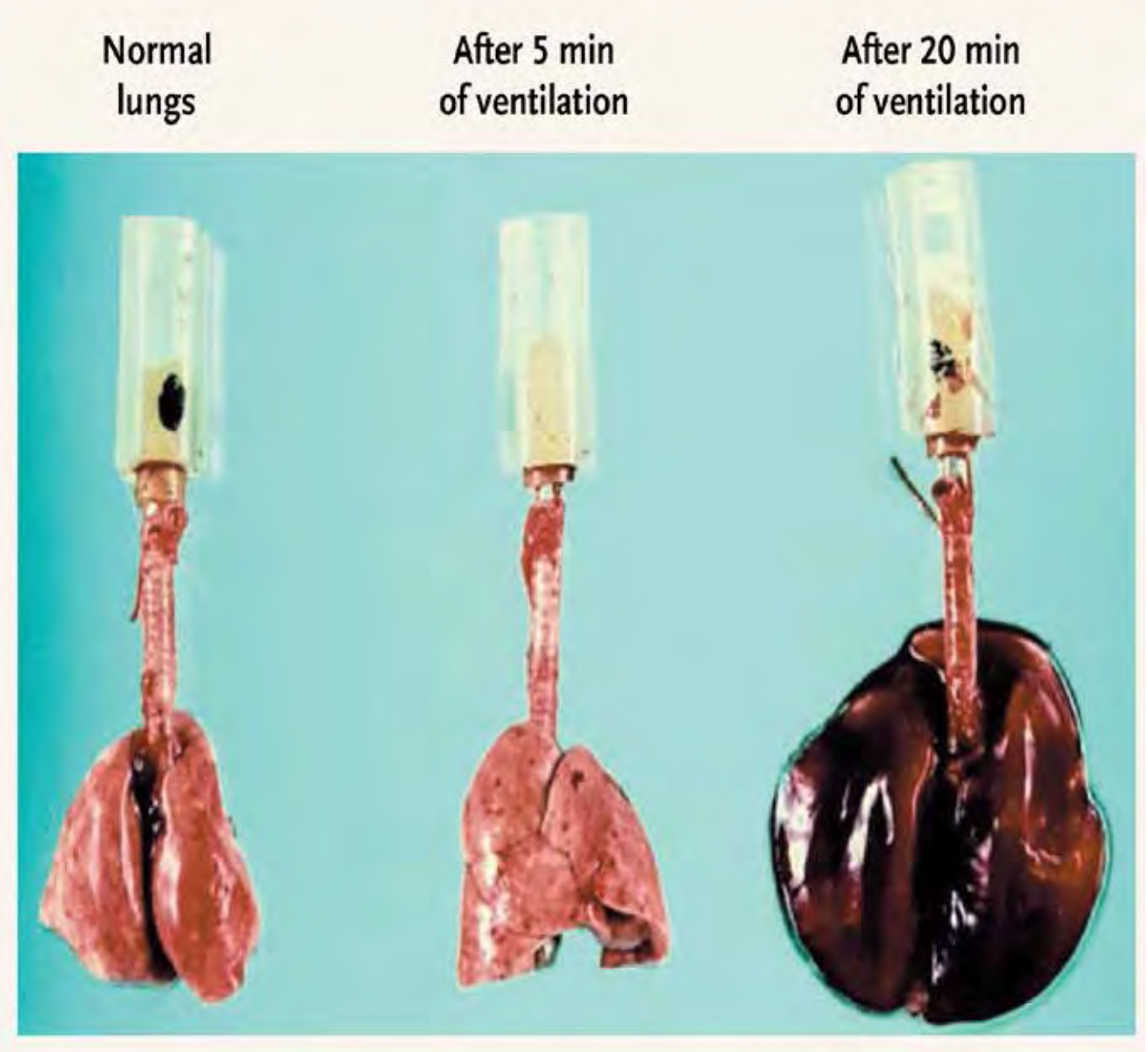
Variable	Subject No.				Group Mean
	1	2	3	4	
pH	7.55	7.45	7.52	7.60	7.53
PaO_2 (mm Hg)†	29.5	19.1	21.0	28.7	24.6
$PaCO_2$ (mm Hg)†	12.3	15.7	15.0	10.3	13.3
Bicarbonate (mmol/liter)‡	10.5	10.67	11.97	9.87	10.8
Base excess of blood‡	−6.3	−9.16	−6.39	−5.71	−6.9
Lactate concentration (mmol/liter)	2.0	2.0	2.9	1.8	2.2
SaO_2 (%)‡	68.1	34.4	43.7	69.7	54.0
Hemoglobin (g/dl)§	20.2	18.7	18.8	19.4	19.3

Michael et coll. AJRCCM 98



ILI prevention

Dreyfuss & Saumon AJRCCM 98



econd-hit

perimental data

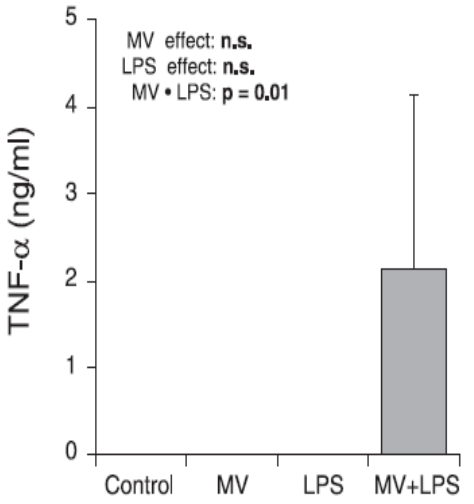
- **Injured lungs**
  - ↗ edema: synergy ANTU - Vt 45 ml/kg

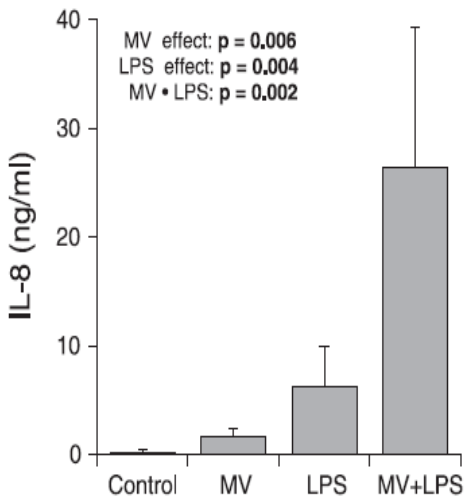
Dreyfuss *et al.* AJRCCM 95

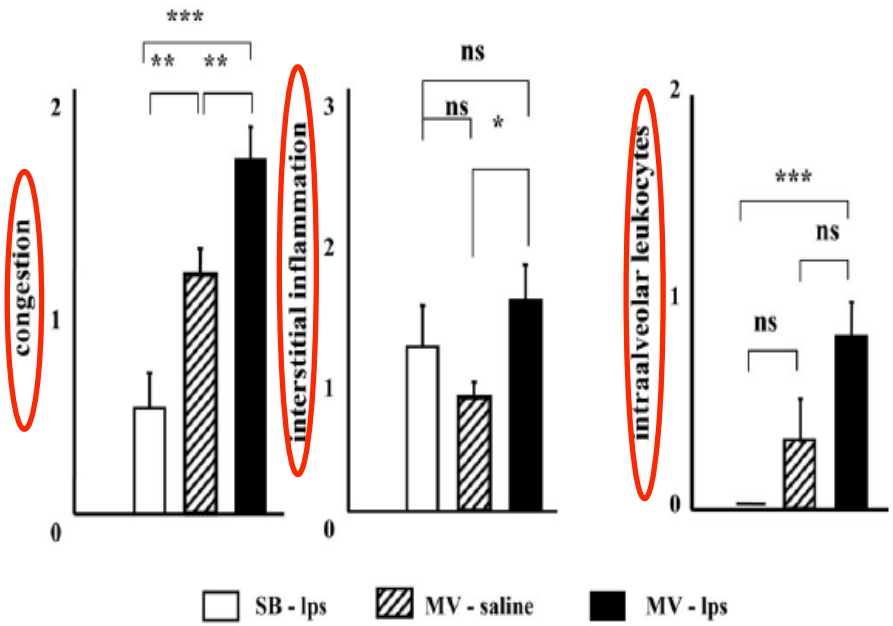
- **Healthy lungs**
  - LPS + MV

Brégeon *et al.* Anesthesiology 2005

Altemeier *et al.* Am J Physiol 2004

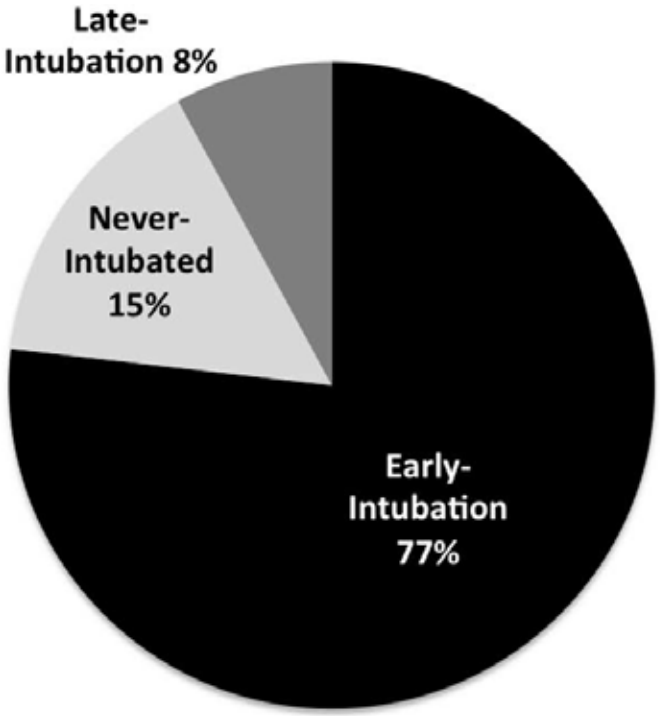




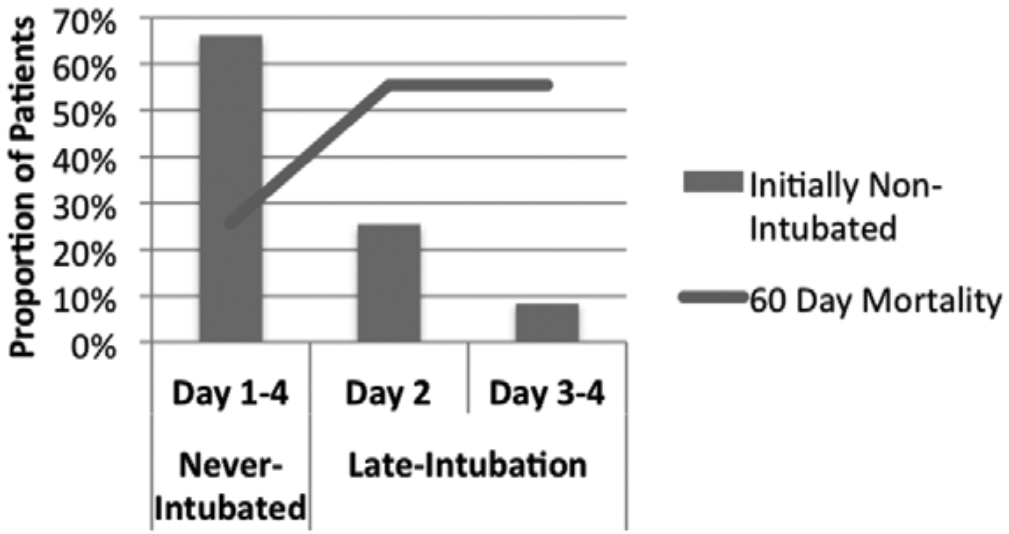


Late intubation is associated with worse outcome

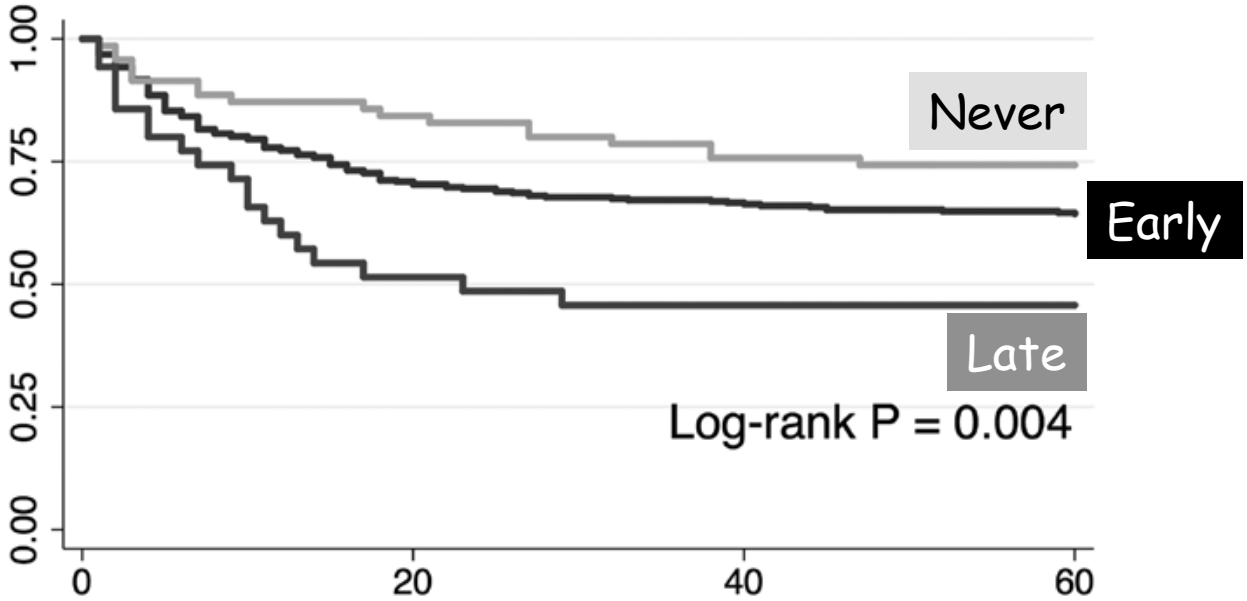
Kangelaris *et al.* CCM 2016



ARDS, N=457

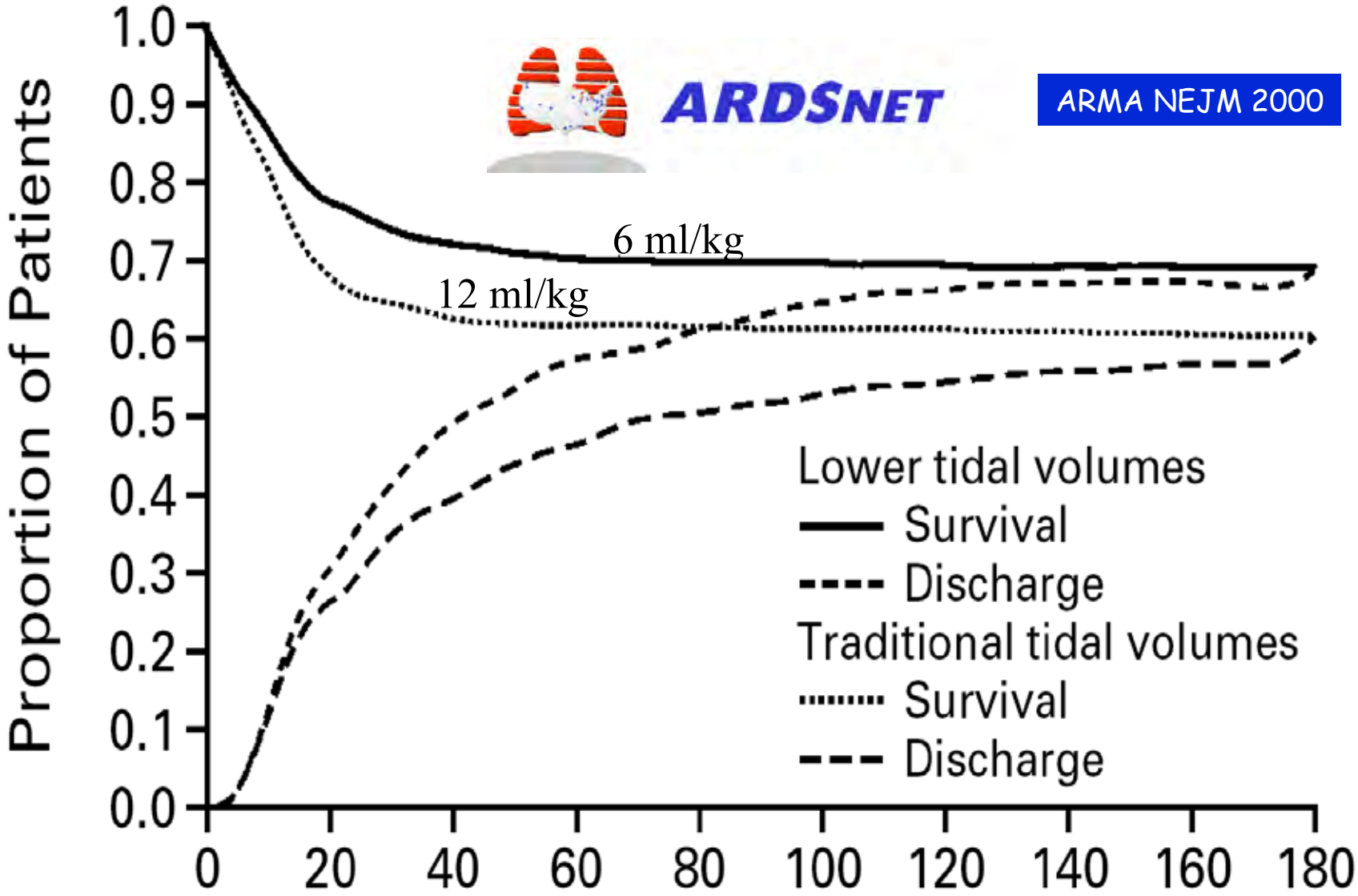


Timing of intubation



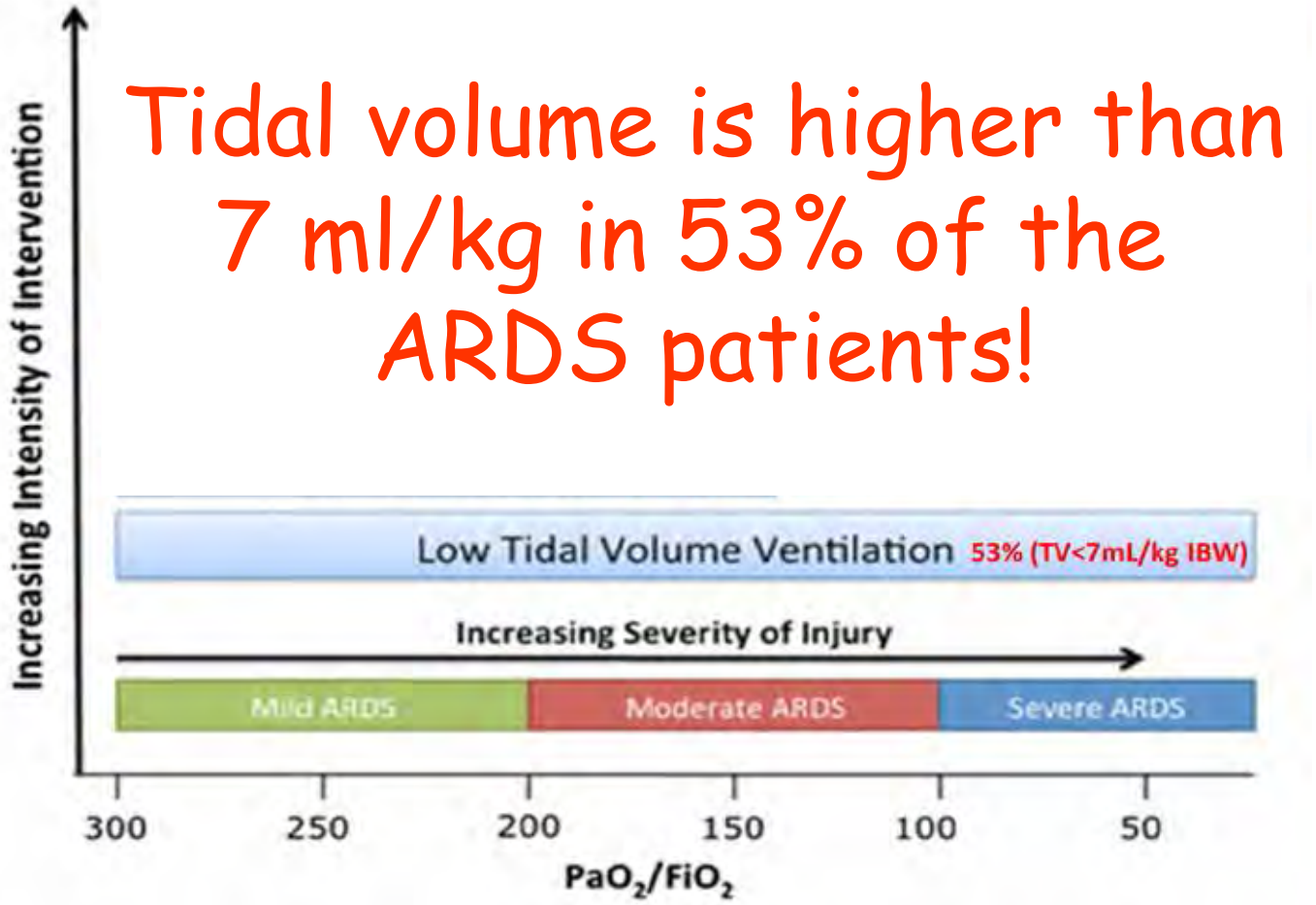
Optimization of ventilator settings

dal volume reduction

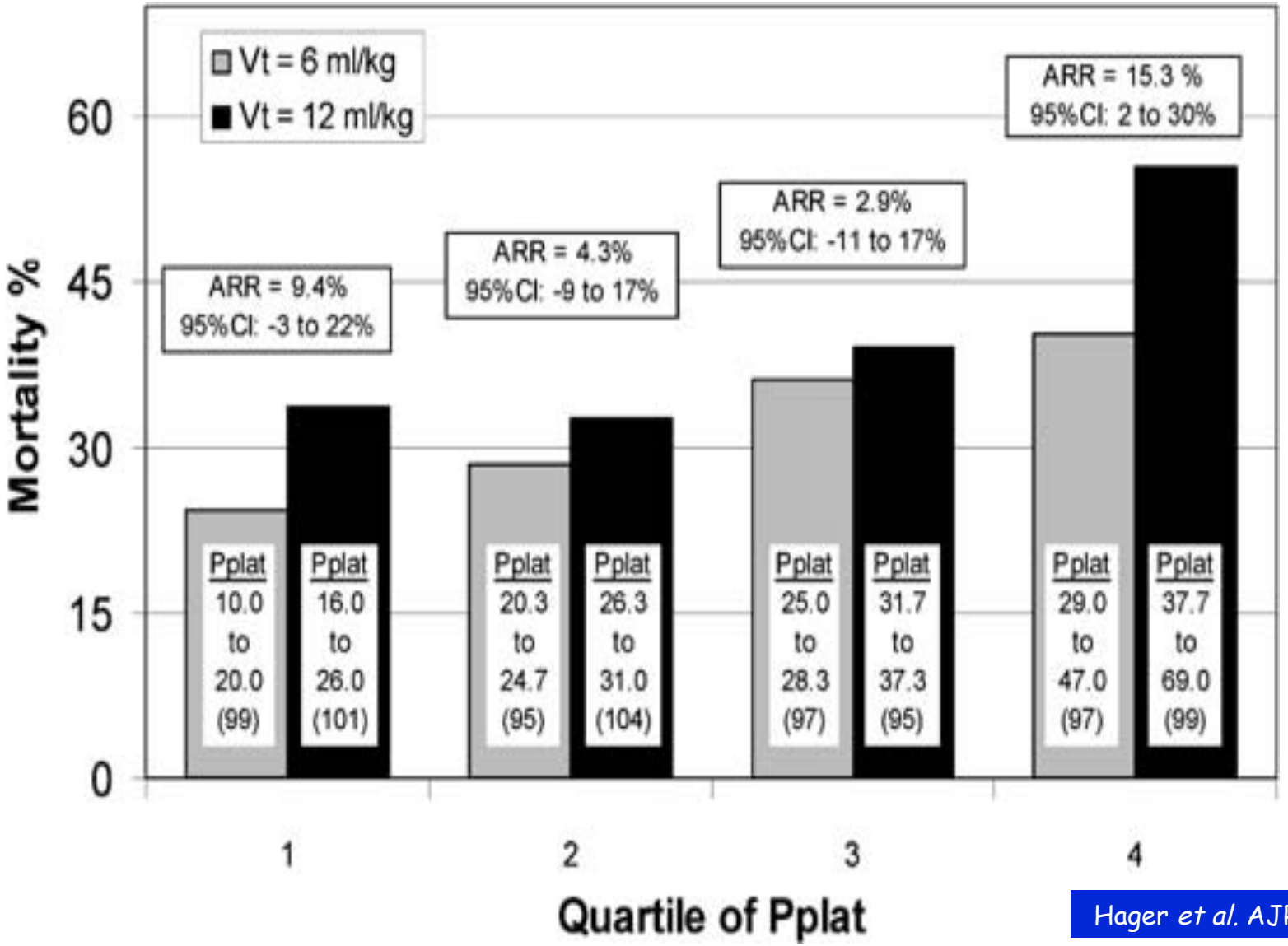


Lungsafe study

Tidal volume is higher than 7 ml/kg in 53% of the ARDS patients!



neficial effects

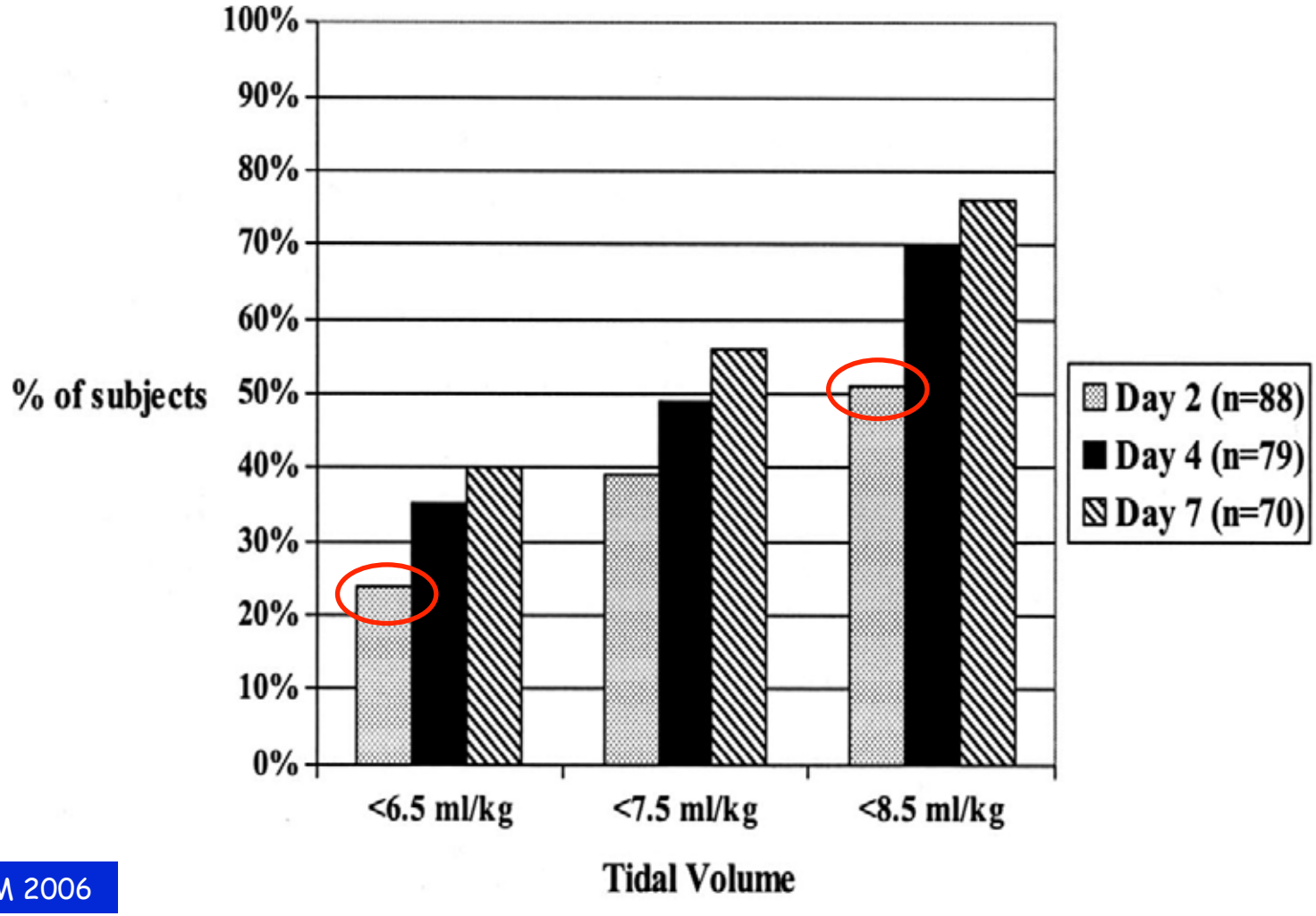


Hager *et al.* AJRCCM 2005

eduction Vt in the real life…

N = 88 ALI

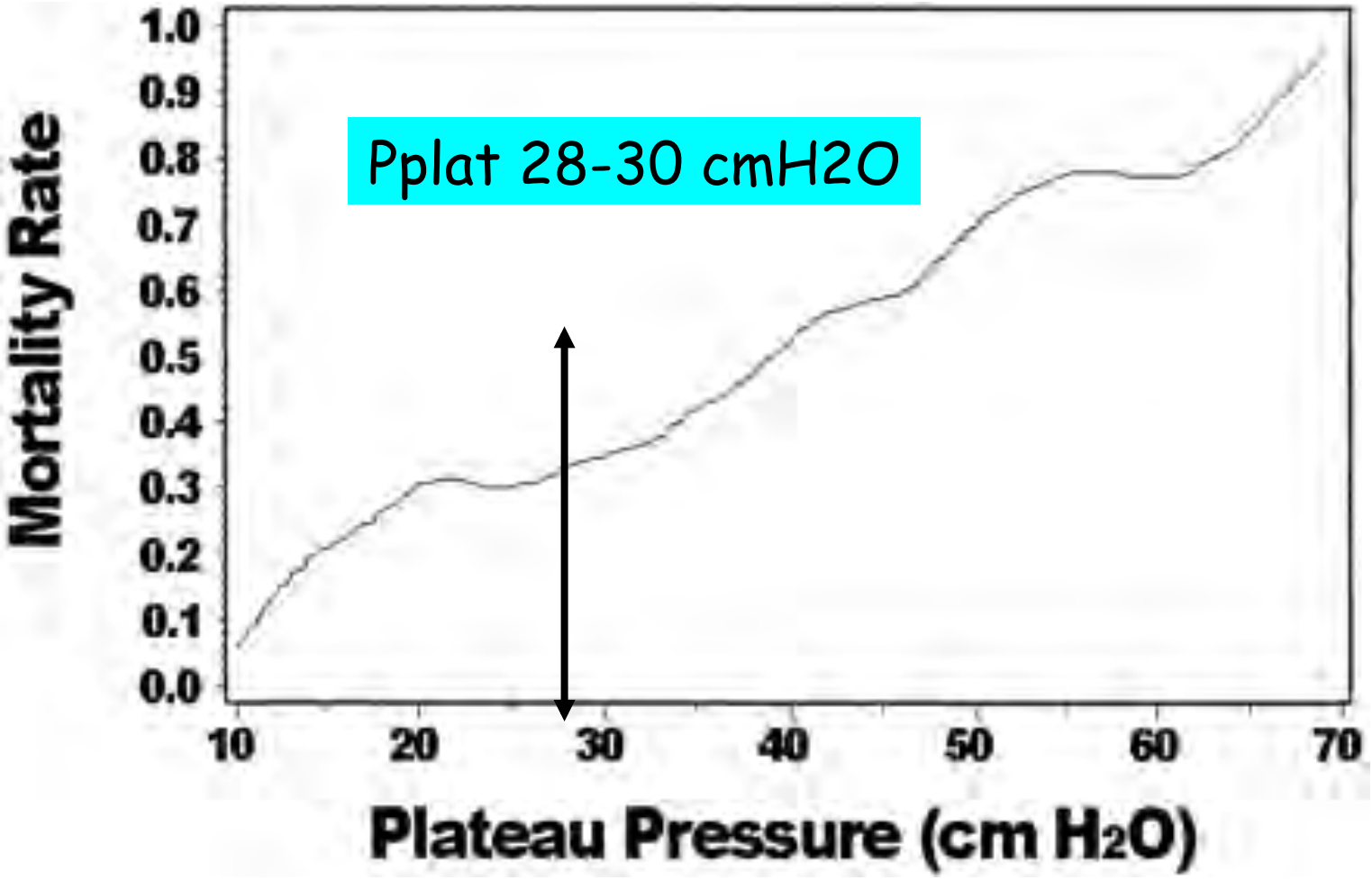
2000-2002



Kalhan *et al.* CCM 2006

Brower et al. AJRCCM 2002

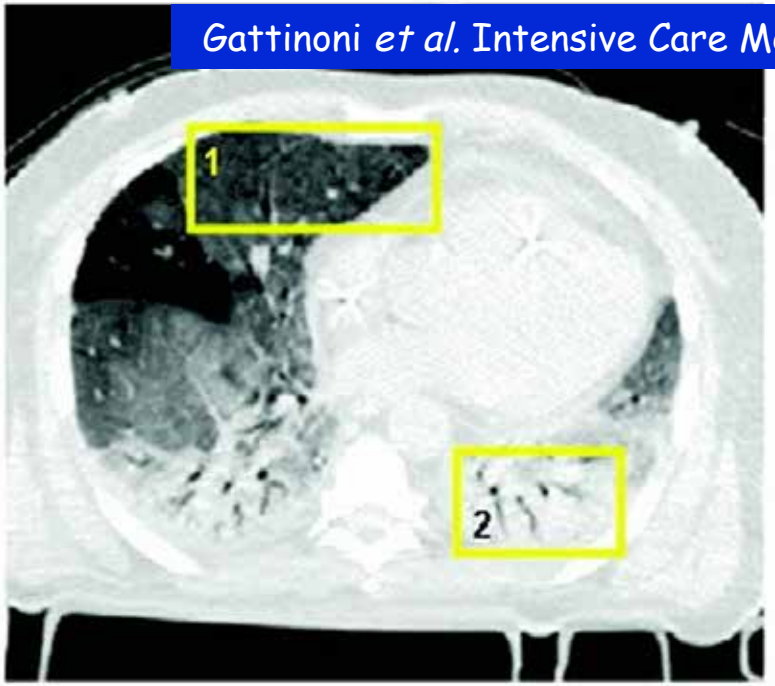
Pplat at D1 – mortality from the ARMA study

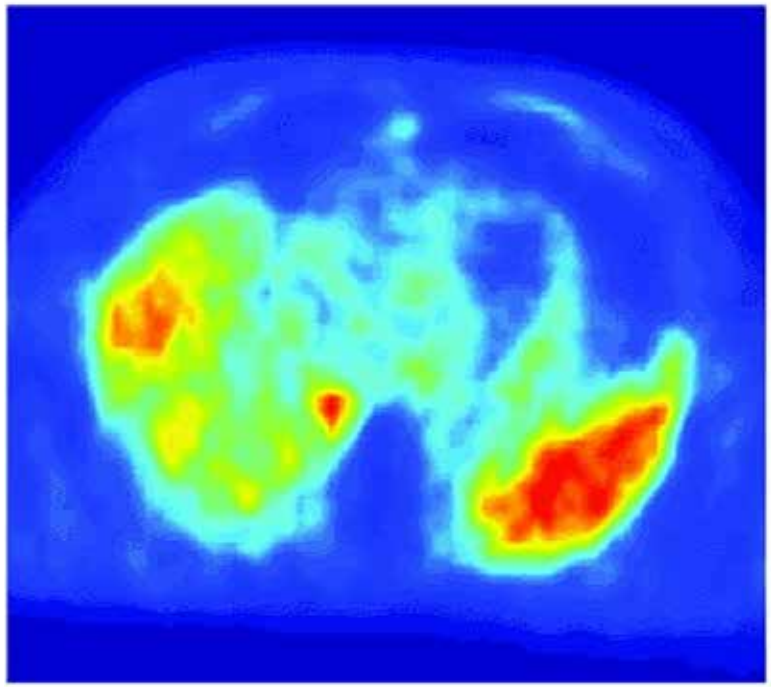


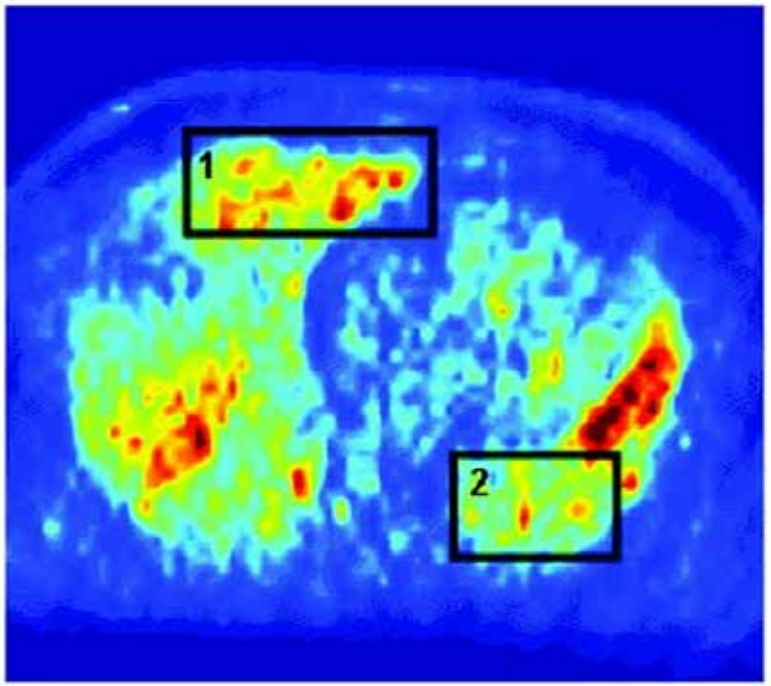

N
ZEEP ↑

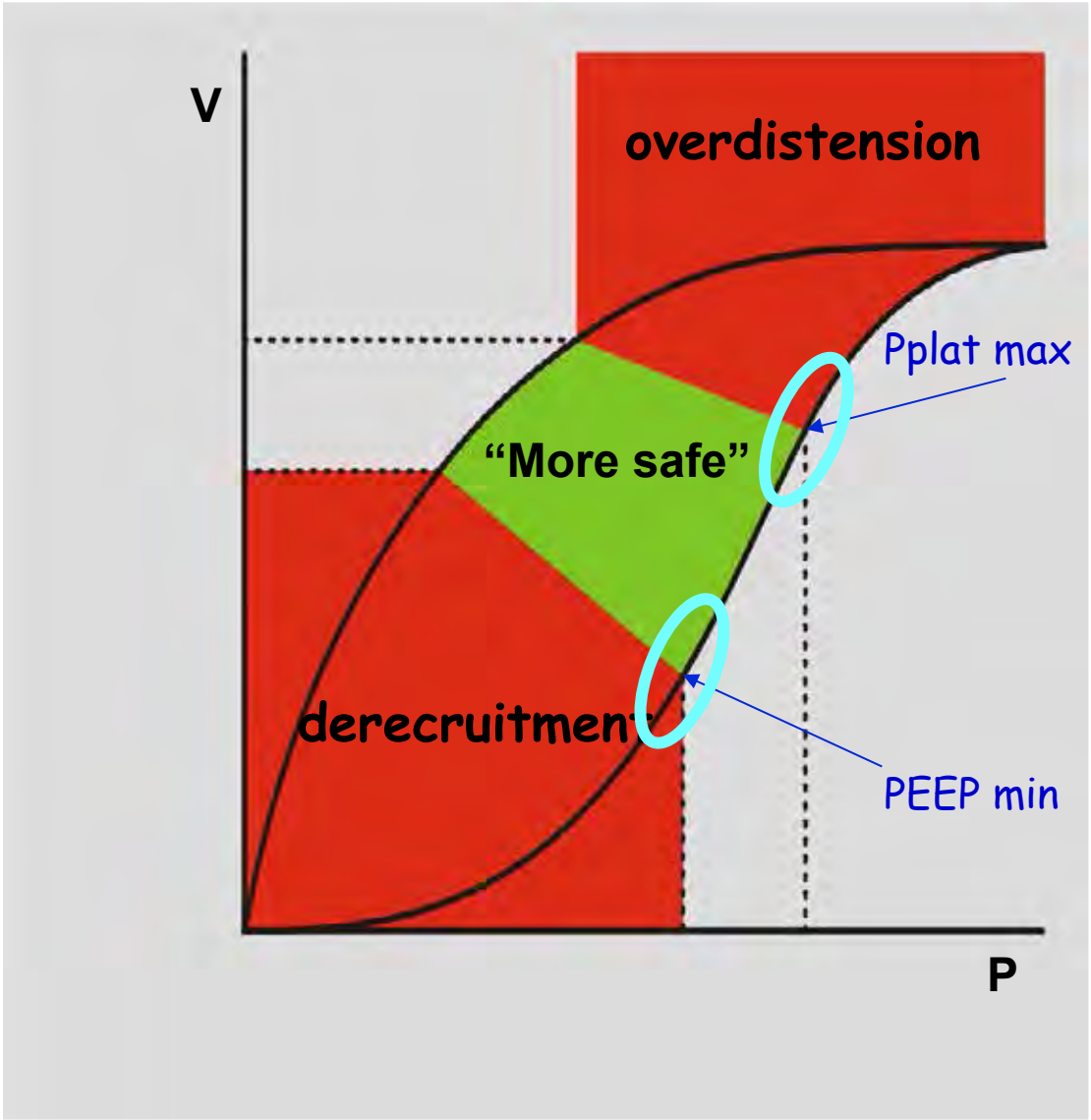

C
ZEEP ↑

Gattinoni *et al.* Intensive Care Medicine 2016



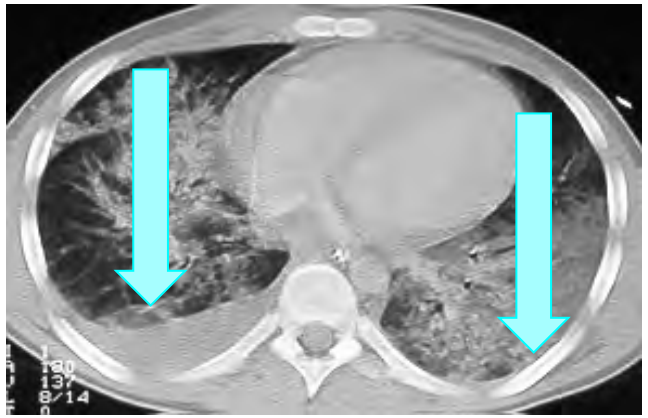





V
overdistension
Pplat max
"More safe"
derecruitment
PEEP min
P

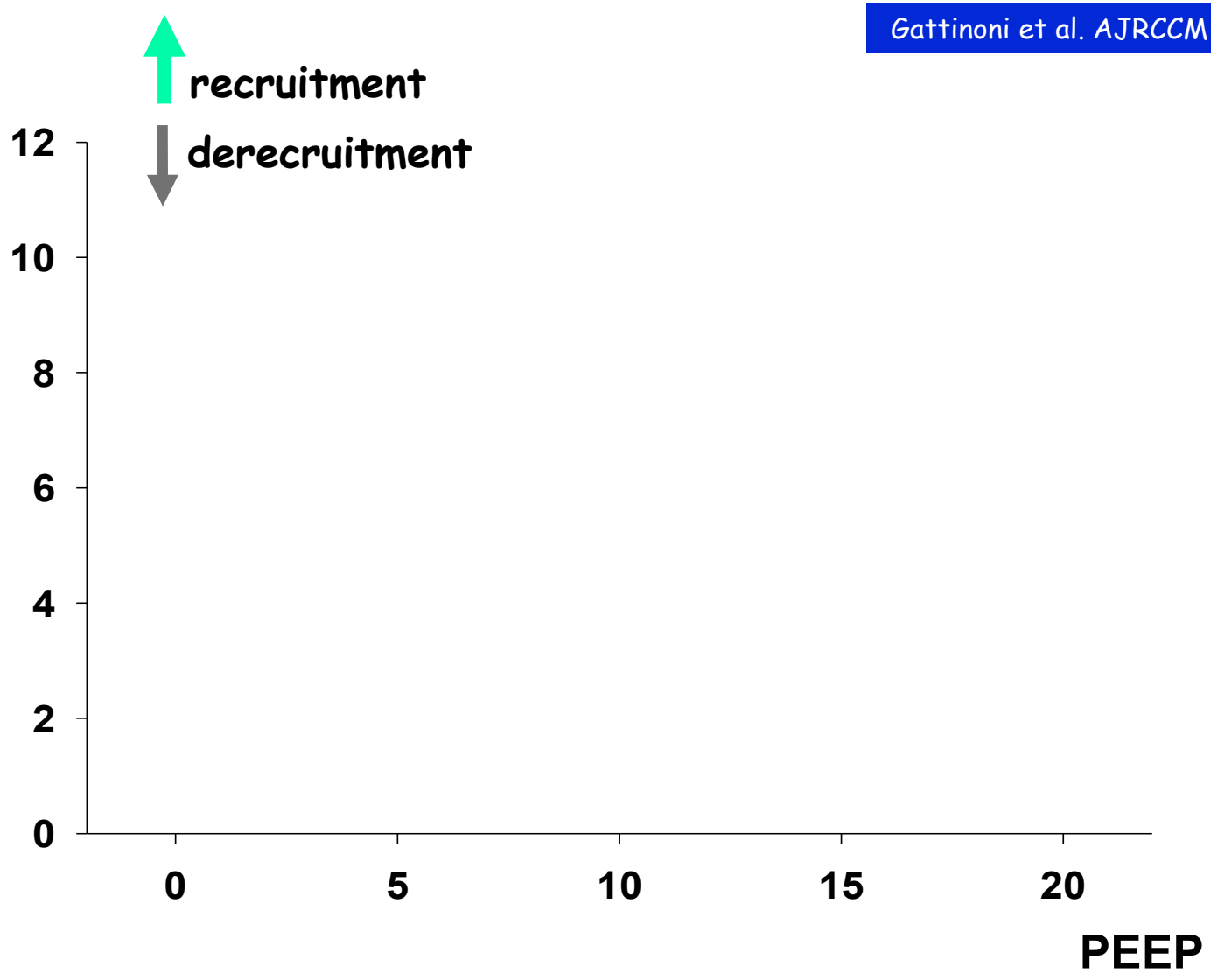
distribution and PEEP

Gattinoni et al. AJRCCM 95



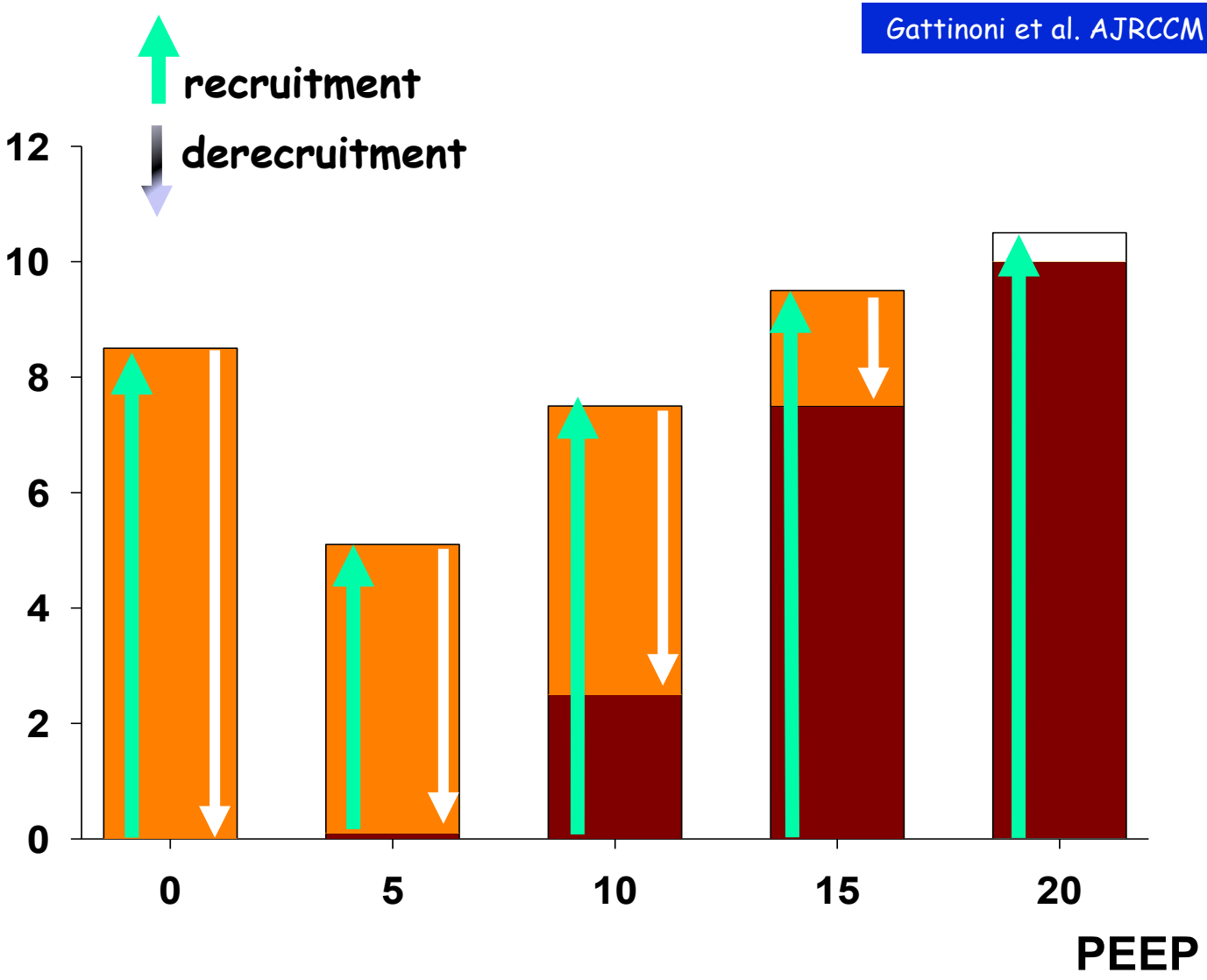
/t, PEEP and recruitment

Gattinoni et al. AJRCCM 95

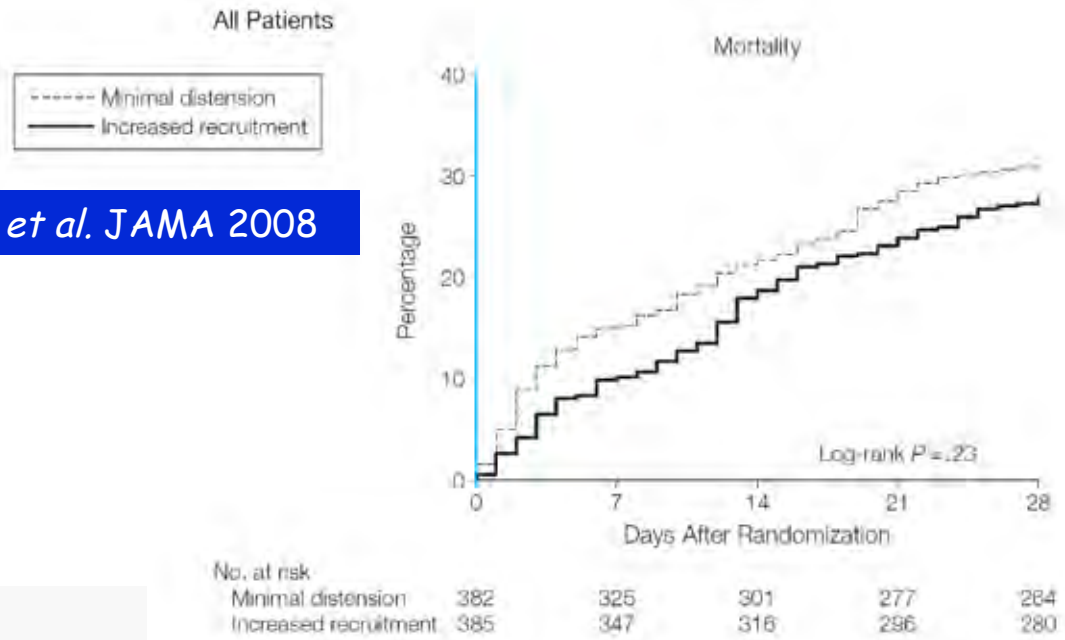


/t, PEEP and recruitment

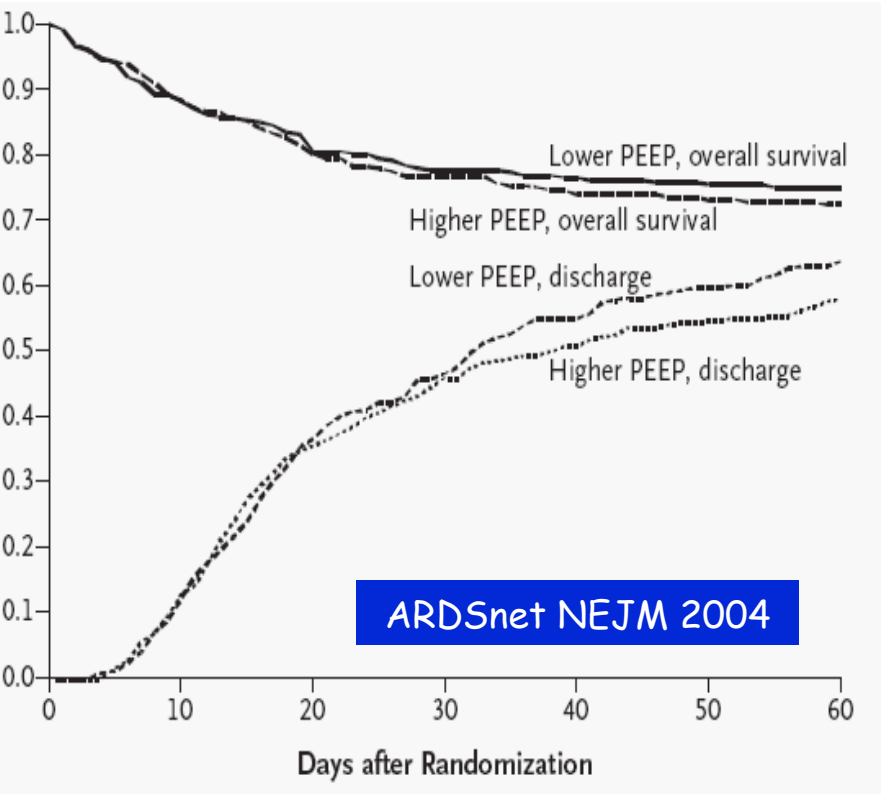
Gattinoni et al. AJRCCM 95



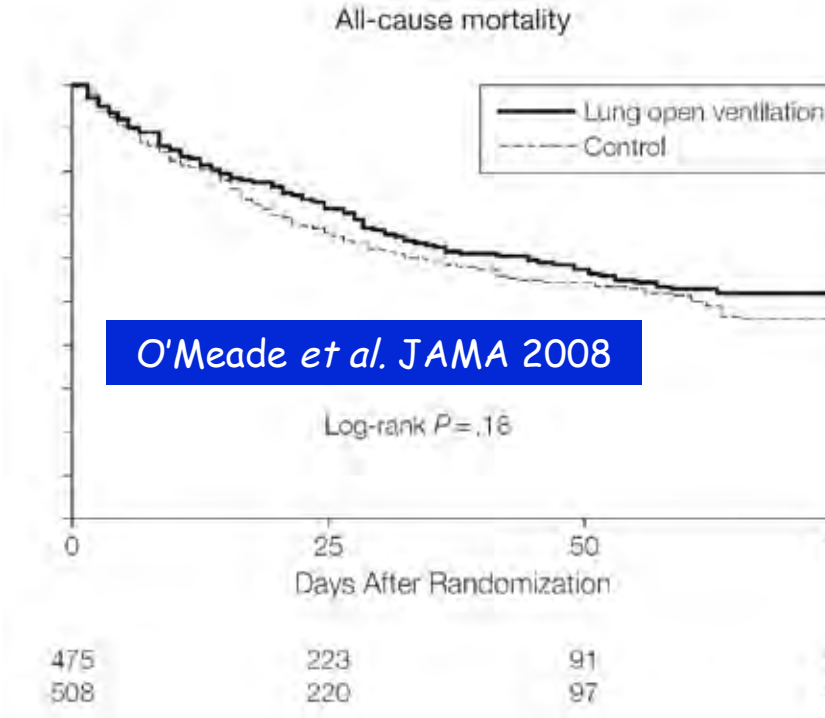
gh/Low PEEP



Mercat *et al.* JAMA 2008



ARDSnet NEJM 2004



O'Meade *et al.* JAMA 2008

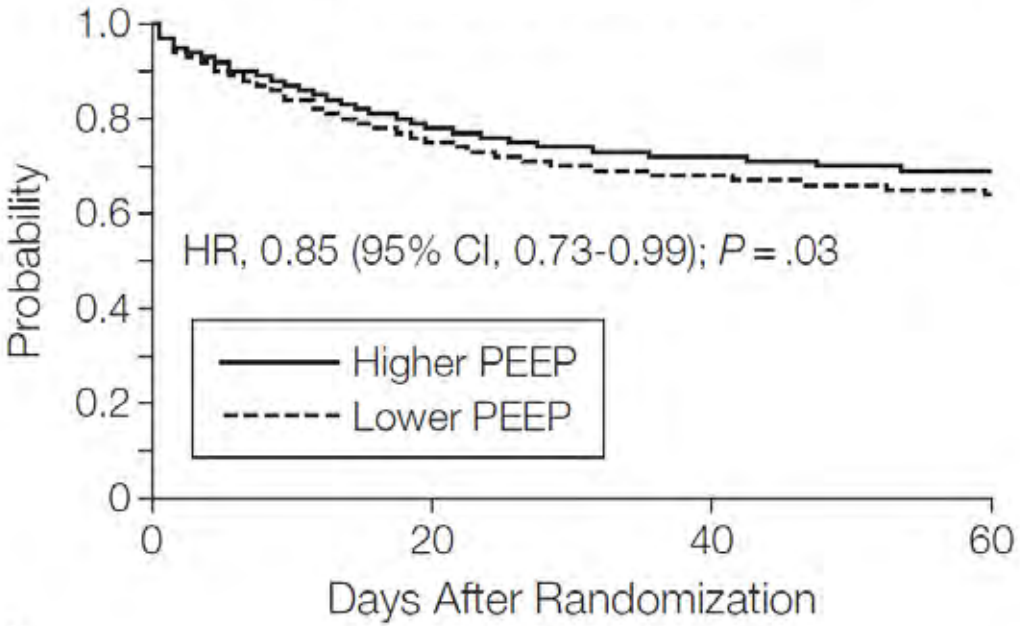
er vs Lower Positive End-Expiratory Pressure tients With Acute Lung Injury Acute Respiratory Distress Syndrome

matic Review and Meta-analysis

Briel *et al.* JAMA 2010

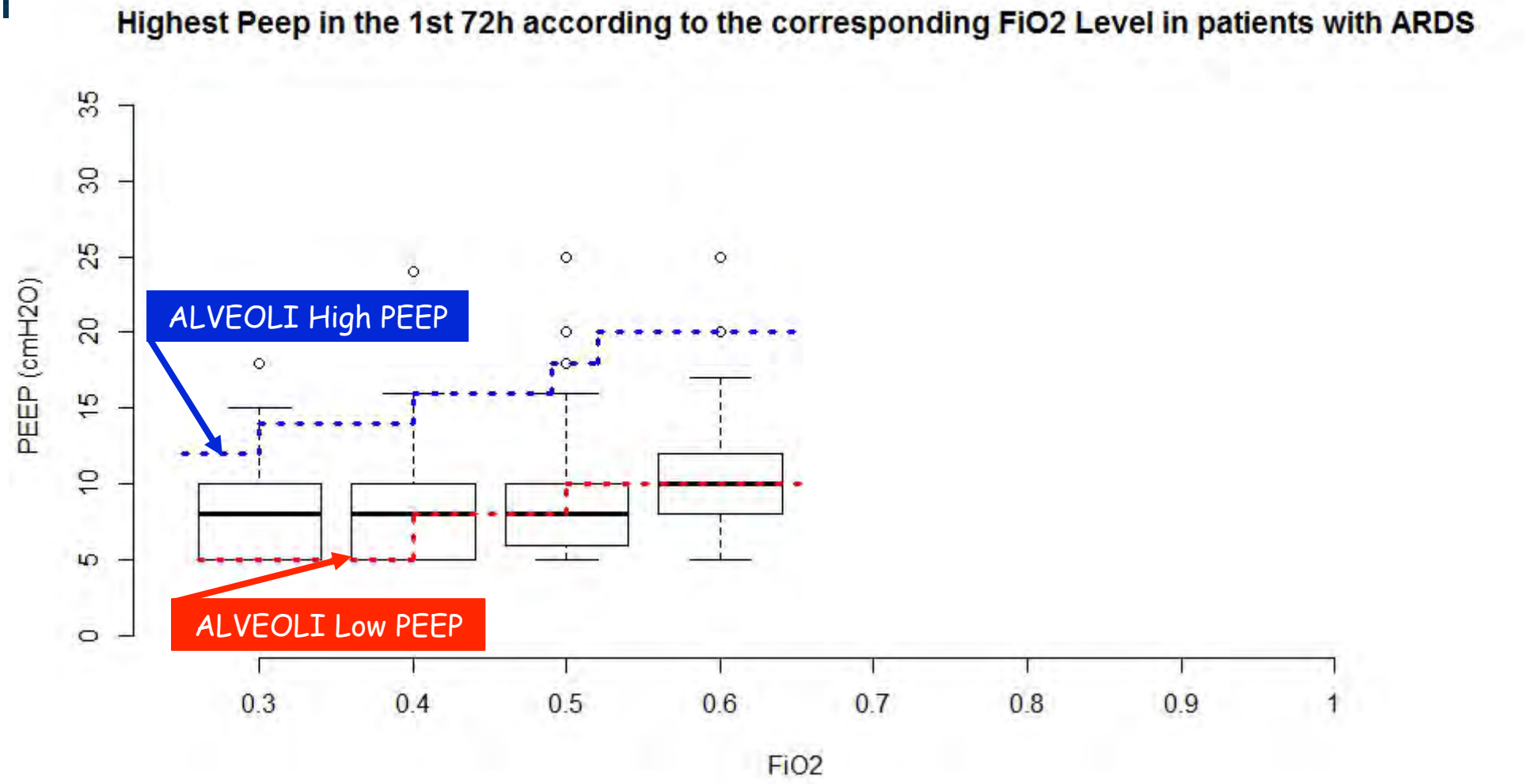
In-hospital time to death

Moderate or severe ARDS



o. at risk								
Higher PEEP	949	760	693	666	183	158	148	144
Lower PEEP	939	723	649	619	219	196	186	183

PEEP versus FiO_2



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			

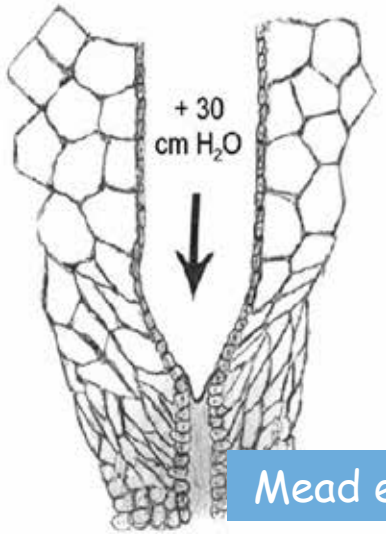
	Fraction of Inspired Oxygen (FIO_2)							
	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0
Control PEEP ranges, cm H_2O	5	5-8	8-10	10	10-14	14	14-18	18-24
Lung open ventilation PEEP ranges, cm H_2O								
Before protocol change	5-10	10-14	14-20	20	20	20	20	20-24
After protocol change	5-10	10-18	18-20	20	20	20-22	22	22-24

PEEP[b]	
Minimal distension group[c]	Total PEEP between 5 and 9 cm H_2O
Increased recruitment group[d]	Plateau pressure between 28 and 30 cm H_2O

EN-DAY PROFILE PUBLICATION

ening pressures and atelectrauma acute respiratory distress syndrome

no Cressoni[1], Davide Chiumello[2,3], Ilaria Algieri[1], Matteo Brioni[3], Chiara Chiurazzi[1], Andrea Colombo[1], Colombo[4], Francesco Crimella[1], Mariateresa Guanziroli[1], Ivan Tomic[5], Tommaso Tonetti[6], no Luca Vergani[3], Eleonora Carlesso[1], Vladimir Gasparovic[5] and Luciano Gattinoni[6*]



Mead et al. J

High PEEP = decrease lung inhomogeneity and prevention in intratidal collapse and reinflation ?

But negative trials

- High PEEP
- HFOV
- RM

Either the atelectrauma is less important than currently believed or the pressures currently used in the “higher PEEP” protocols are insufficient to prevent its occurrence

Mechanical ventilation at 30 cmH2O of plateau pressure and 15 cmH2O of PEEP “opens the lung and keeps it open” ?

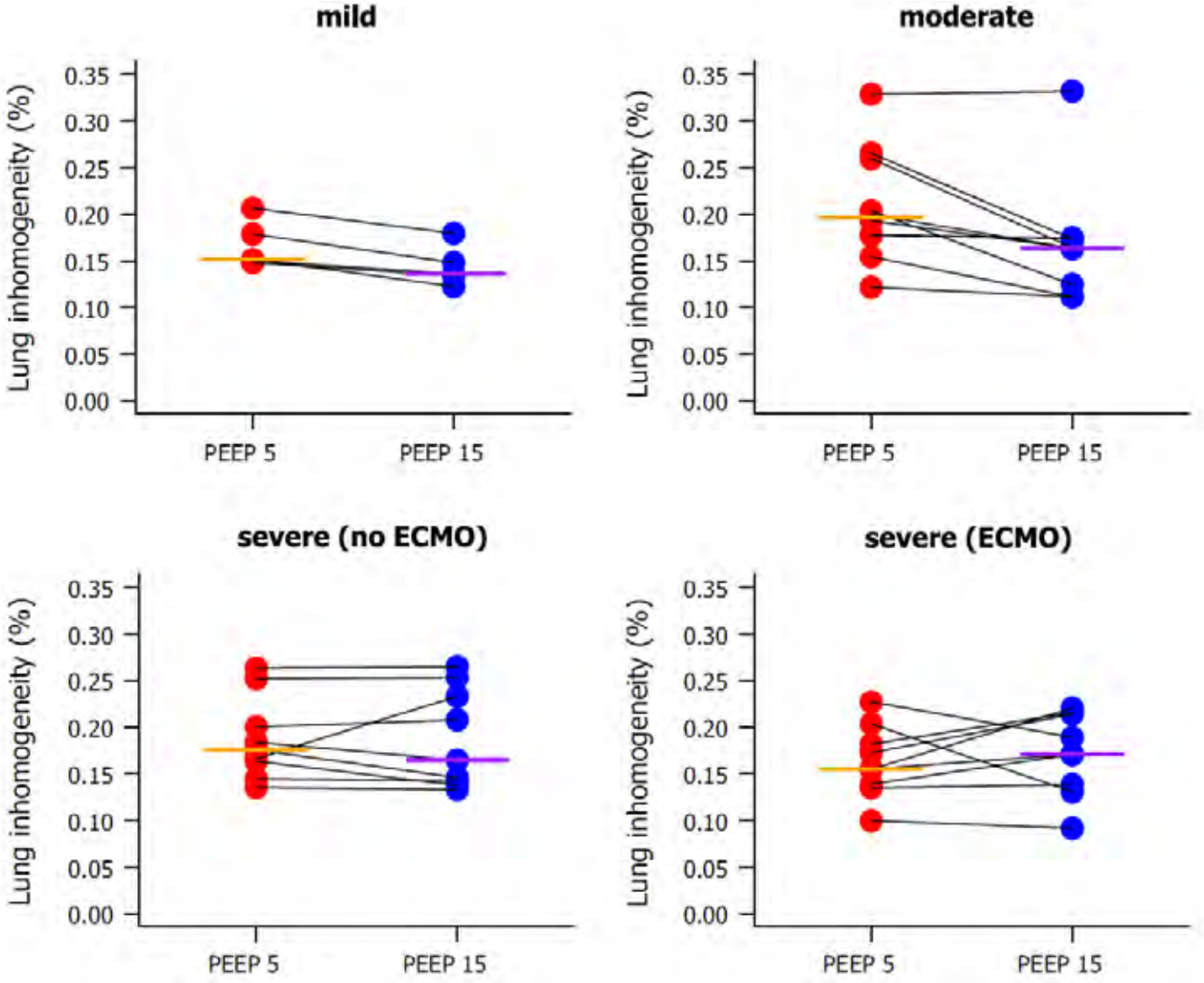
	Mild ($n = 5$)	Moderate ($n = 10$)	Severe No ECMO ($n = 9$)	Severe With ECMO ($n = 9$)	p value
e (years)	59 ± 24	49 ± 12	59 ± 17	57 ± 12	0.45
nale, *n* (%)	2 (40%)	4 (40%)	2 (22%)	2 (22%)	0.77
dy mass index (kg/m^2)	27 ± 9	26 ± 6	28 ± 9	26 ± 3	0.91
al volume/ideal body weight (ml/kg IBW)[b]	7.8 (1)	7.8 (1.2)	8.4 (1.5)	4.8 (1.4)*†‡	<0.0001
nute ventilation (l/min)[a]	8 ± 1	9 ± 2	10 ± 2	4 ± 1*†‡	<0.0001
piratory rate (breaths/min)[a]	15 ± 2	18 ± 4	18 ± 4	11 ± 2†‡	<0.001
EP (cmH_2O)[a]	11 ± 2	10 ± 4	12 ± 3	14 ± 4†	0.04
use of ARDS					
neumonia	0 (0%)	0 (0%)	6 (67%)	9 (100%)	<0.0001
epsis	3 (60%)	7 (70%)	2 (22%)	0 (0%)	<0.01
auma	1 (20%)	1 (10%)	0 (0%)	0 (0%)	0.37
spiration	0 (0%)	0 (0%)	1 (11%)	0 (0%)	0.43
ther	1 (20%)	2 (20%)	0 (0%)	0 (0%)	0.27

he intratidal collapses were similar at PEEP and 15 cmH2O

ams of lung tissue undergoing intratidal collapse and reinflation at PEEP 5 cmH2O and PEEP 15 cmH2O at constant tidal volume

severity	ECMO	Number of patients	Collapse/reinflation grams of tissue (% of lung weight)		p
			PEEP 5 cmH_2O	PEEP 15 cmH_2O	
	–	5	63 ± 26 (5 ± 2.1%)	39 ± 32 (3.2 ± 2.6%)	0
rate	–	10	92 ± 53 (6.2 ± 3.6%)	78 ± 142 (5.3 ± 9.6%)	0
e	No	9	110 ± 91 (6 ± 5%)	89 ± 93 (5 ± 5%)	0
	Yes	9	135 ± 100 (7 ± 5%)	104 ± 80 (5 ± 4%)	0

ung inhomogeneities and PEEP



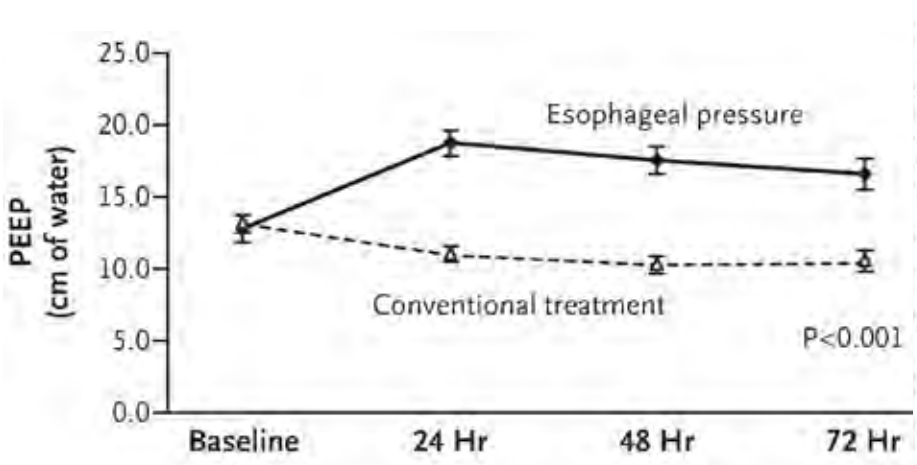
Δ PEEP et Δ P trans-pulmonaire

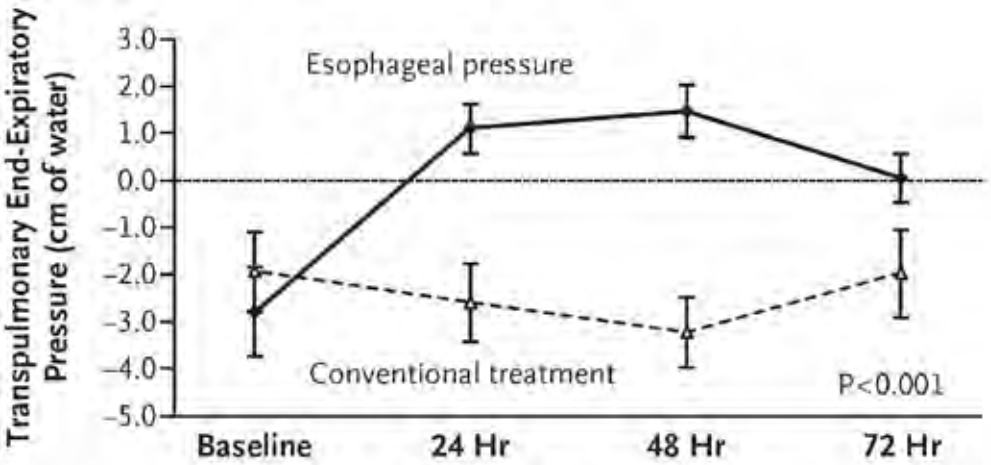
Talmor *et al.* NEJM 2008

- **Standardisation durant 3 jours**

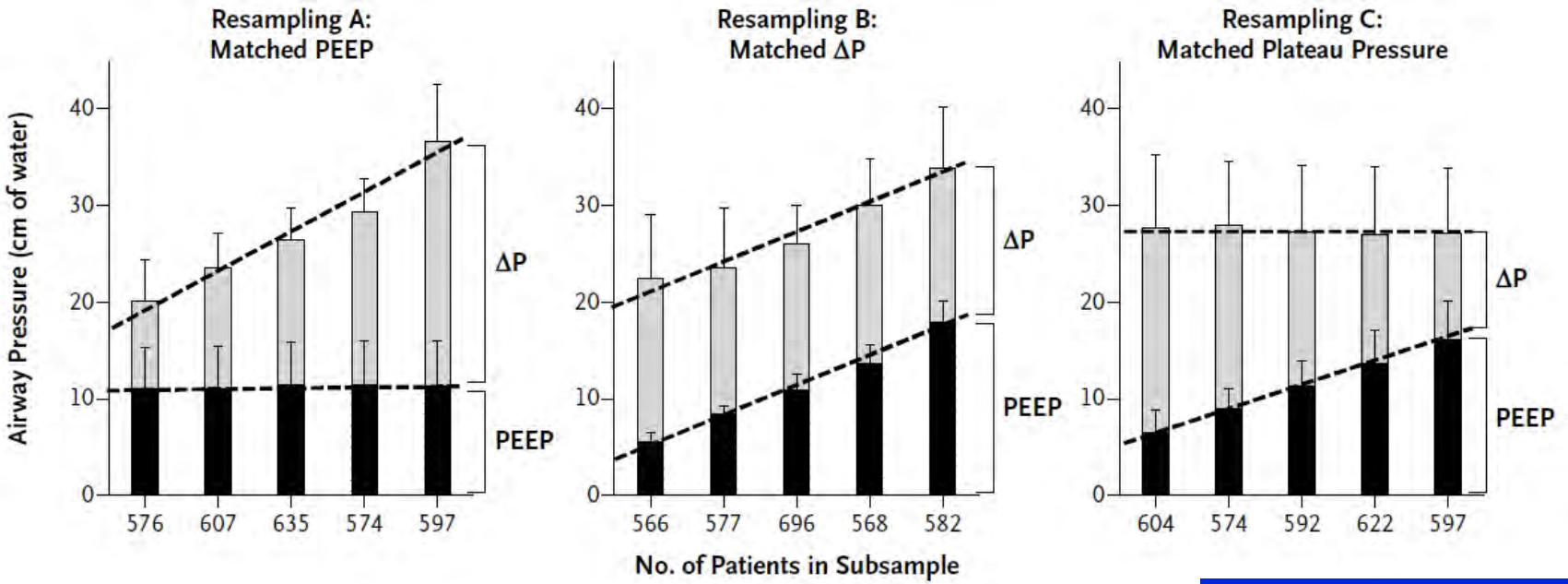
The primary end point of the study was arterial oxygenation, as measured by the ratio of PaO_2 to FiO_2 (PaO_2:FiO_2) 72 hours after randomization.

Esophageal-Pressure–Guided Group												
FiO_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
Control 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	20–24

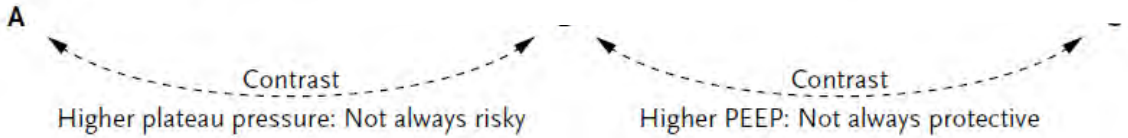




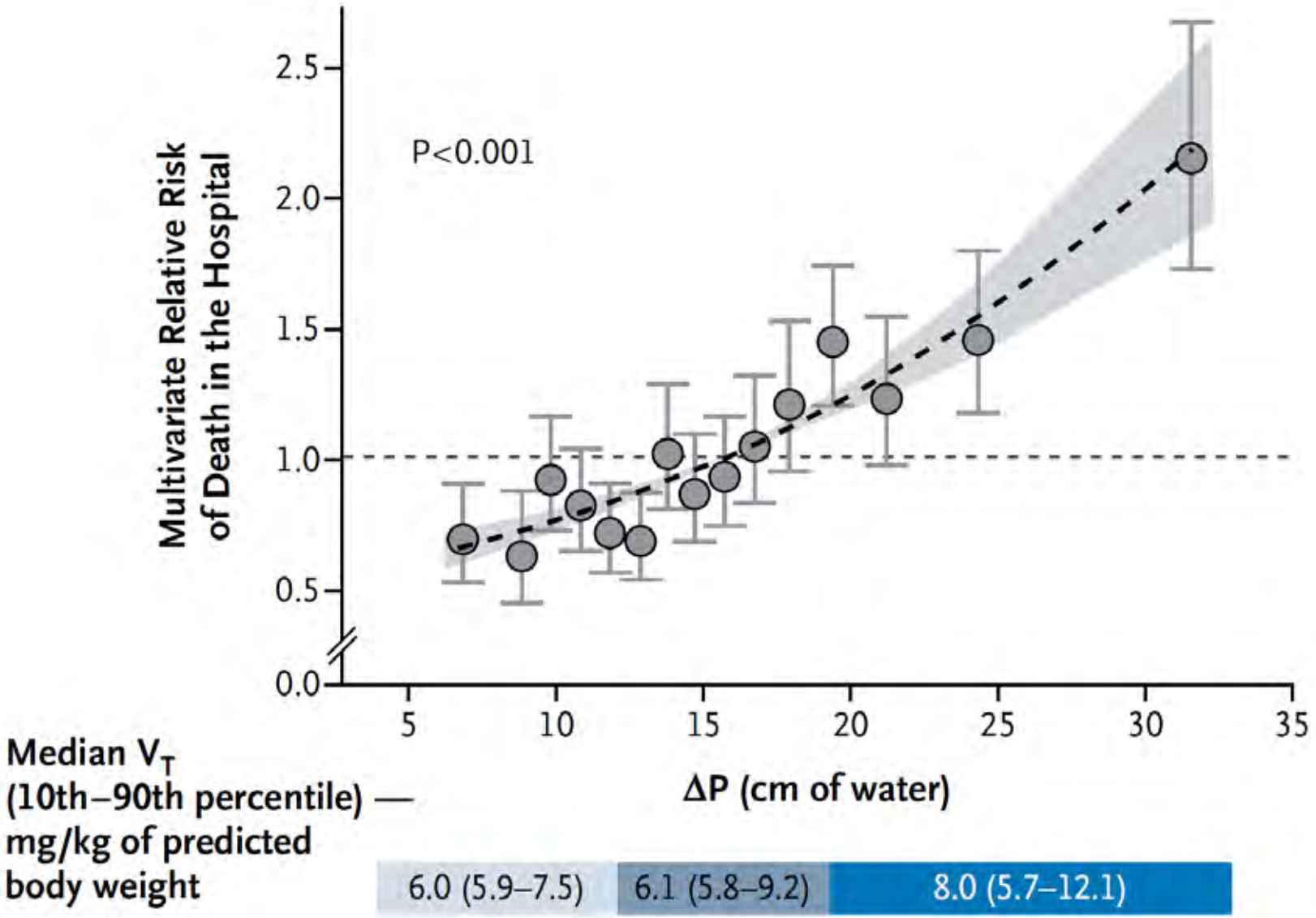
Treatment Group	Change in PEEP				
	−1 to −6 cm of Water	0 to 5 cm of Water	6 to 10 cm of Water	11 to 15 cm of Water	16 to 20 cm of Water
			no. of patients		
Esophageal-pressure–guided group	3	9	12	4	2
Control group	12	18	1	0	0



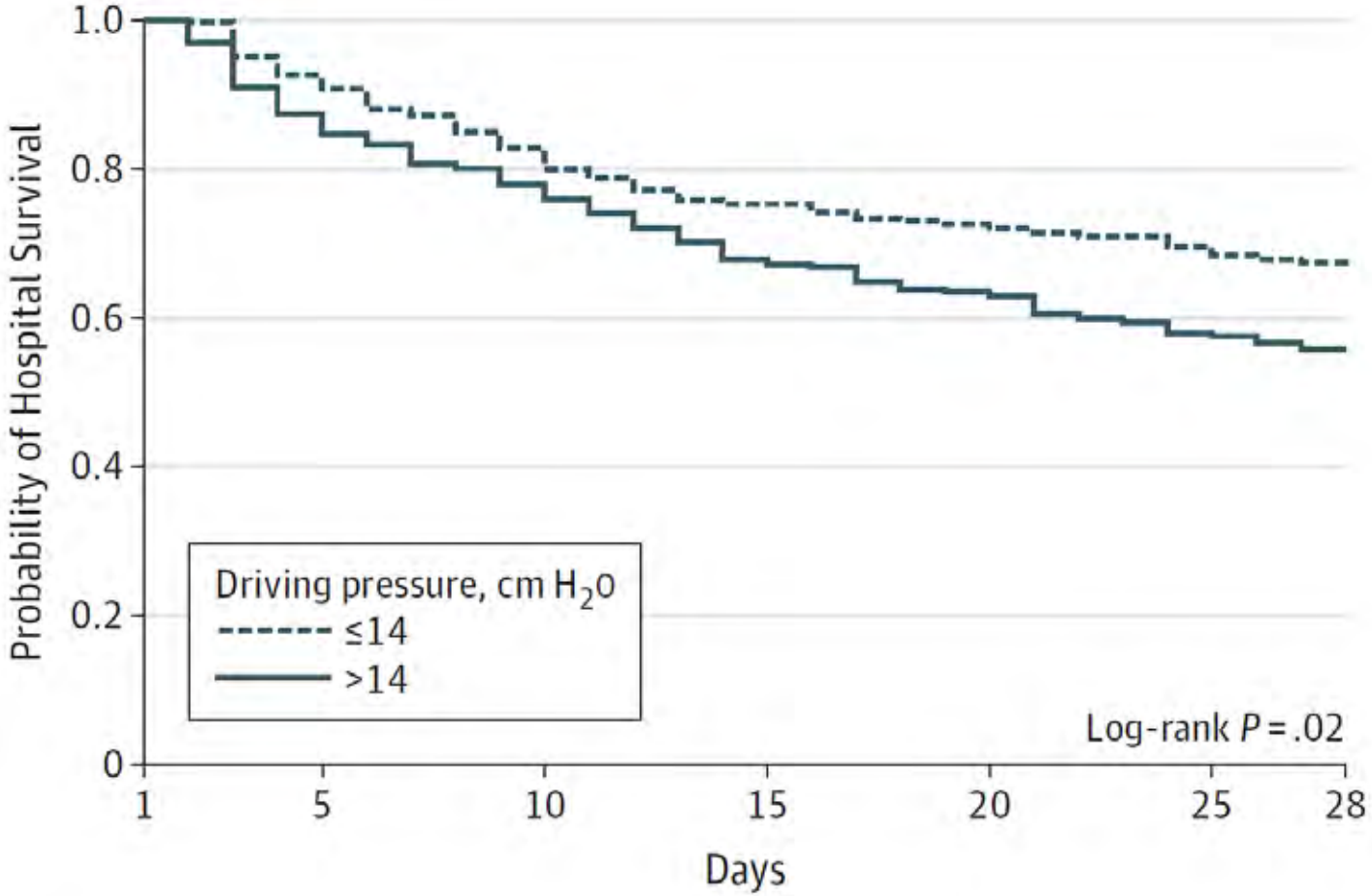
Amato *et al.* NEJM 2015



Amato *et al.* NEJM 2015



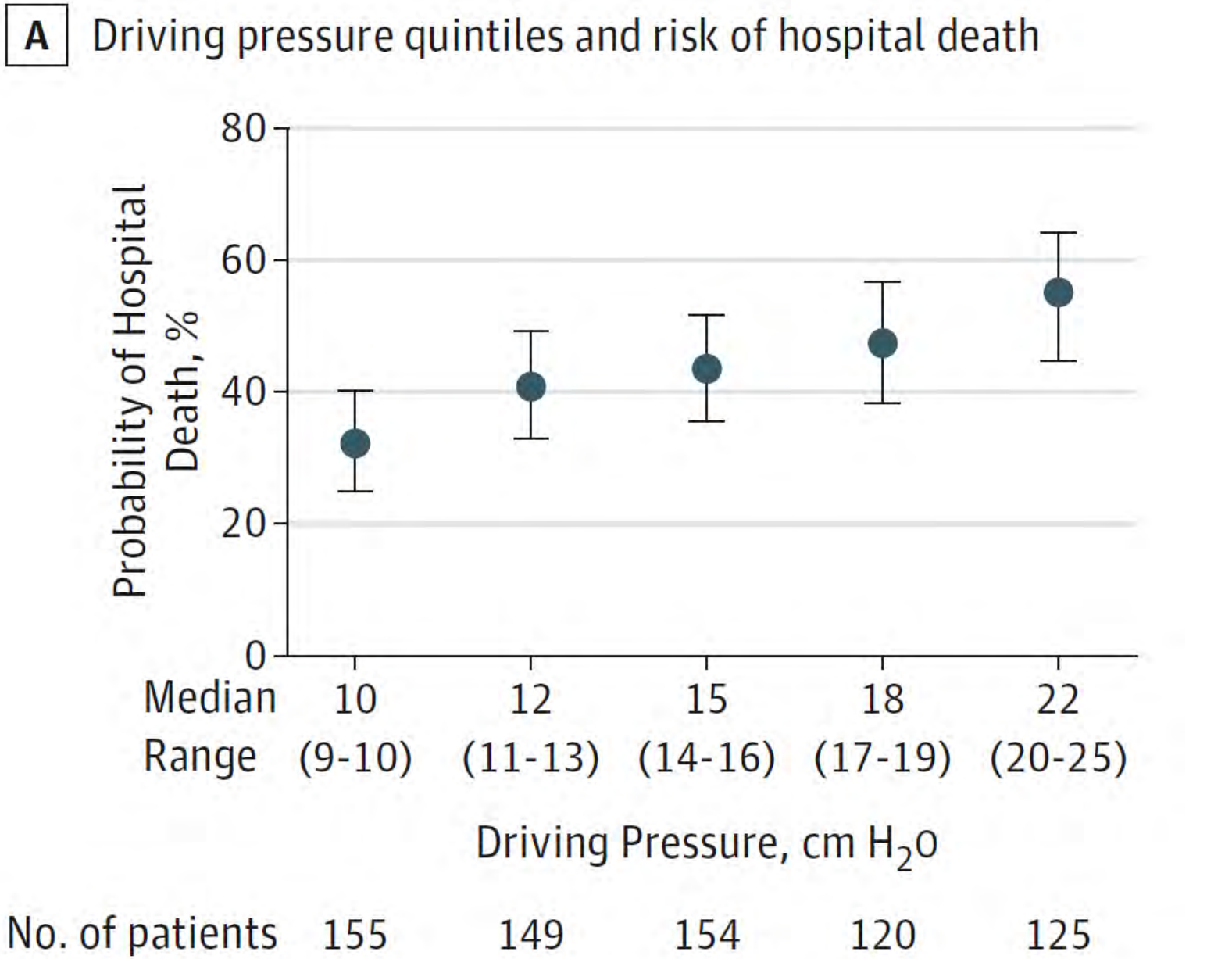
Bellani *et al.* JAMA 2016

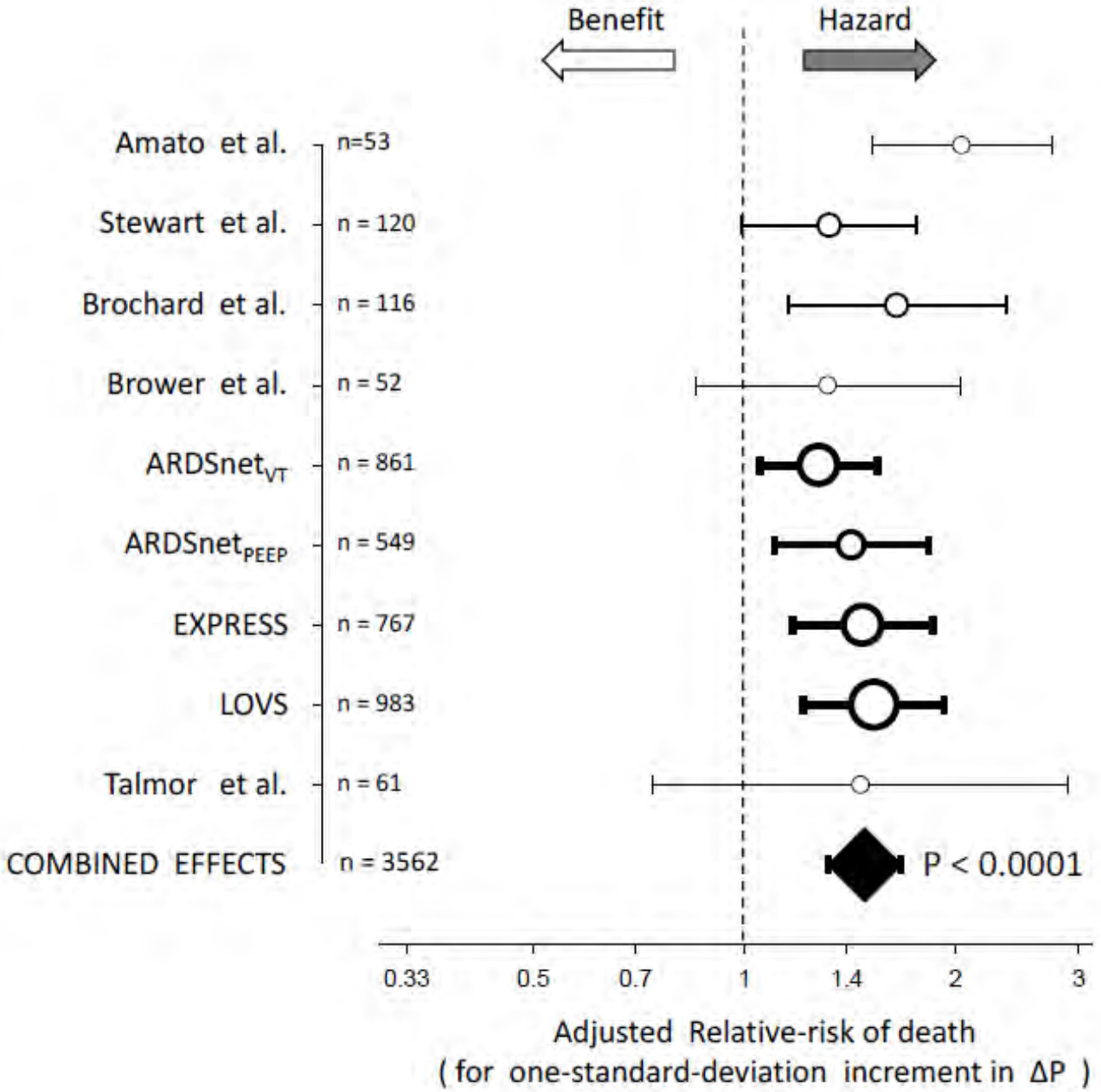


No. at risk

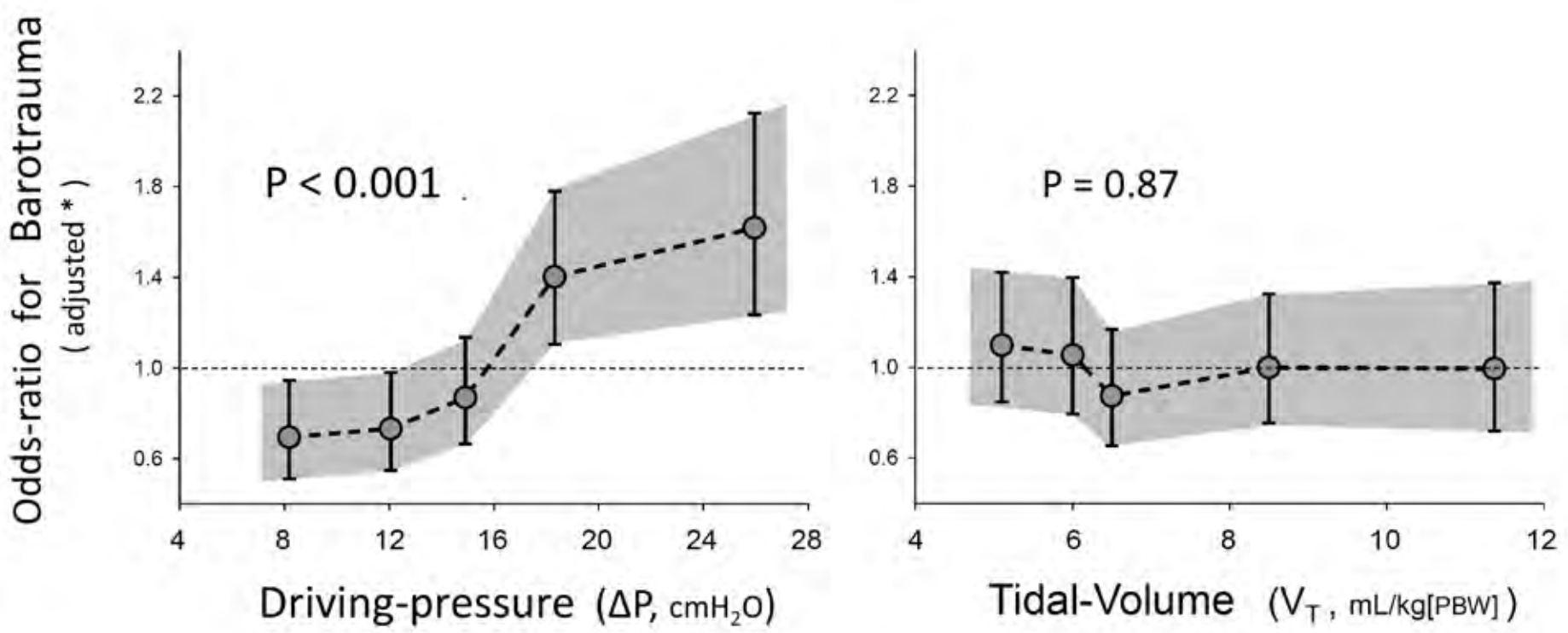
Driving pressure, cm H_2O							
≤14	370	342	306	277	266	254	245
>14	342	298	262	225	211	192	185

Bellani *et al.* JAMA 2016




Benefit
Hazard
Amato et al.
n=53
Stewart et al.
n = 120
Brochard et al.
n = 116
Brower et al.
n = 52
ARDSnet$_{VT}$
n = 861
ARDSnet$_{PEEP}$
n = 549
EXPRESS
n = 767
LOVS
n = 983
Talmor et al.
n = 61
COMBINED EFFECTS
n = 3562
P < 0.0001
0.33
0.5
0.7
1
1.4
2
3
Adjusted Relative-risk of death
(for one-standard-deviation increment in ΔP)

dds for Barotrauma across quintiles of driving essure or Vt

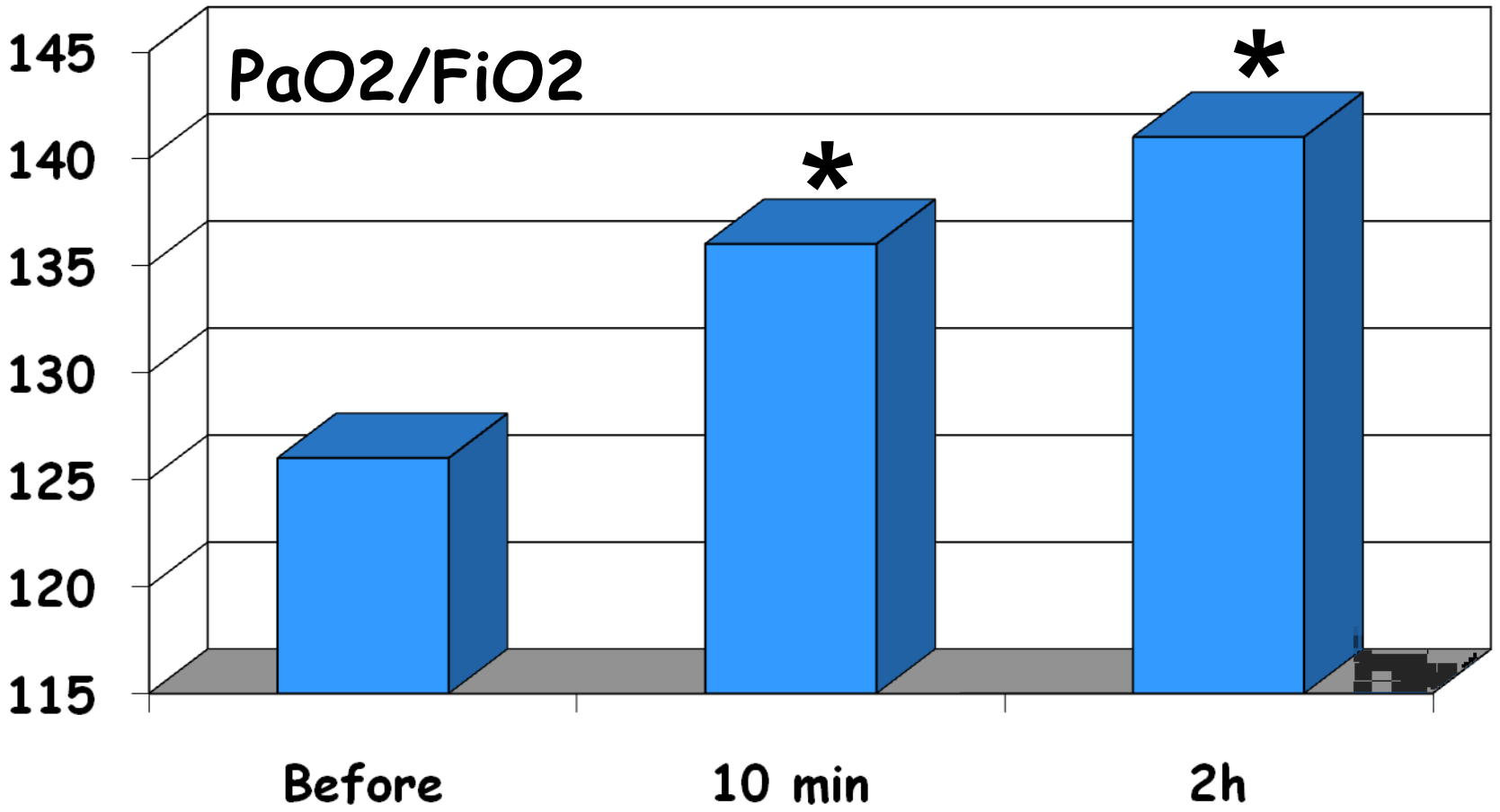


Amato *et al.* NEJM 2015

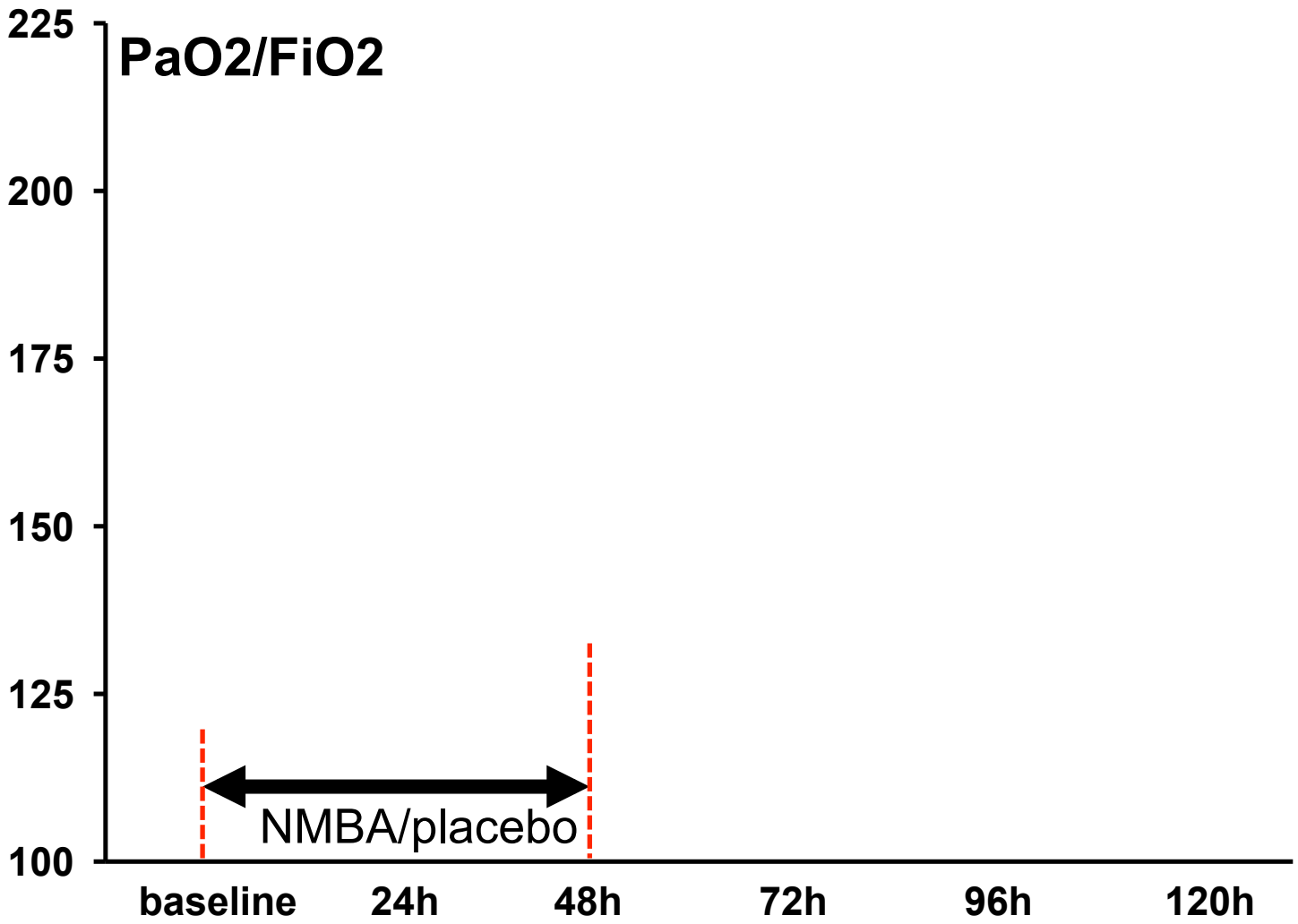
Adjuvants for severe ARDS

ysiological effects of neuromuscular blockers

Lagneau *et al.* ICM 2002



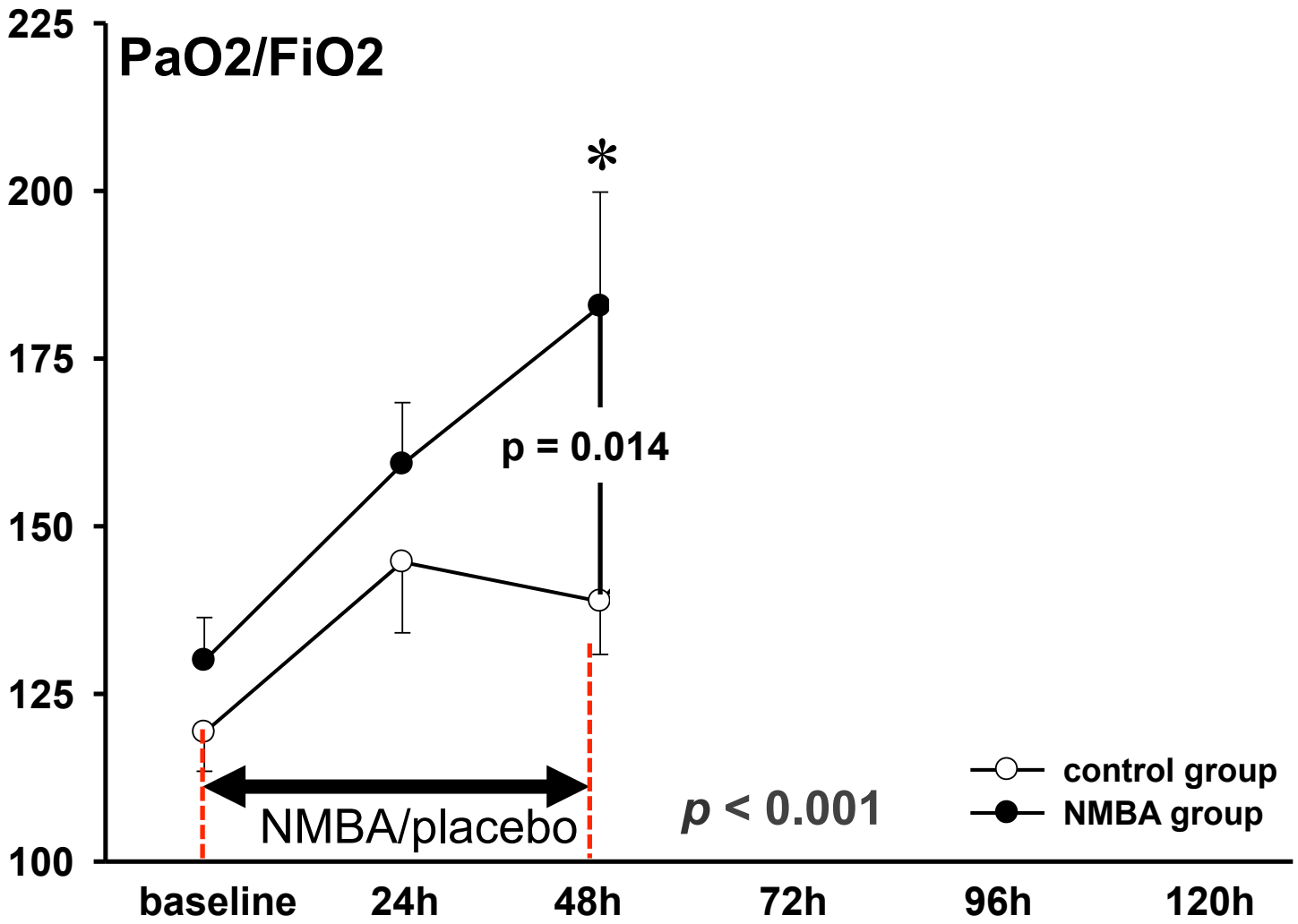
fect of cisatracurium on oxygenation



4 ICUs - 56 patients

Gainnier *et al.* Crit Care Med 2004

fect of cisatracurium on oxygenation



4 ICUs - 56 patients

Gainnier *et al.* Crit Care Med 2

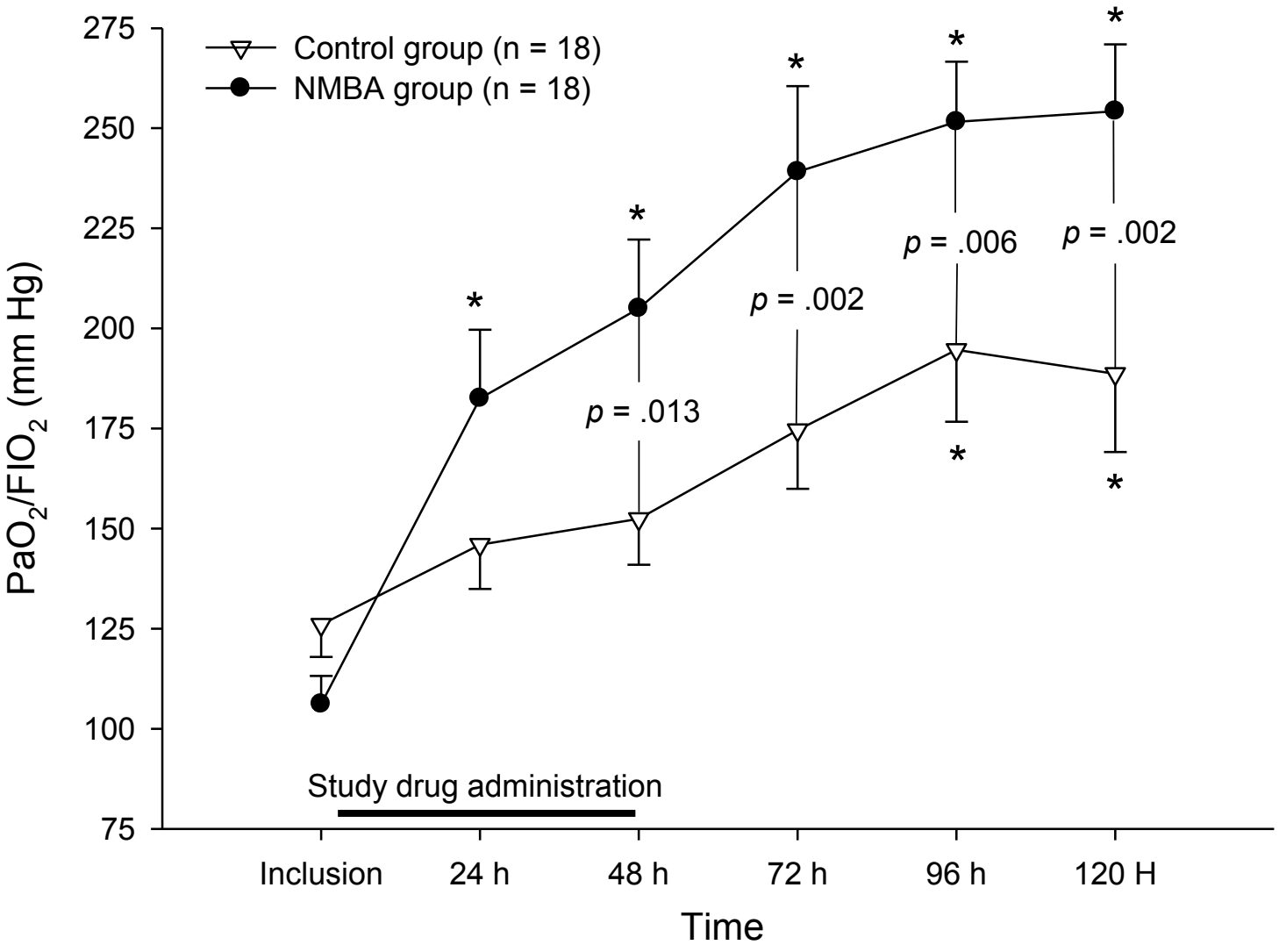
	NMBA Group (n = 28)	Control Group (n = 28)	*p* Value
VFD at day 28, days	3.7 ± 7.2	1.7 ± 5.3	.24
Median (25th–75th percentiles)	0 (0–5)	0 (0–0)	.24
VFD at day 60, days	19.0 ± 20.3	9.8 ± 16.9	.071
Median (25th–75th percentiles)	14 (0–37)	0 (0–18)	.11
Mortality at day 28 after inclusion, n (%)	10 (35.7)	17 (60.7)	.061
Mortality at day 60 after inclusion, n (%)	13 (46.4)	18 (64.3)	.18
ICU mortality, n (%)	13 (46.4)	20 (71.4)	.057

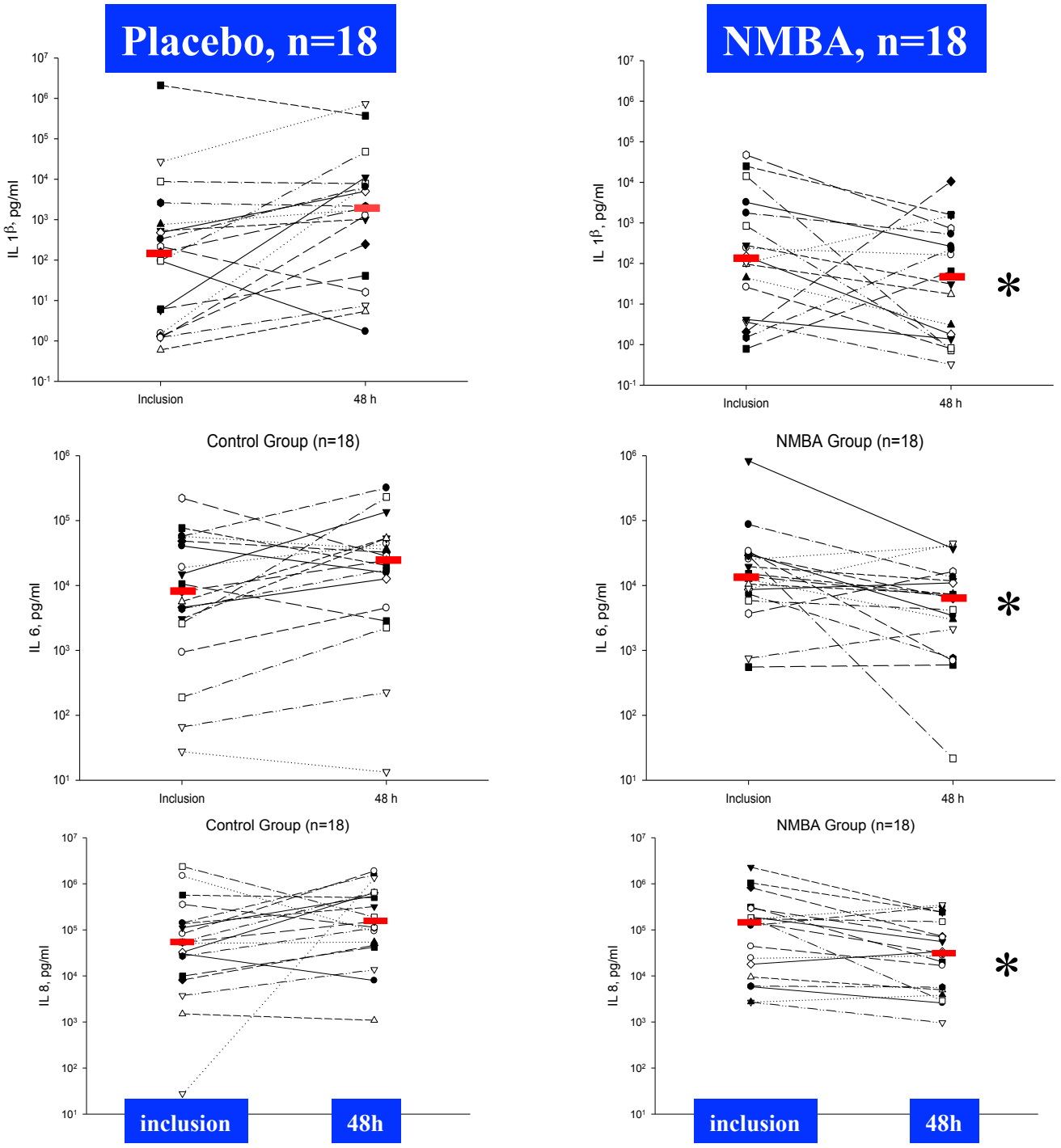
Gainnier *et al.* Crit Care Med 2004

Neuromuscular blocking agents decrease inflammatory response in patients presenting with acute respiratory distress syndrome*

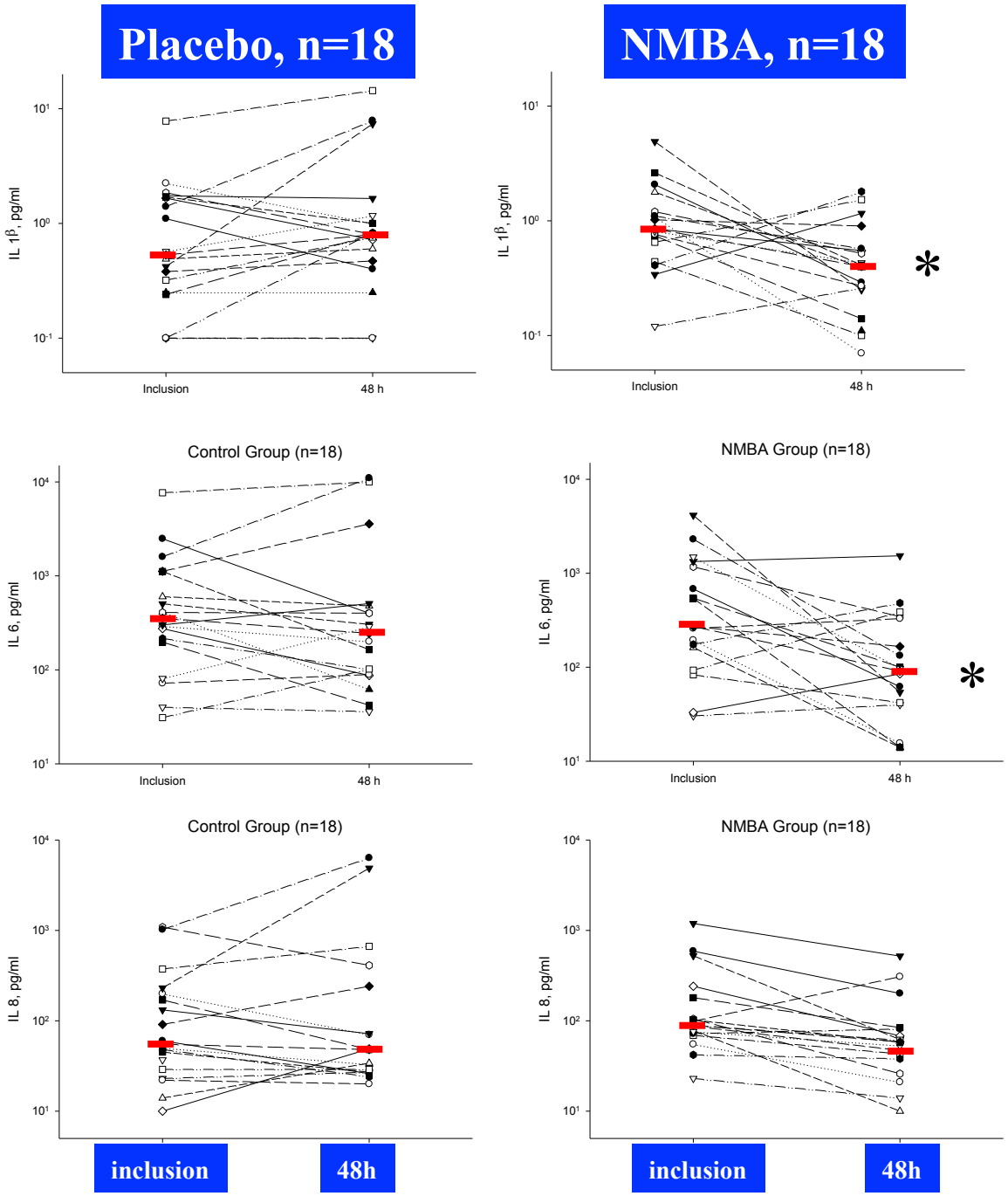
Jean-Marie Forel, MD; Antoine Roch, MD, PhD; Valérie Marin, MD, PhD; Pierre Michelet, MD; Didier Demory, MD; Jean-Louis Blache, MD; Gilles Perrin, MD; Marc Gainnier, MD, PhD; Pierre Bongrand, MD, PhD; Laurent Papazian, MD, PhD

Forel *et al.* CCM 2006




Placebo, n=18
NMBA, n=18
BAL
IL 1β, pg/ml
Inclusion
48 h
*
IL1β
Control Group (n=18)
NMBA Group (n=18)
IL 6, pg/ml
IL6
IL 8, pg/ml
IL8
inclusion
48h
Forel et al. CCM 20

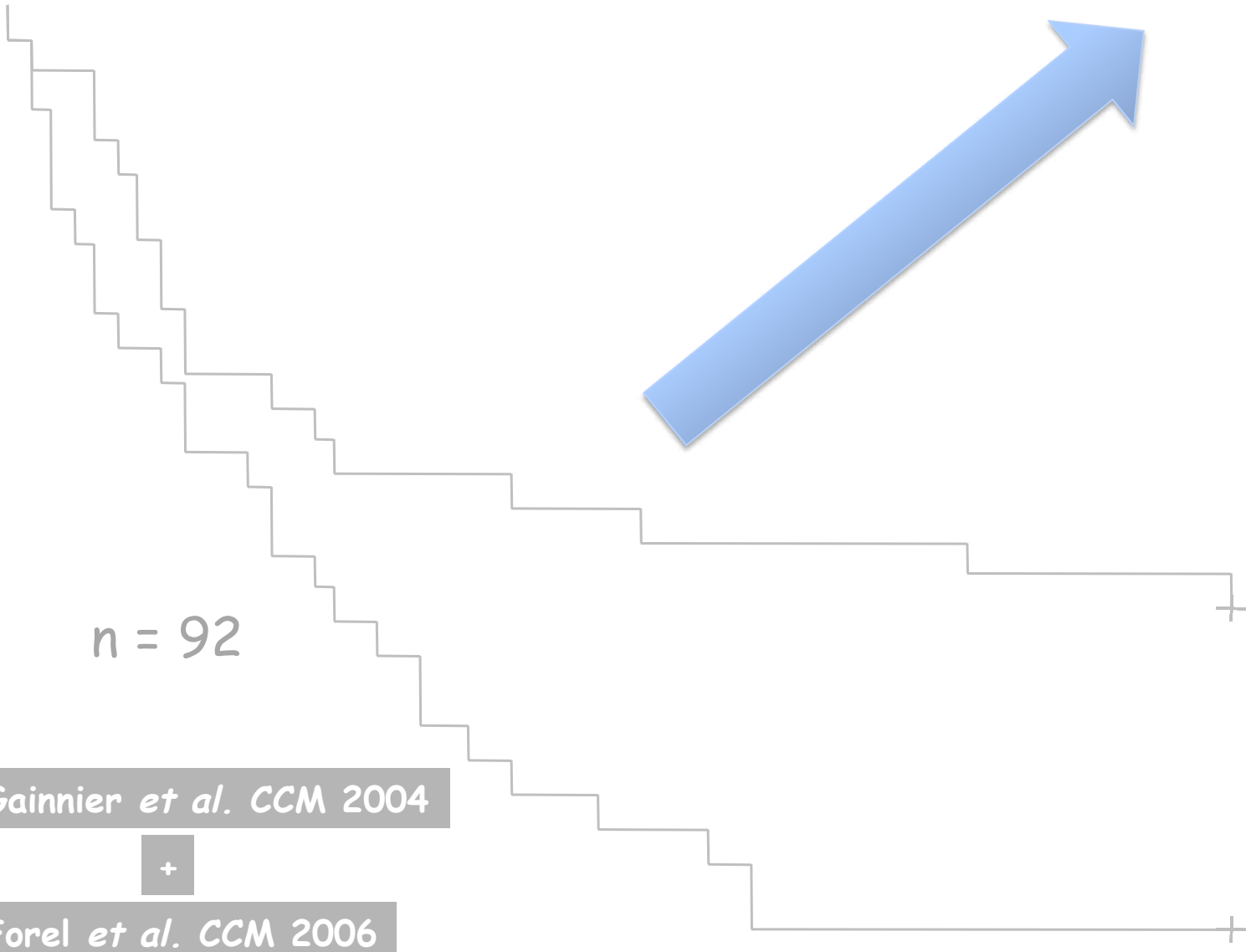
Blood



Forel *et al.* CCM 200

ortality

ACURASYS



n = 92

Gainnier *et al.* CCM 2004

+

Forel *et al.* CCM 2006

Important methodological aspects (1)

- Prospective, randomized, double-blind study

  cisatracurium *vs.* placebo

- Vt 6-8 ml/kg, Pplat ≤ 32 cmH2O

- Inclusion criteria:

  PaO_2:FiO_2 < 150 (PEEP ≥ 5) for < 48 h

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Important methodological aspects (2)

- Prior to infusion : Ramsay 6
- Cisatracurium: 6 x 150 mg / day for 2 days

- Volume-assist control mode
- PEEP and FiO2 according to the ARMA study
- Weaning started on day 3 if FiO2 ≤ 0.6

ACURASYS

ACURASYS

48 hrs

NMBA + → lung protection

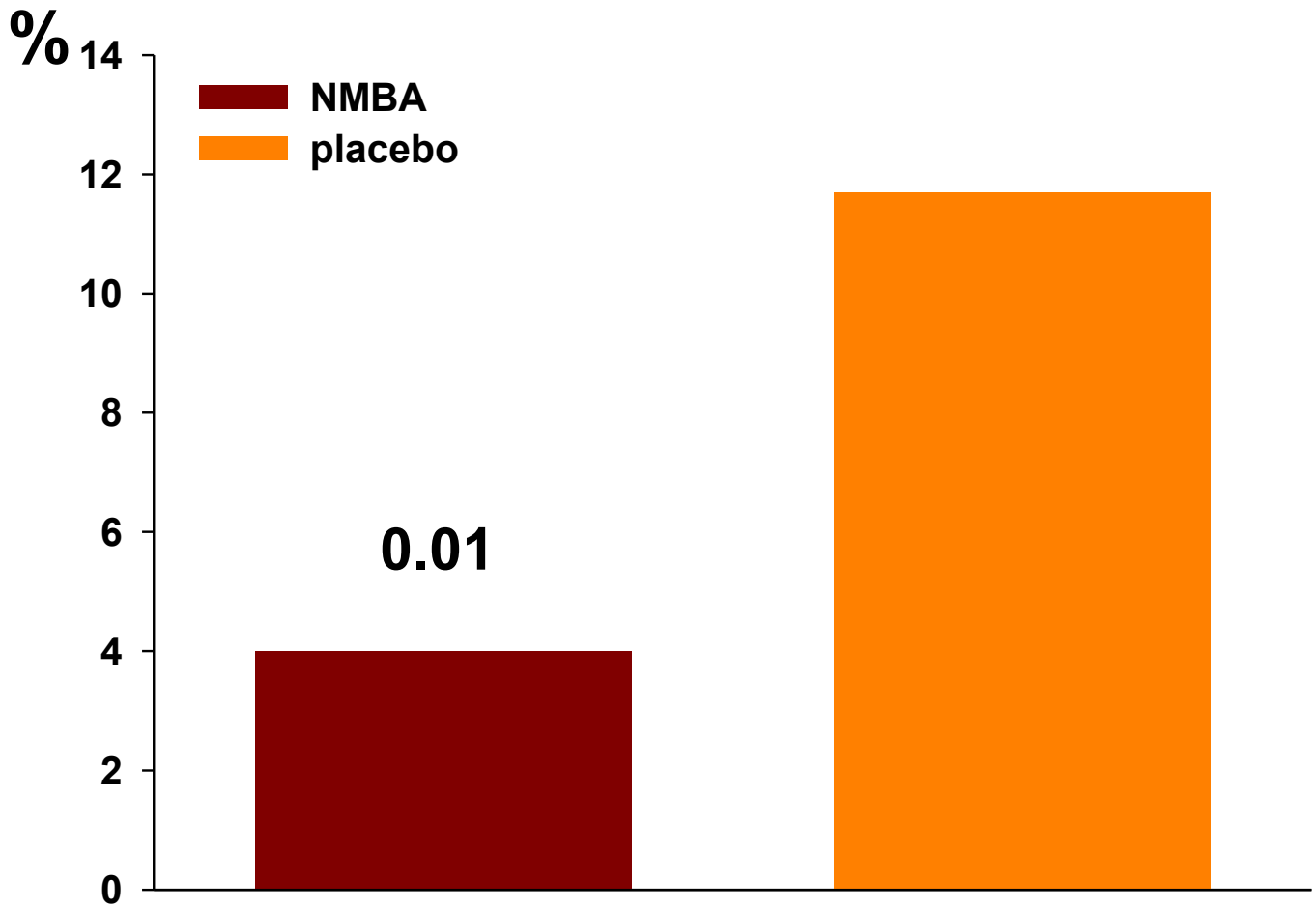
Stop NMBA + → weaning

Table 1. Summary of the Ventilation Procedure.*

Variable
Ventilator mode: volume assist–control
Initial tidal volume: 6–8 ml/kg of predicted body weight
Plateau pressure: ≤32 cm of water
Oxygenation goal: PaO_2 of 55–80 mm Hg or SpO_2 of 88–95%
Permitted combinations of FiO_2 and PEEP, respectively (cm of water): 0.3 and 5, 0.4 and 5, 0.4 and 8, 0.5 and 8, 0.5 and 10, 0.6 and 10, 0.7 and 10, 0.7 and 12, 0.7 and 14, 0.8 and 14, 0.9 and 14, 0.9 and 16, 0.9 and 18, 1.0 and 18, 1.0 and 20, 1.0 and 22, and 1.0 and 24
pH goal: 7.20–7.45
Procedure when oxygenation goal not achieved despite adjustments to FiO_2 and PEEP: use inhaled nitric oxide, almitrine mesylate, prone positioning, or any combination thereof
Procedure when plateau pressure is >32 cm of water for at least 10 min (in the following order, as needed): increase sedation, reduce tidal volume to 4 ml/kg, decrease PEEP by decrements of 2 cm of water, and perform injection of cisatracurium in a bolus of 20 mg (not to be given again if plateau pressure decreased by <2 cm of water because further doses would probably be futile, but permitted if the drug had its intended effect)
Procedure to correct hypercapnia when pH is <7.20 (in the following order, as needed): connect Y-piece directly to endotracheal tube, increase respiratory rate to a maximum of 35 cycles per min, and increase tidal volume to a maximum of 8 ml/kg
Weaning attempt: starting on day 3, if FiO_2 ≤0.6
Goals during weaning procedure: SpO_2 ≥88% and respiratory rate 26–35 cycles per min
Weaning procedure: decrease PEEP over 20–30 min to 5 cm of water
Pressure-support ventilation levels used during weaning procedure: 20, 15, 10, and 5 cm of water
If weaning procedure fails at a pressure-support ventilation level of 20 cm of water, switch to volume assist–control mode of ventilation
After at least 2 hr of successful pressure-support ventilation at a level of 5 cm of water, disconnect patient from the ventilator

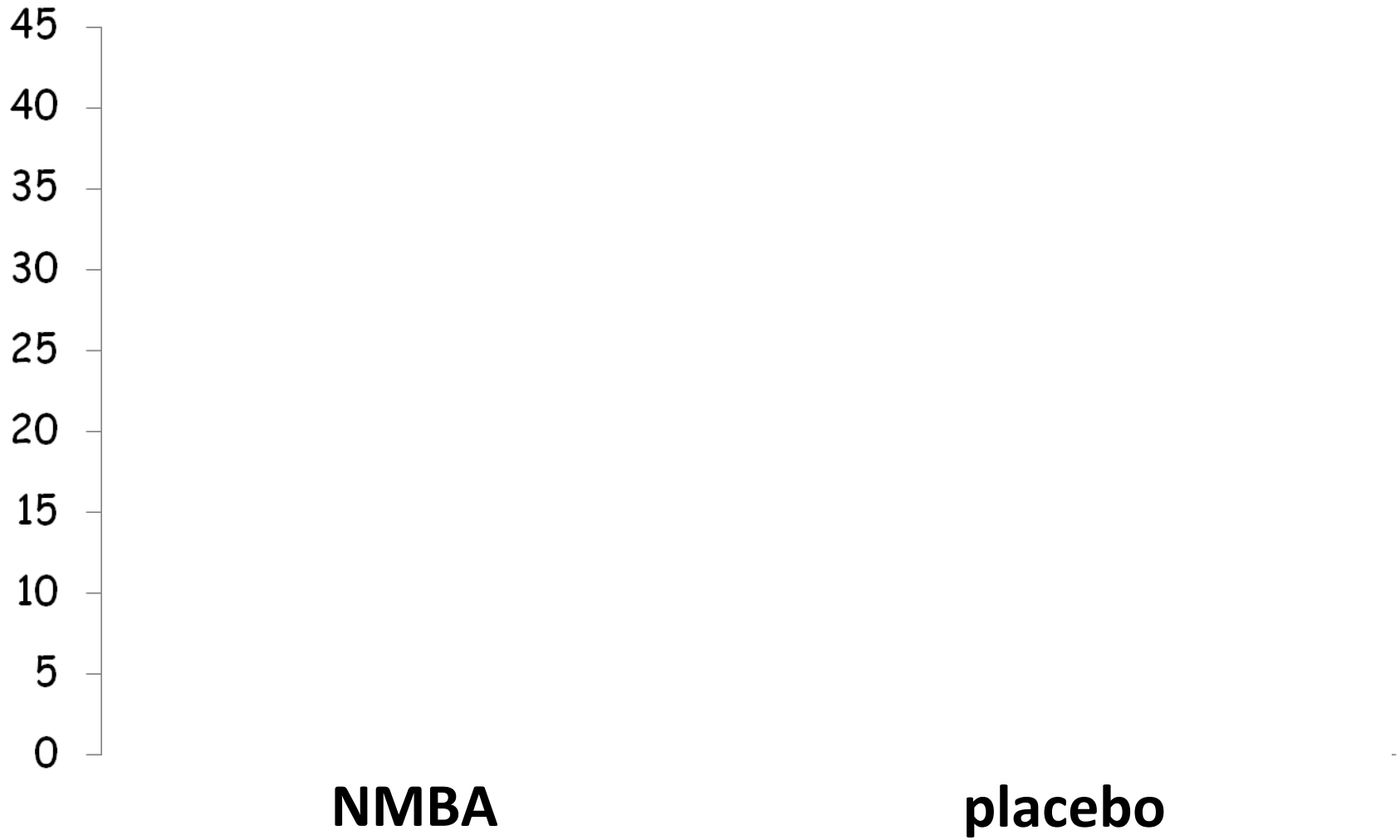
neumothorax

ACURASYS



Unadjusted day 90 mortality

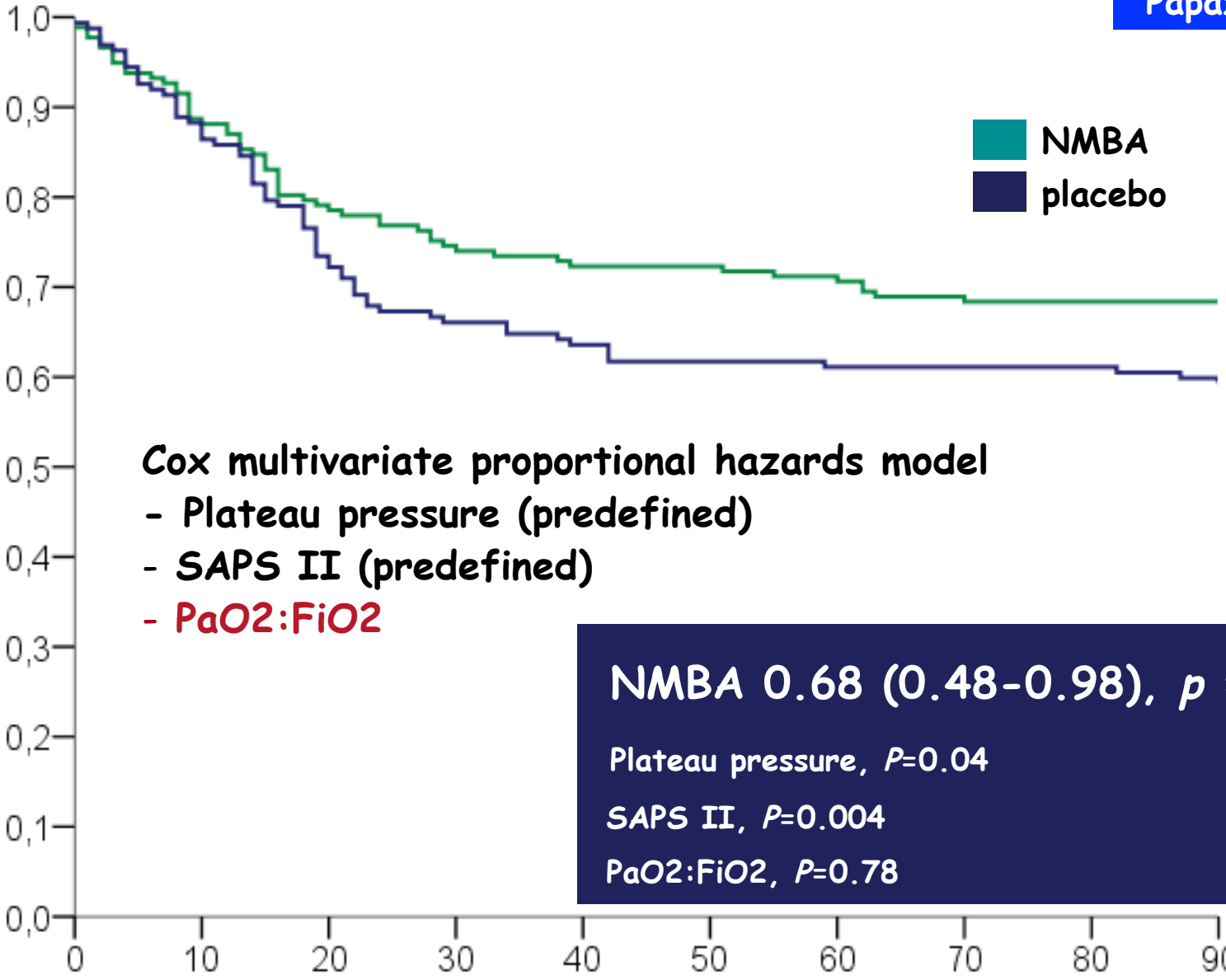
ACURASYS



ralytics

ACURASYS

Papazian *et al.* NEJM 20



Cox multivariate proportional hazards model
- Plateau pressure (predefined)
- SAPS II (predefined)
- PaO2:FiO2

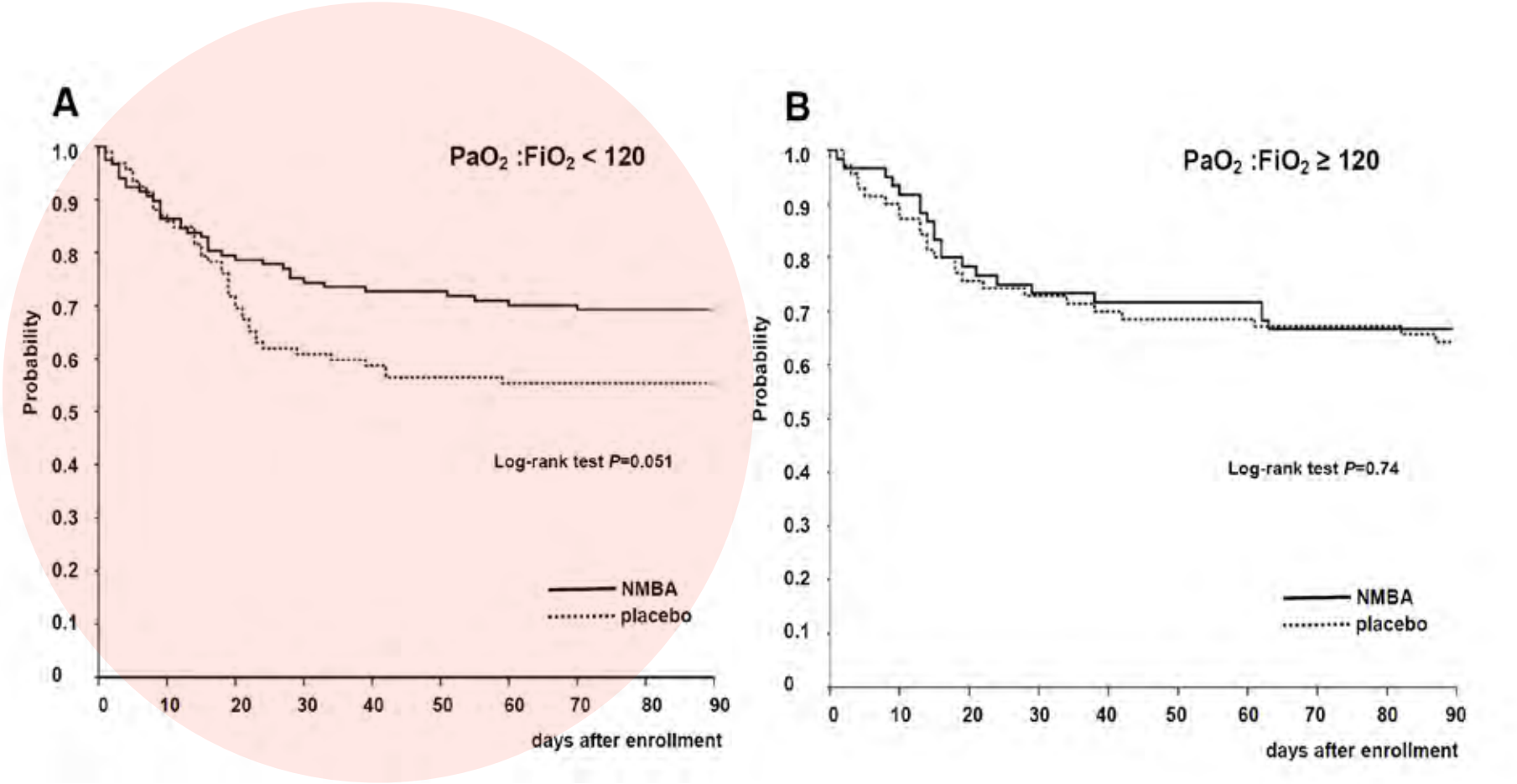
NMBA 0.68 (0.48-0.98), *p* = 0.04

Plateau pressure, *P*=0.04

SAPS II, *P*=0.004

PaO2:FiO2, *P*=0.78

Mortality according to P/F ratio



ACURASYS

Neuromuscular Blocking Agent Cisatracurium Attenuates Lung Injury by Inhibition of Nicotinic Acetylcholine Receptor-α1

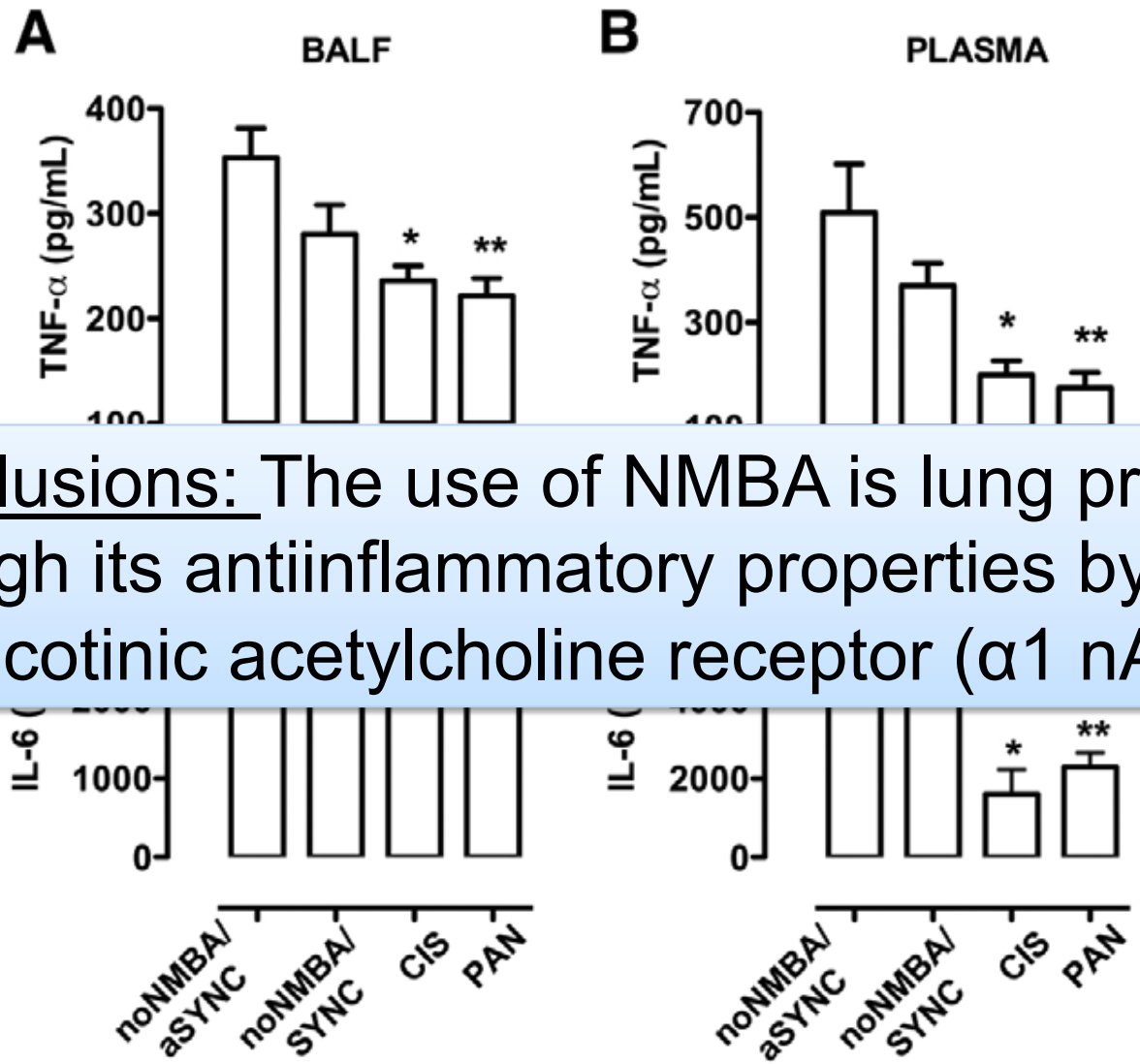
Vito Fanelli, M.D., Ph.D., Yasumasa Morita, M.D., Ph.D., Paola Cappello, Ph.D., Mirna Ghazarian, M.Sc., Bina Sugumar, B.Sc., Luisa Delsedime, M.D., Jane Batt, M.D., Ph.D., V. Marco Ranieri, M.D., Haibo Zhang, M.D., Ph.D., Arthur S. Slutsky, M.D.

Evaluate the inflammatory response that may be modulated by cisatracurium using a rat and mouse model of lung injury

Nicotinic acetylcholine receptors mediate proinflammatory effects in a variety of cell types

Nicotinic acetylcholine receptors are antagonized by cisatracurium

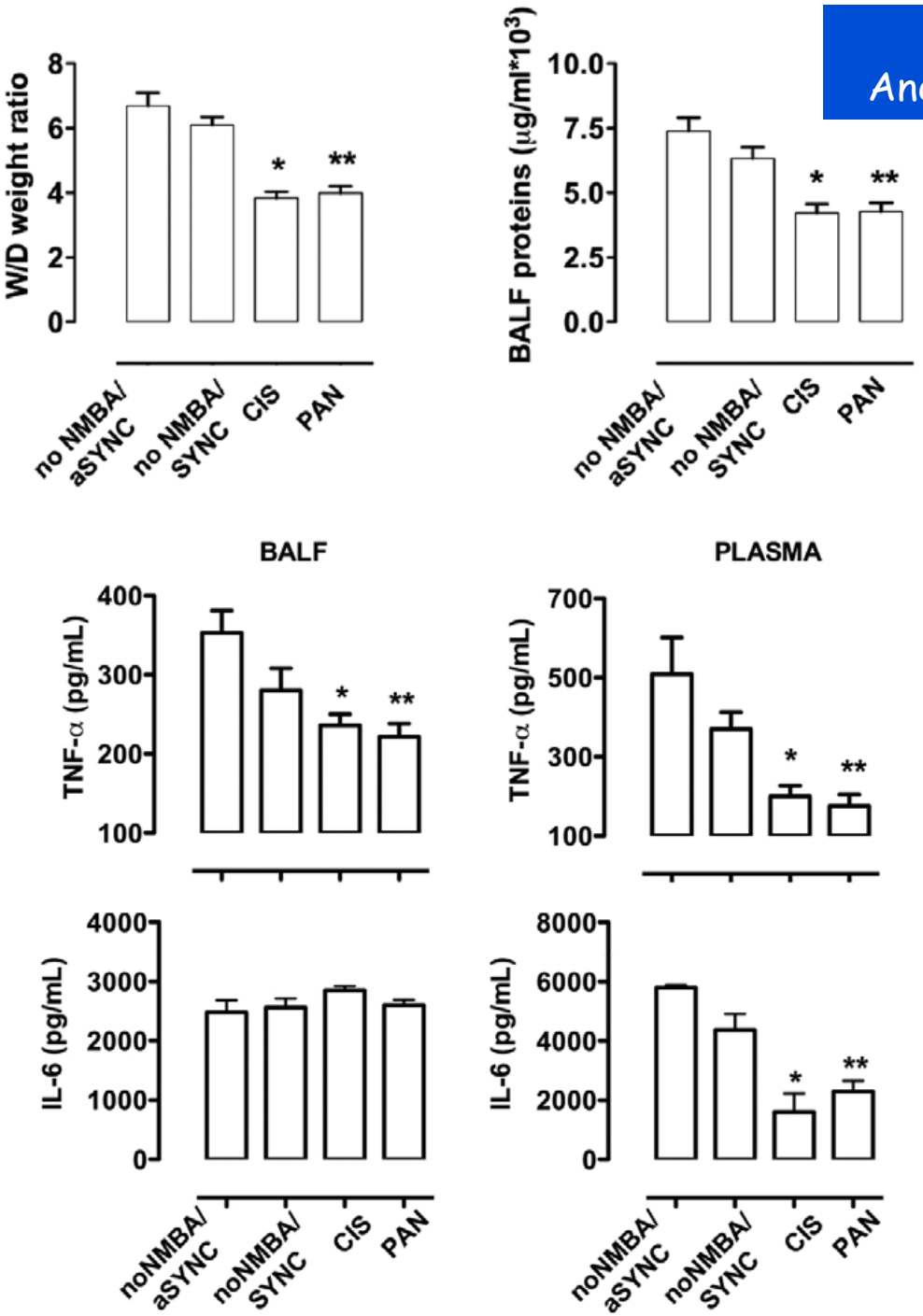
Fanelli *et al.* Anesthesiology 2016



Conclusions: The use of NMBA is lung protective through its antiinflammatory properties by blocking the nicotinic acetylcholine receptor (α1 nAChRα1).

Fanelli *et al.* Anesthesiology 2016

Fanelli *et al.*
Anesthesiology 2016



Reevaluation Of Systemic Early Neuromuscular Blockade (ROSE)

This study is not yet open for participant recruitment. (see Contacts and Locations)

Verified July 2015 by Massachusetts General Hospital

Sponsor:
Massachusetts General Hospital

Collaborator:
National Heart, Lung, and Blood Institute (NHLBI)

Information provided by (Responsible Party):
David Alan Schoenfeld, Massachusetts General Hospital

ClinicalTrials.gov Identifier:
NCT02509078

First received: July 24, 2015
Last updated: NA
Last verified: July 2015
History: No changes posted

Purpose

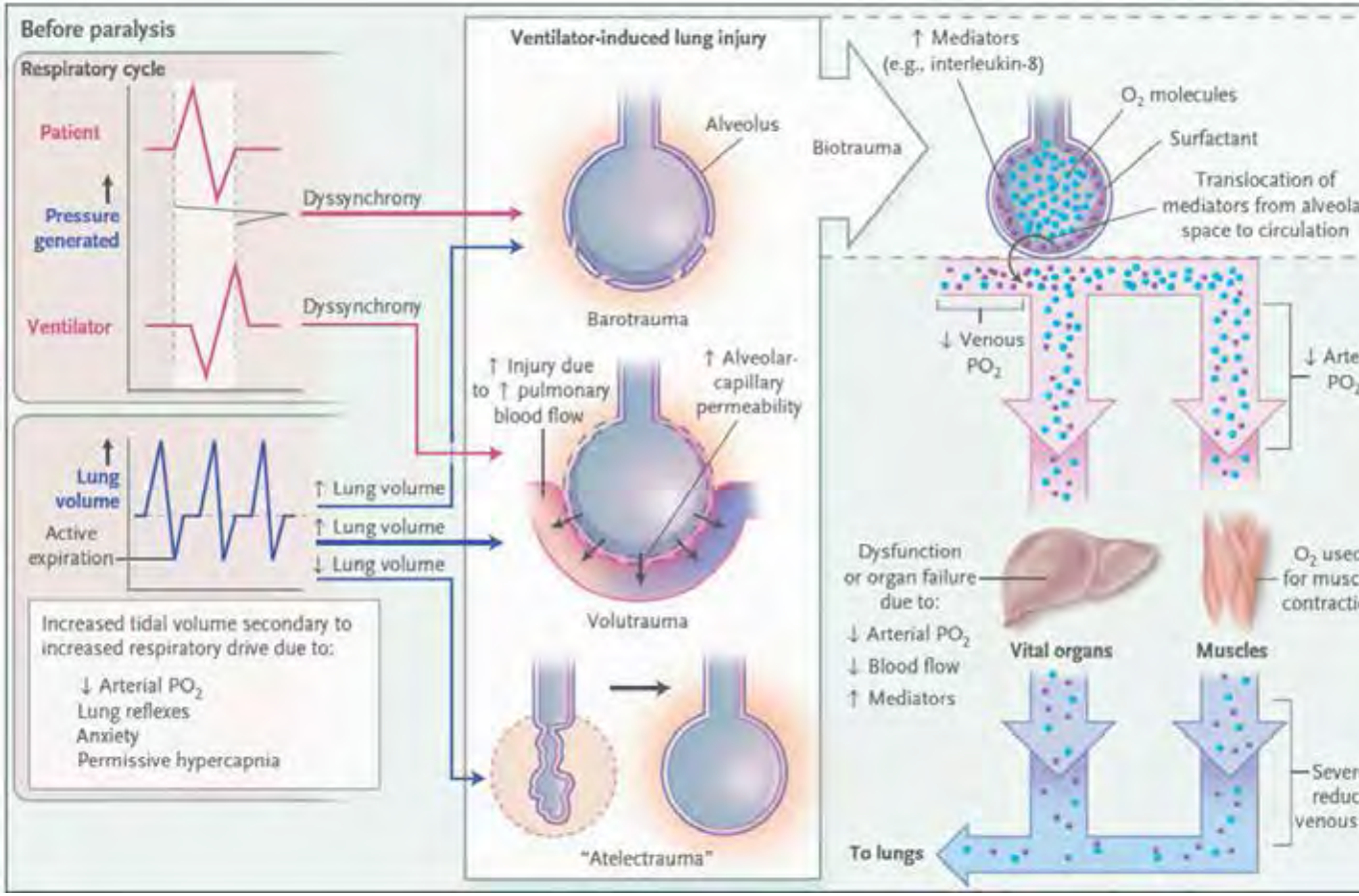
This study evaluates whether giving a neuromuscular blocker (skeletal muscle relaxant) to a patient with acute respiratory distress syndrome will improve survival. Half of the patien
two days and in the other half the use of neuromuscular blockers will be discouraged .

Condition	Intervention
Acute Respiratory Distress Syndrome	Drug: cisastracurium besylate

NAL

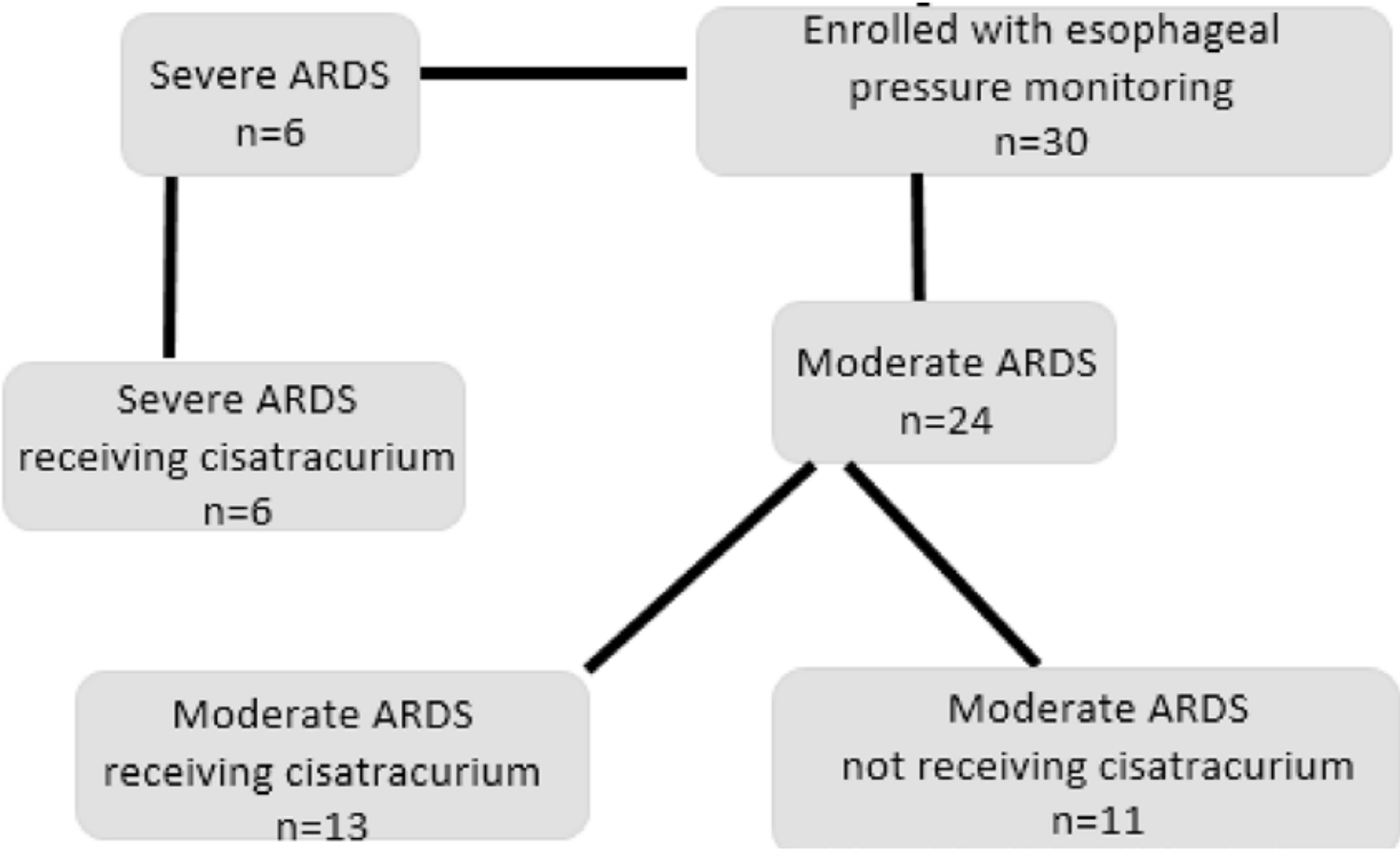
cts of neuromuscular blockers ranspulmonary pressures in moderate evere acute respiratory distress syndrome

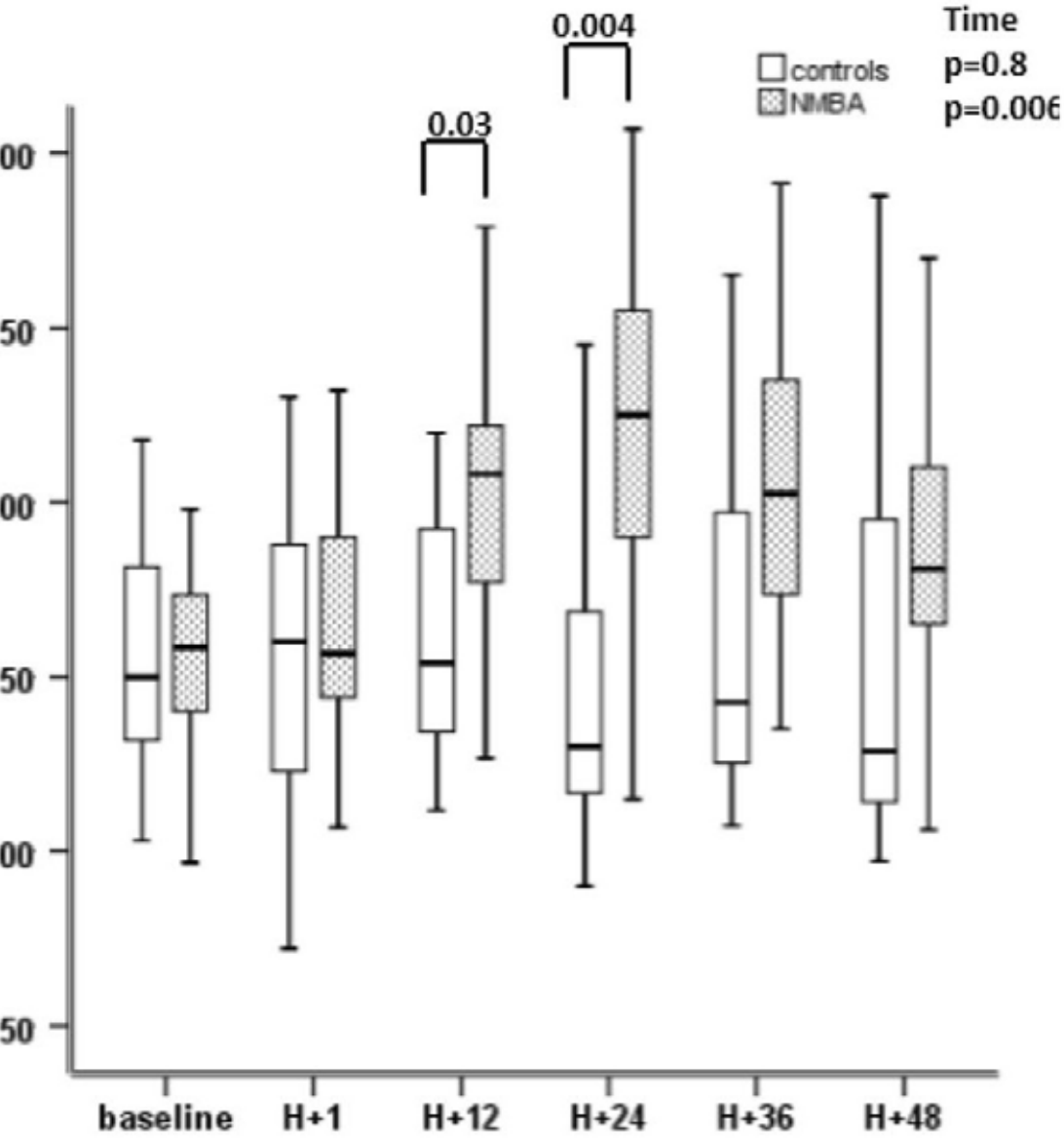
ne Guervilly[1*], Magali Bisbal[2,3], Jean Marie Forel[1], Malika Mechati[3], Samuel Lehingue[1], ourenne[3], Gilles Perrin[3], Romain Rambaud[1], Melanie Adda[1], Sami Hraiech[1], Elisa Marchi[1], Roch[1,4], Marc Gainnier[3] and Laurent Papazian[1]

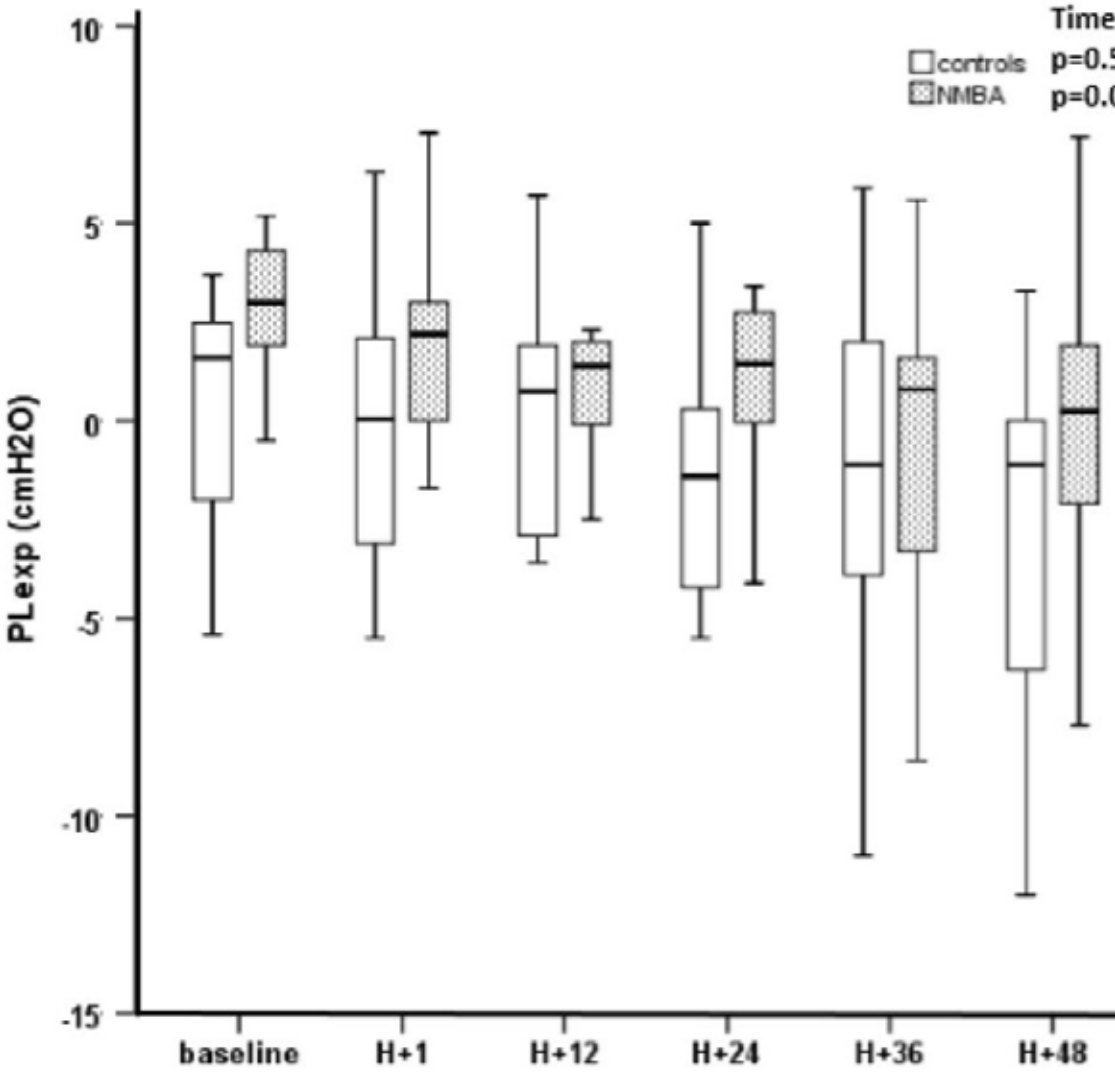


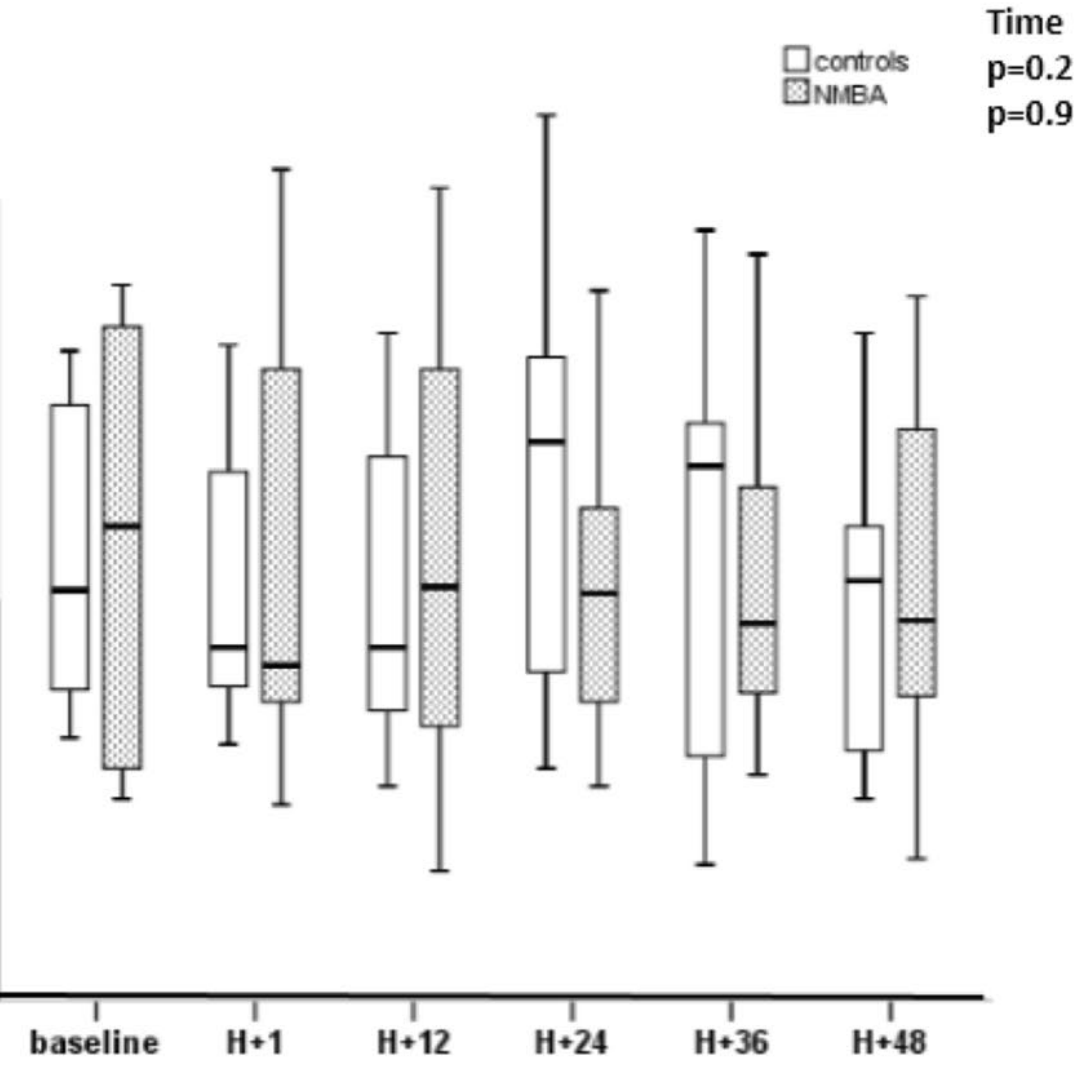
Neuromuscular Blocking Agents in ARDS

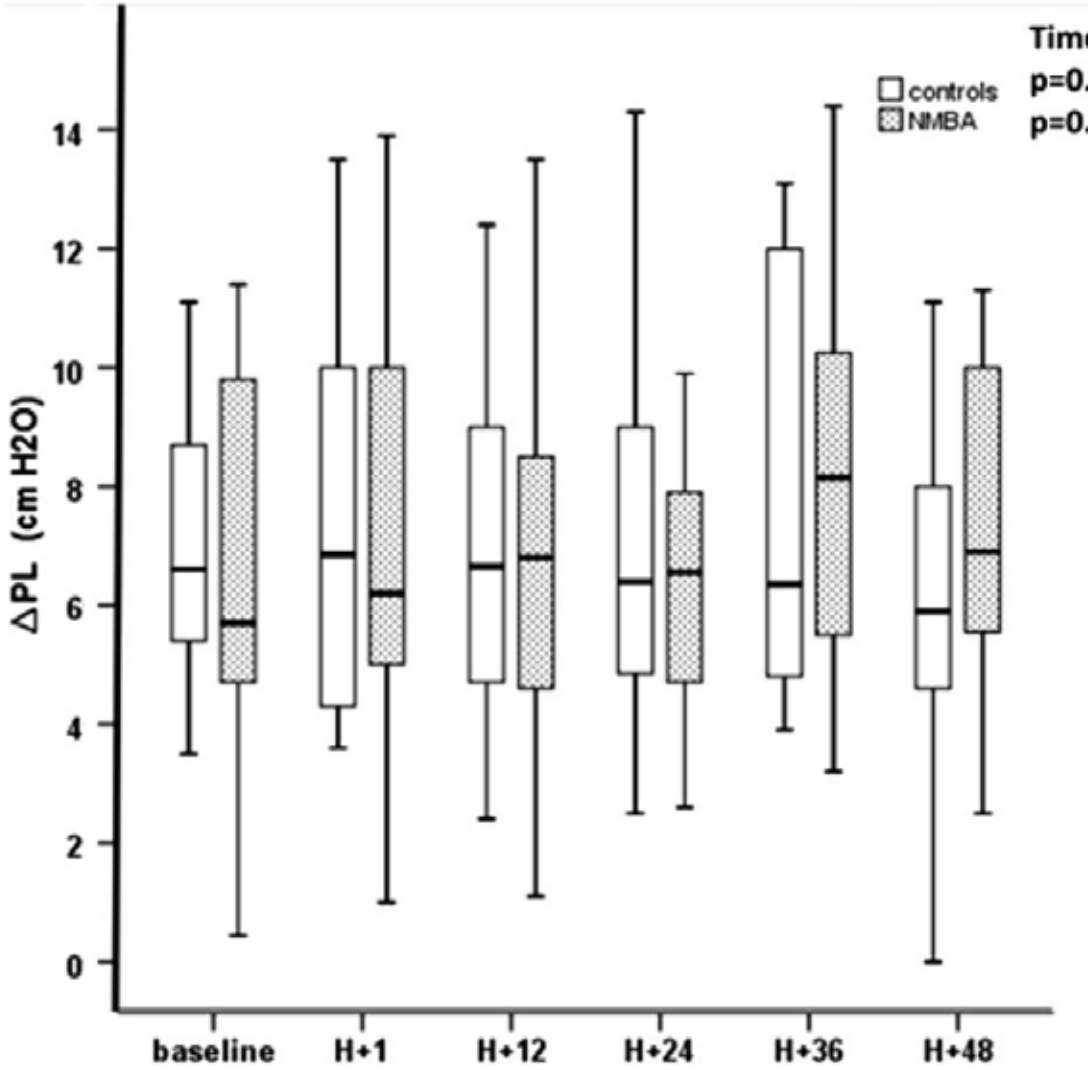
Arthur S. Slutsky, M.D.


Enrolled with esophageal pressure monitoring n=30
Severe ARDS n=6
Severe ARDS receiving cisatracurium n=6
Moderate ARDS n=24
Moderate ARDS receiving cisatracurium n=13
Moderate ARDS not receiving cisatracurium n=11

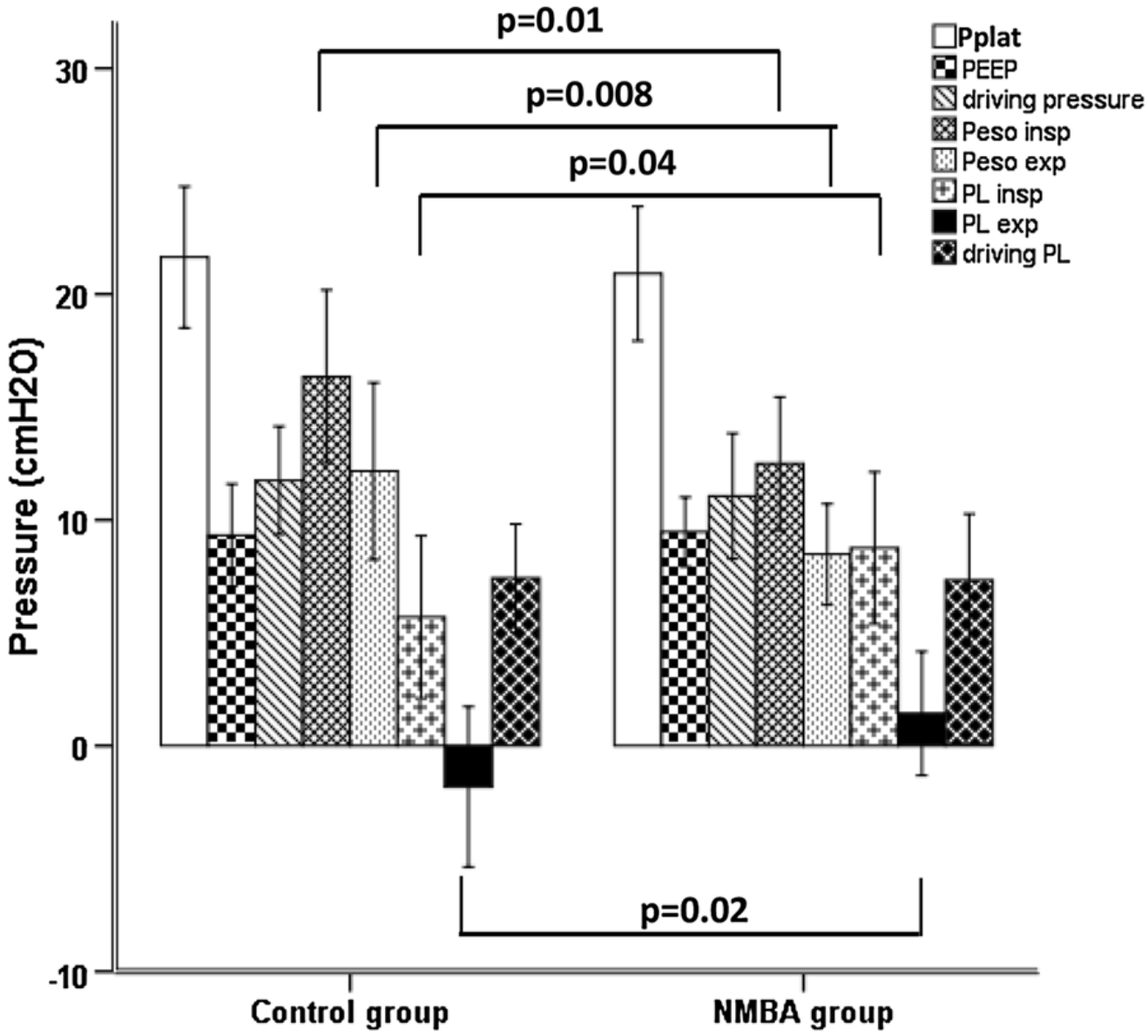

0.004
0.03
controls
NMBA
Time
p=0.8
p=0.006
baseline
H+1
H+12
H+24
H+36
H+48


PLexp (cmH2O)
10
5
0
-5
-10
-15
controls
NMBA
Time
p=0.5
p=0.0
baseline
H+1
H+12
H+24
H+36
H+48


Time
p=0.2
p=0.9
controls
NIMBA
baseline
H+1
H+12
H+24
H+36
H+48


Tim
p=0.
p=0.
controls
NIMBA
ΔPL (cm H2O)
0
2
4
6
8
10
12
14
baseline
H+1
H+12
H+24
H+36
H+48

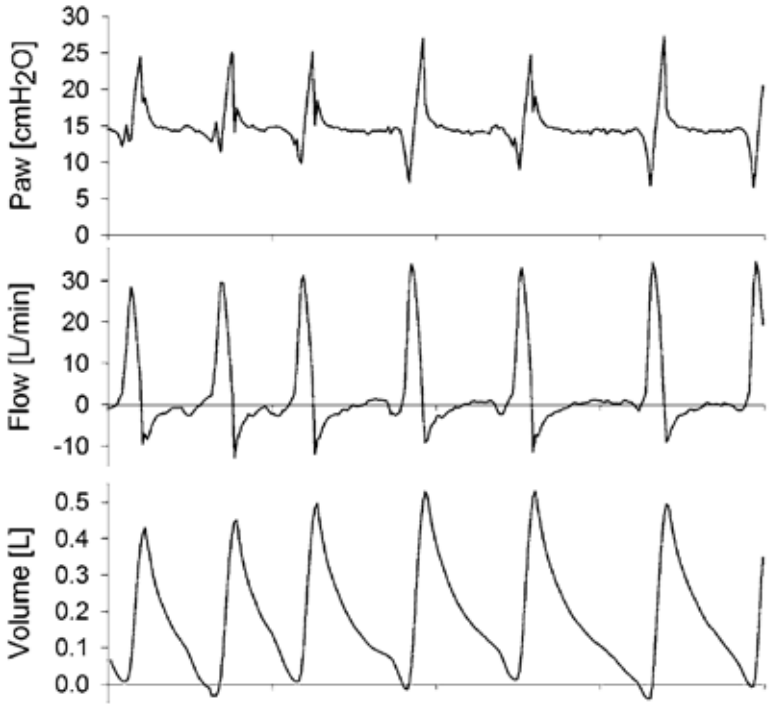
mparisons of averages over the 48 h in each
tient of Pplat, PEEP tot, ΔP, PL insp, PL exp, and
L



nely high transpulmonary pressure ontaneously breathing patient with early ARDS on ECMO

ri[1], Thomas Langer[2], Alberto Zanella[1], Giacomo Grasselli[1] and Antonio Pesenti[1,2*]

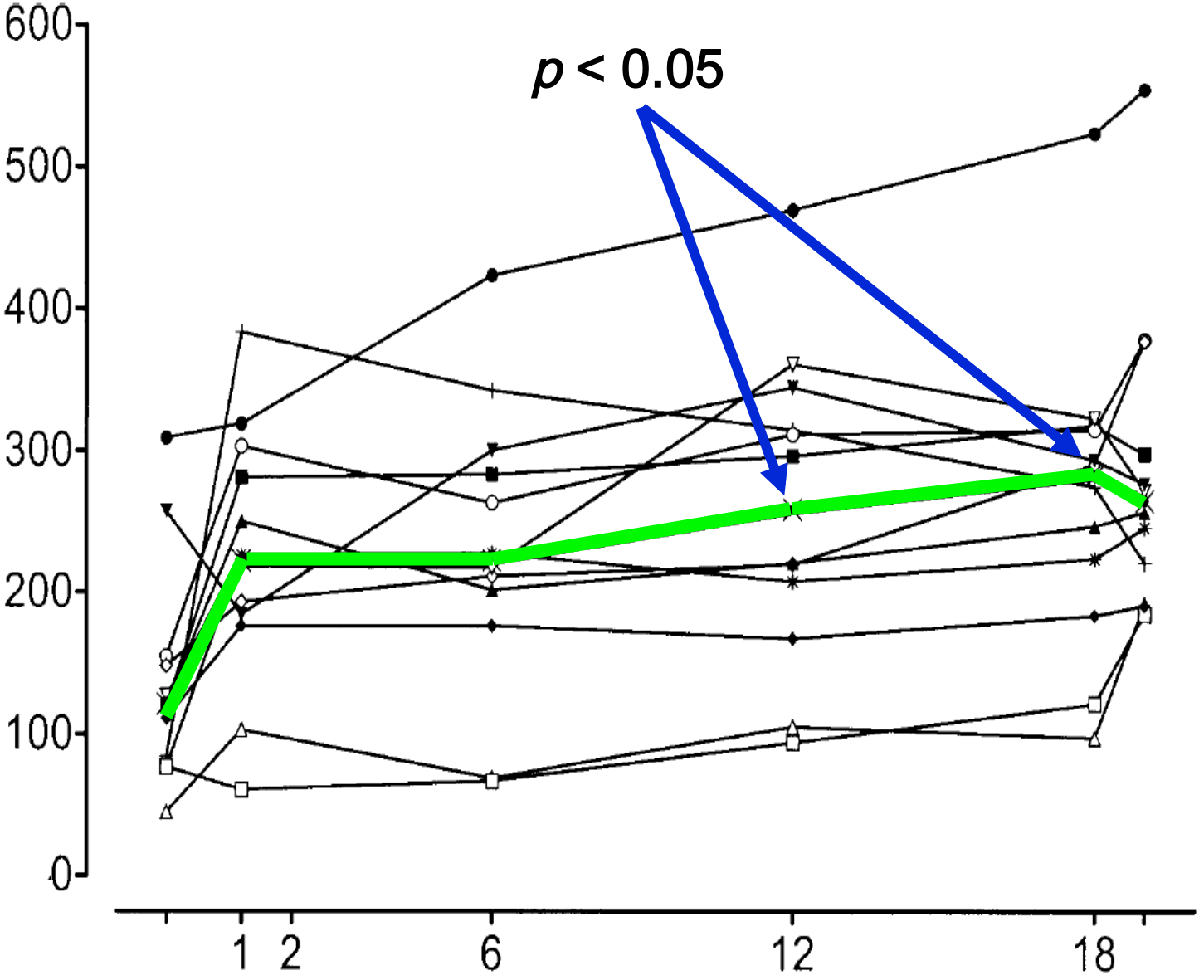
	Volume controlled	Pressure support
PEEP (cmH_2O)	15	15
Vt (ml/kg PBW)	4	6.5
RR (bpm)	10	21
Ppeak (cmH_2O)	37	24
ECMO GF (l/min)	6.5	11.0
pH	7.42	7.47
PaO_2 (mmHg)	63	63
$PaCO_2$ (mmHg)	45	37



one positionning

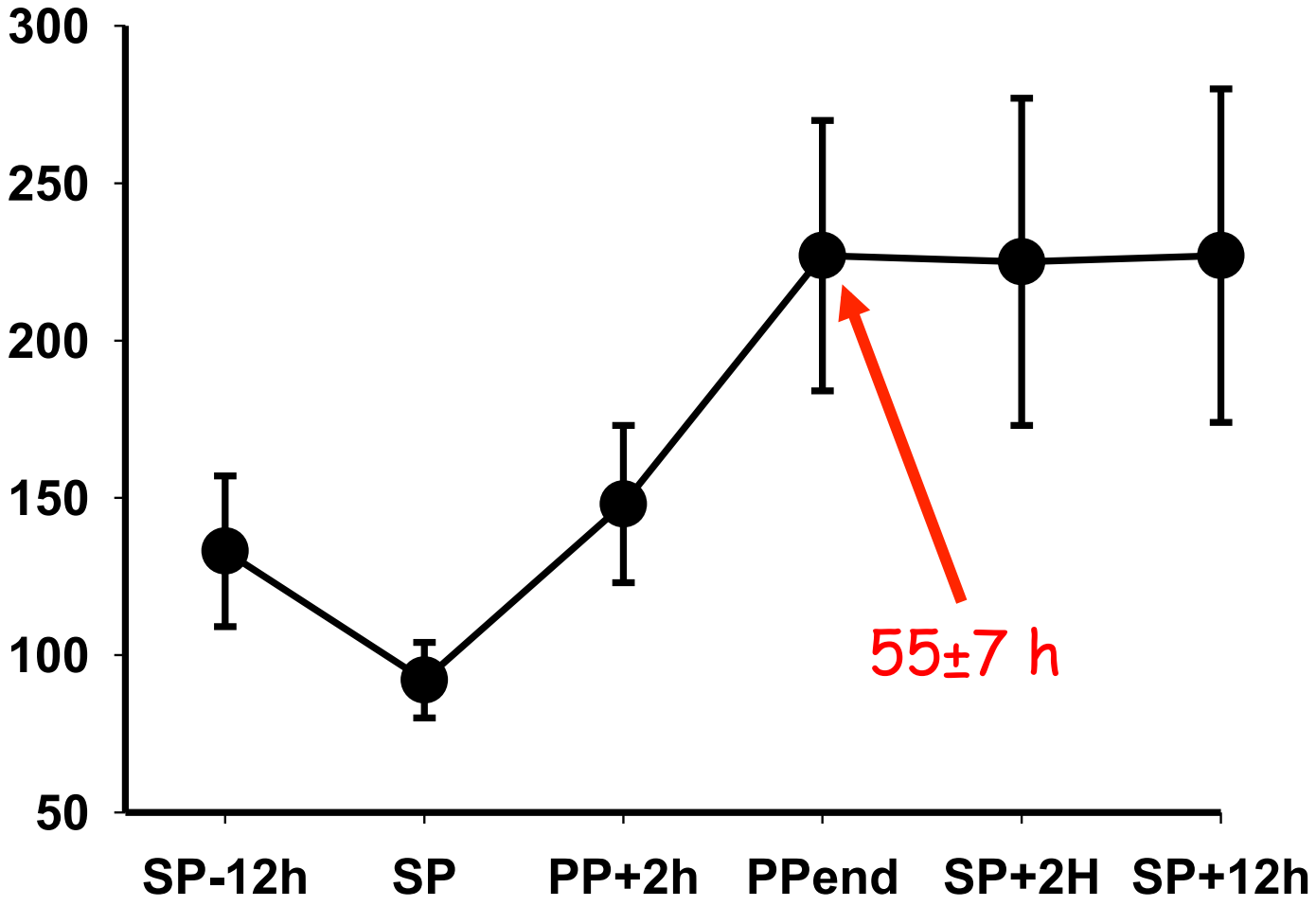
PP duration

McAuley *et al.* Intensive Care Med 2002



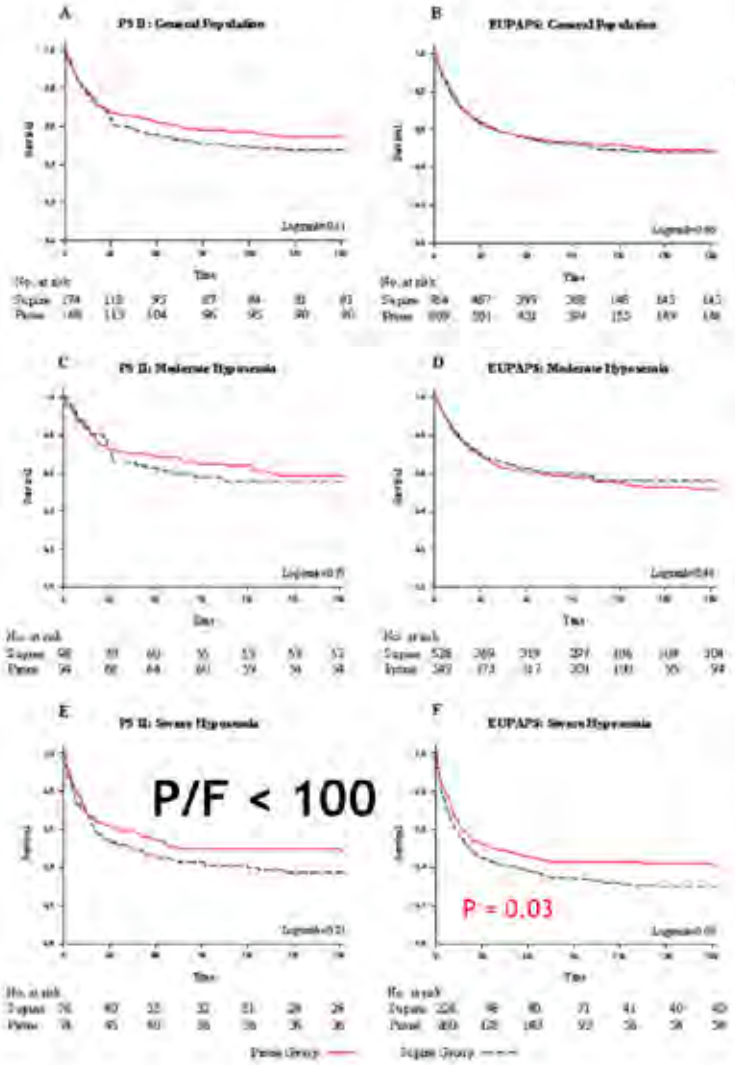
Romero *et al.* J Crit Care 2009

PP duration

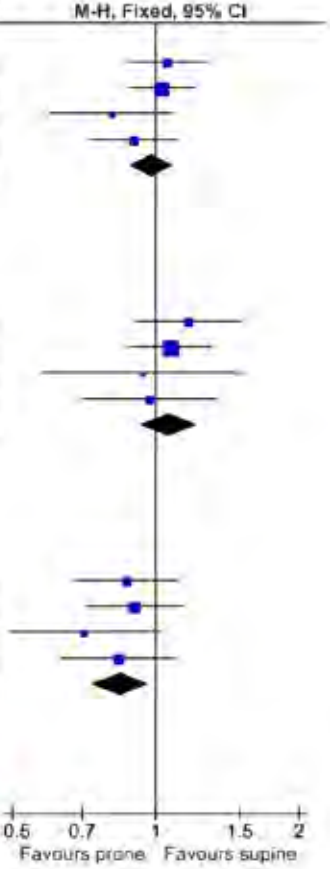


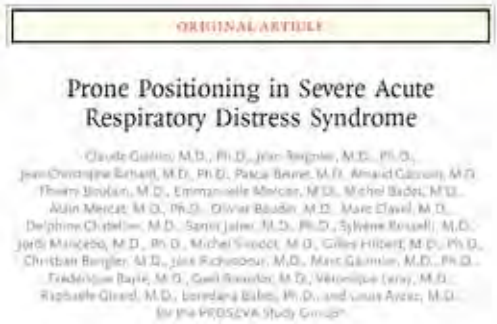
PS II

Meta-analysis



	Prone group Events	Total	Supine group Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
EUPAPS: general population						
Gattinoni 2001	92	152	87	152	22.7%	1.06 [0.88, 1.28]
Guerin 2004	179	413	159	378	43.3%	1.03 [0.88, 1.21]
Mancebo 2006	38	76	37	60	10.8%	0.81 [0.60, 1.10]
Gattinoni 2008	79	168	91	174	23.3%	0.90 [0.73, 1.11]
Subtotal (95% CI)		809		764	100.0%	**0.98 [0.89, 1.09]**
Total events	388		374			
Heterogeneity: Chi² = 3.15, df = 3 (P = 0.37); I² = 5%						
Test for overall effect: Z = 0.35 (P = 0.73)						
EUPAPS: moderate hypoxemia						
Gattinoni 2001	57	99	52	106	22.6%	1.17 [0.91, 1.52]
Guerin 2004	126	323	110	303	51.1%	1.07 [0.88, 1.32]
Mancebo 2006	16	33	16	31	7.4%	0.94 [0.58, 1.53]
Gattinoni 2008	40	94	43	98	18.9%	0.97 [0.70, 1.34]
Subtotal (95% CI)		549		538	100.0%	**1.07 [0.93, 1.22]**
Total events	239		221			
Heterogeneity: Chi² = 1.12, df = 3 (P = 0.77); I² = 0%						
Test for overall effect: Z = 0.92 (P = 0.36)						
EUPAPS: severe hypoxemia						
Gattinoni 2001	35	53	35	46	22.9%	0.87 [0.67, 1.12]
Guerin 2004	53	90	49	75	32.7%	0.90 [0.71, 1.14]
Mancebo 2006	22	43	21	29	15.4%	0.71 [0.49, 1.02]
Gattinoni 2008	39	74	48	76	29.0%	0.83 [0.63, 1.10]
Subtotal (95% CI)		260		226	100.0%	**0.84 [0.74, 0.97]**
Total events	149		153			
Heterogeneity: Chi² = 1.24, df = 3 (P = 0.74); I² = 0%						
Test for overall effect: Z = 2.41 (P = 0.02)						P = 0.02





ORIGINAL ARTICLE

Prone Positioning in Severe Acute Respiratory Distress Syndrome

Slide provided by C. Guérin

Inclusion criteria

1. Aged 18 years or more
2. Both genders
3. Intubated for ARDS for < 36 hours
4. ARDS according to AECC criteria
5. Criteria confirmed 12-24 hours later
6. AND severity criteria at that time
   - $PaO_2/FiO_2 < 150$ with $F_IO_2 \geq 0.6$ + PEEP ≥ 5 cm H_2O + VT 6 ml/kg IBW
7. Information sheet given to next of kin

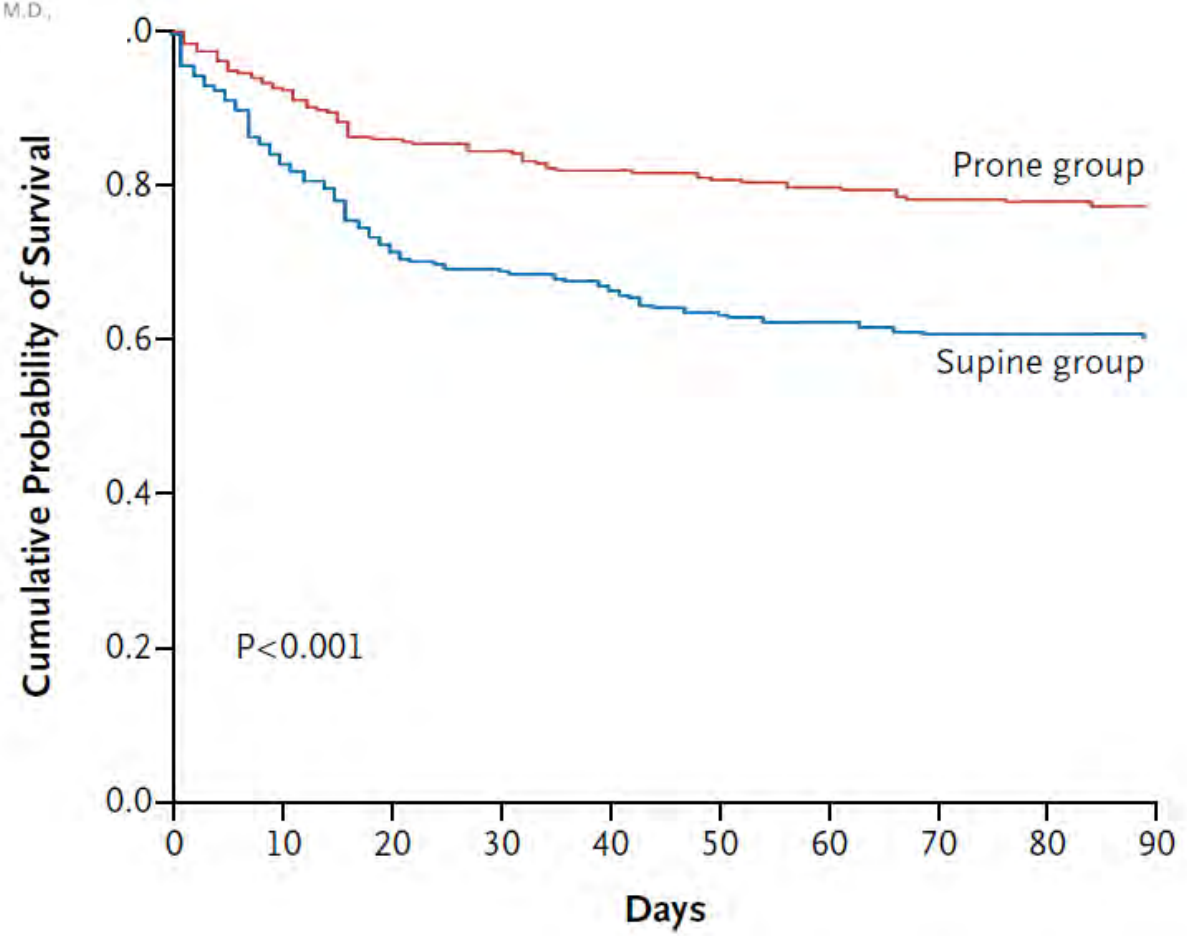
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

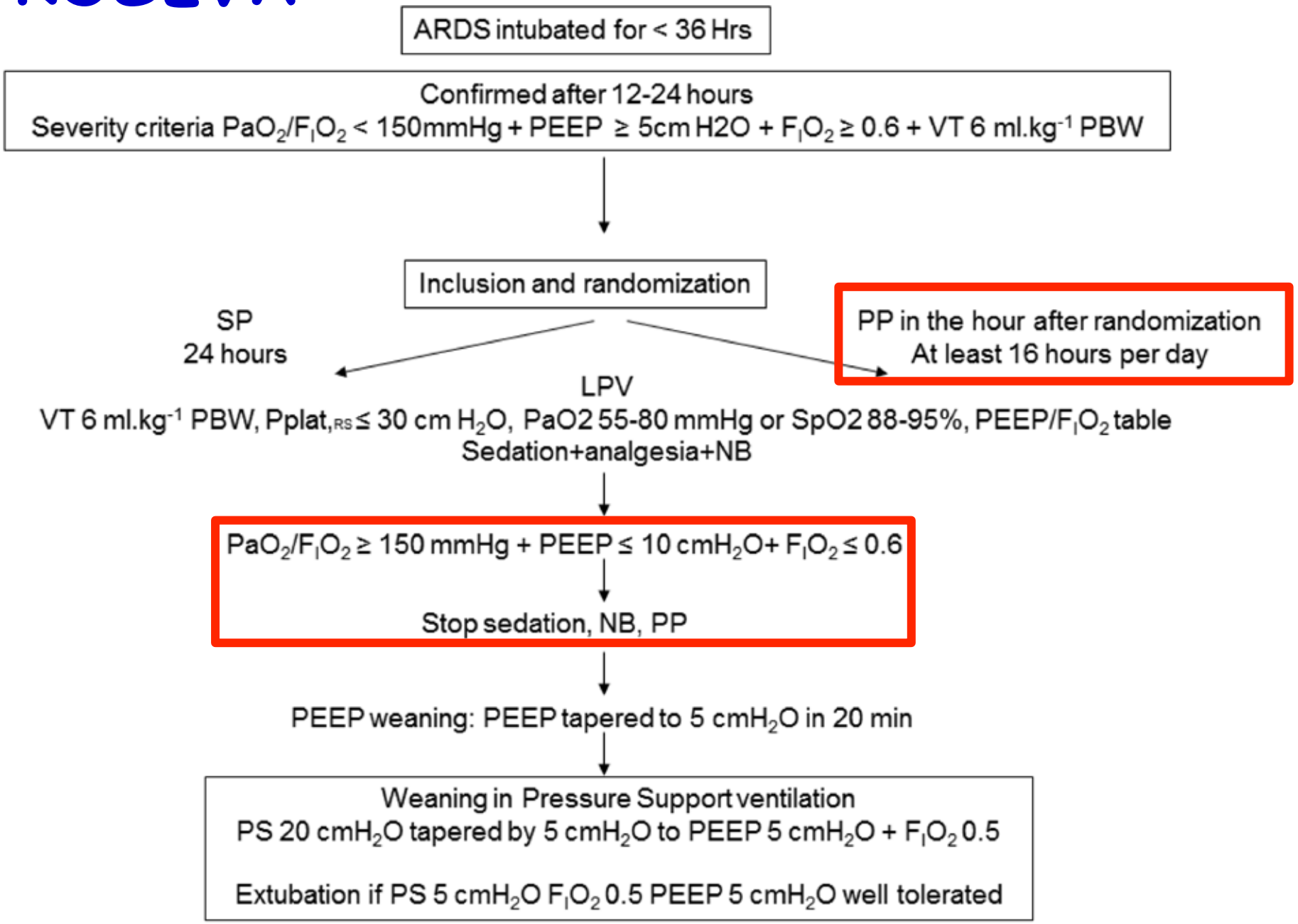
Prone Positioning in Severe Acute Respiratory Distress Syndrome

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

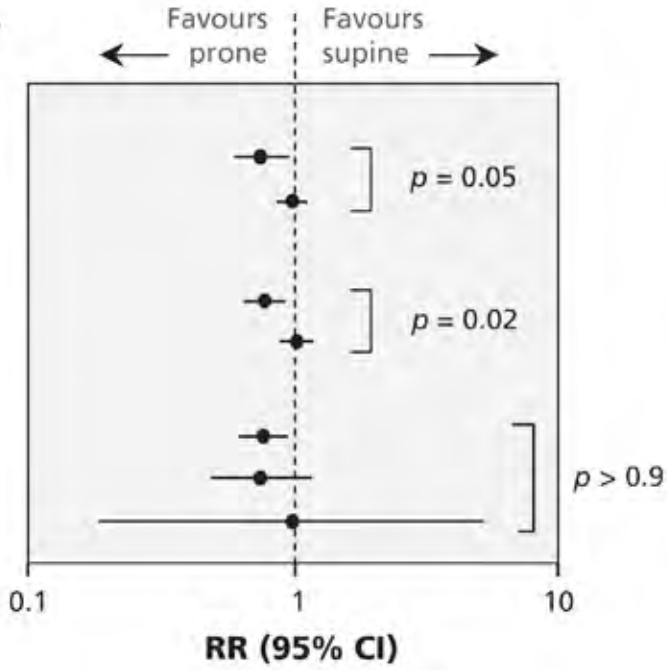
- Mean P/F ratio, 100 mmHg
- 4 sessions of PP (17±3 h)



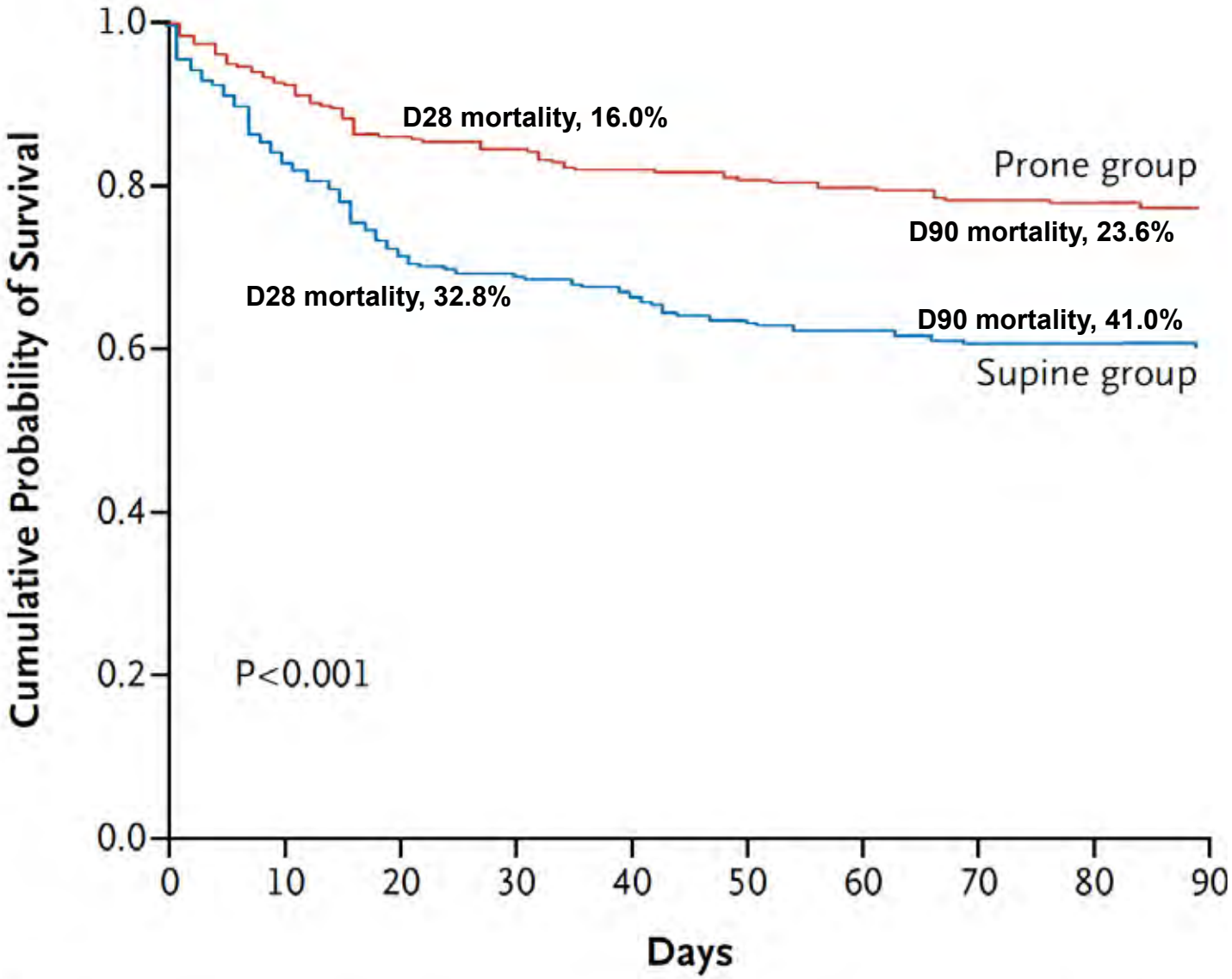
PROSEVA


ARDS intubated for < 36 Hrs
Confirmed after 12-24 hours
Severity criteria PaO_2/F_IO_2 < 150mmHg + PEEP ≥ 5cm H2O + F_IO_2 ≥ 0.6 + VT 6 ml.kg^{-1} PBW
Inclusion and randomization
SP
24 hours
PP in the hour after randomization
At least 16 hours per day
LPV
VT 6 ml.kg^{-1} PBW, $P_{plat,RS}$ ≤ 30 cm H_2O, PaO2 55-80 mmHg or SpO2 88-95%, $PEEP/F_IO_2$ table
Sedation+analgesia+NB
PaO_2/F_IO_2 ≥ 150 mmHg + PEEP ≤ 10 cmH_2O + F_IO_2 ≤ 0.6
Stop sedation, NB, PP
PEEP weaning: PEEP tapered to 5 cmH_2O in 20 min
Weaning in Pressure Support ventilation
PS 20 cmH_2O tapered by 5 cmH_2O to PEEP 5 cmH_2O + F_IO_2 0.5
Extubation if PS 5 cmH_2O F_IO_2 0.5 PEEP 5 cmH_2O well tolerated

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



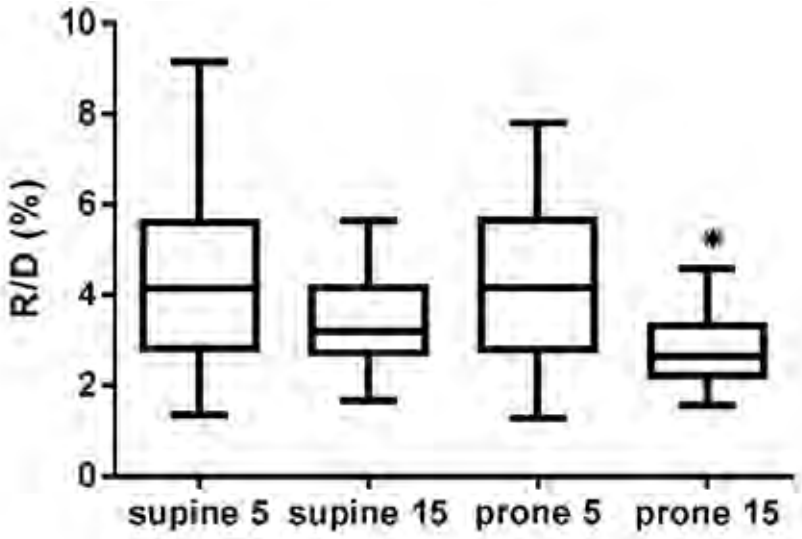
Sud *et al.* CMAJ 2014

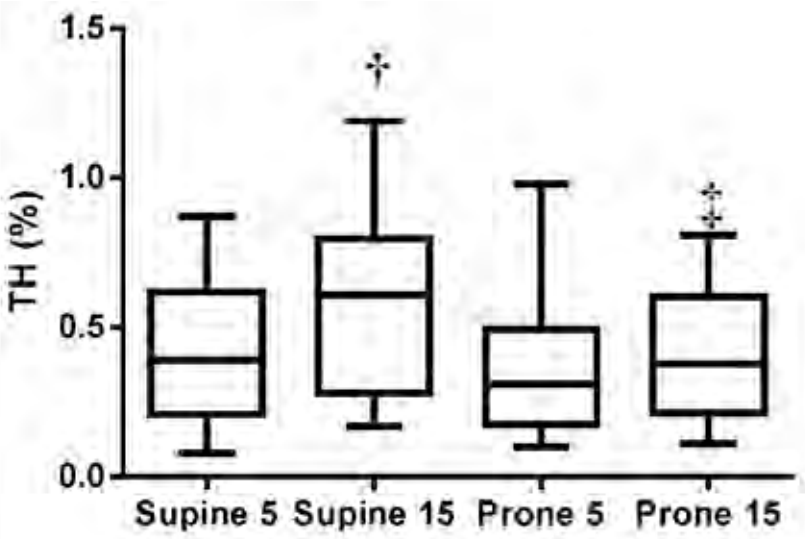


No. at Risk

Prone group	237	202	191	186	182
Supine group	229	163	150	139	136

ects of PEEP and PP on cyclic recruitment/derecruitm
tidal hyperinflation

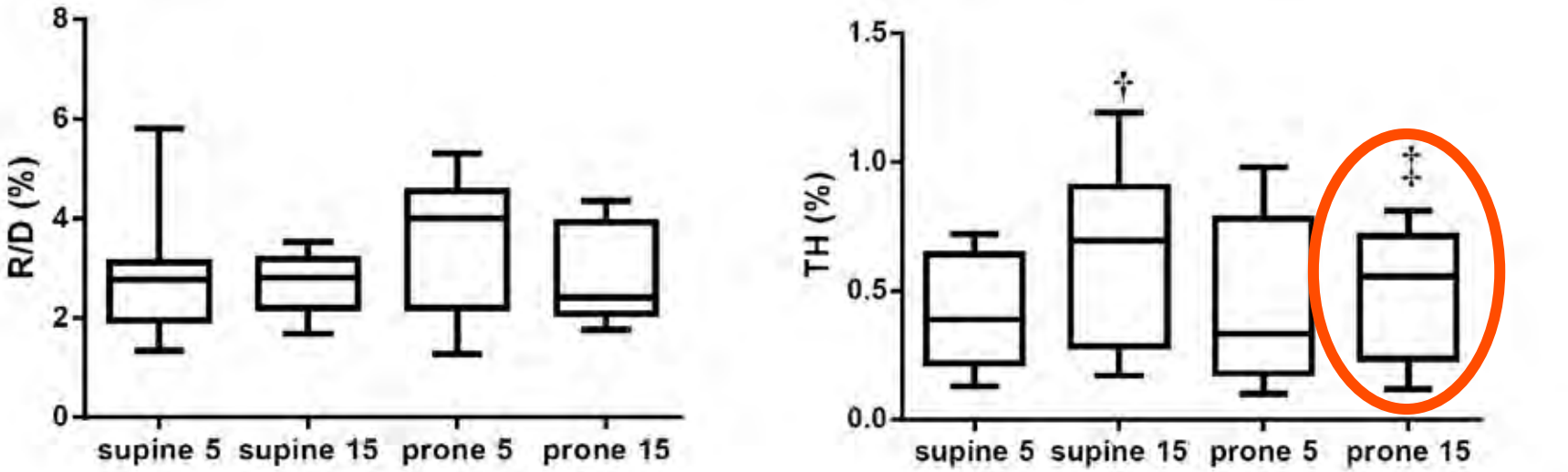




All 24 patients

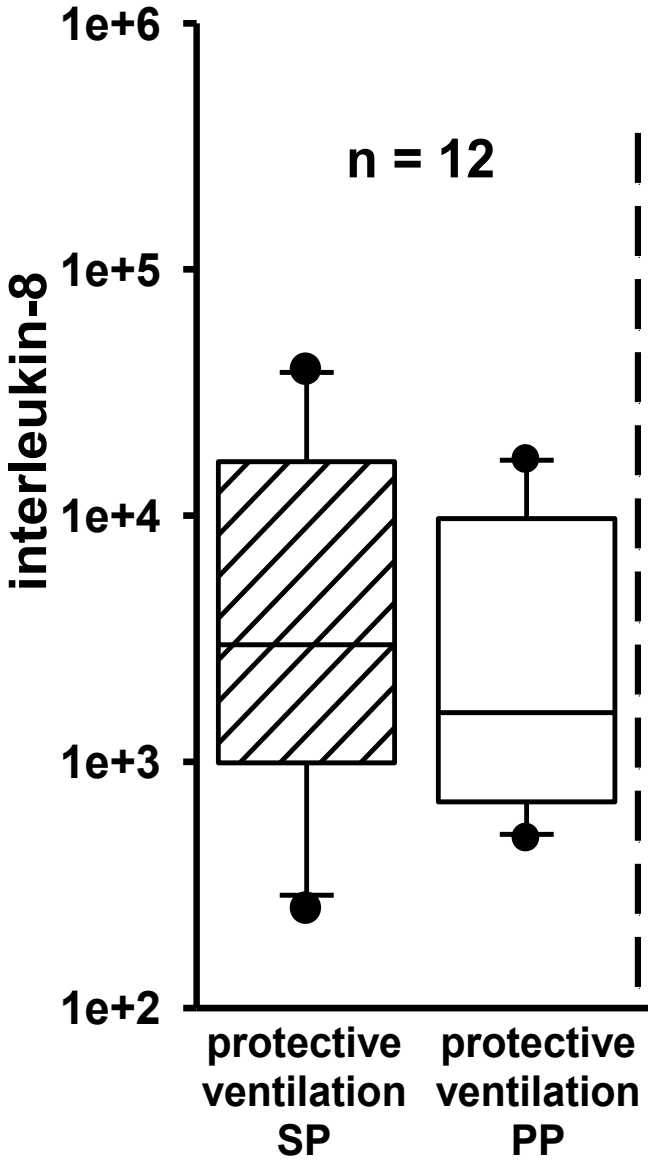
Cornejo *et al.* AJRCCM 2013

Only the 10 patients with low lung recruitability



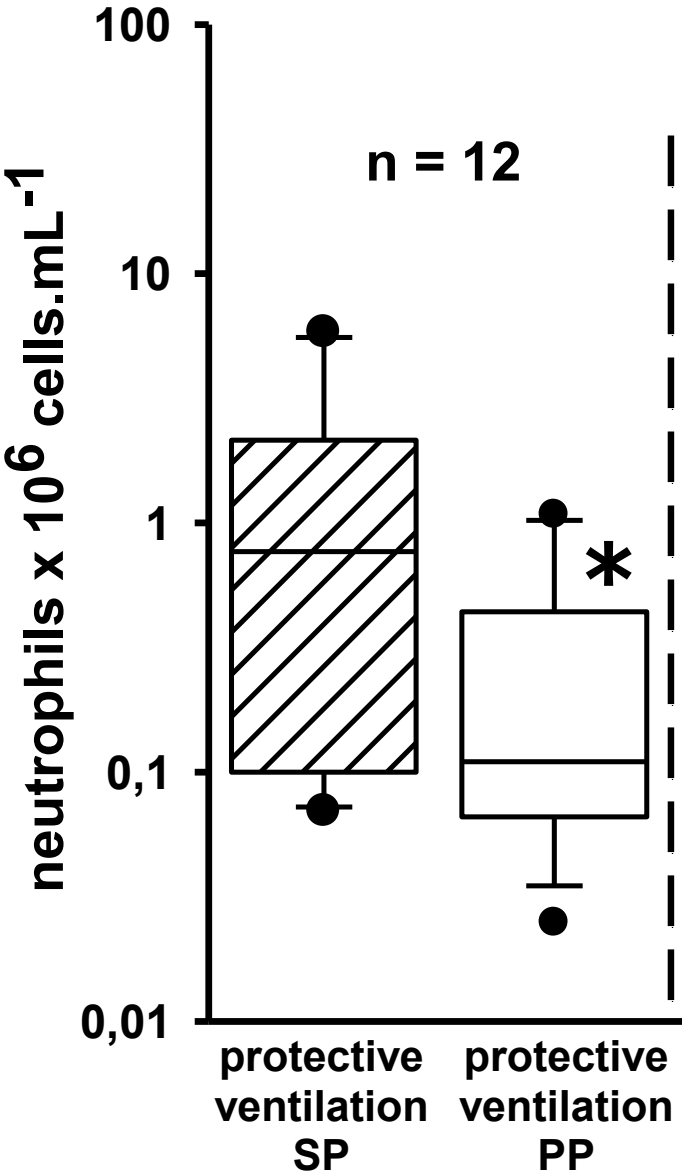
Cornejo *et al.* AJRCCM 2013

V et VILI…



Papazian *et al.* CCM 2006

V et VILI…


100
10
1
0,1
0,01
neutrophils x 10^6 cells.mL^-1
n = 12
*
protective ventilation SP
protective ventilation PP

PP should be done by well-trained ICU teams

Table 5. Incidence of Complications During the 28 Days After Randomization

	Supine Position			Prone Position		
	Patient-Days	No. of Occurrences	Incidence per 100 Days (95% CI)	Patient-Days	No. of Occurrences	Incidence per 100 Days (95% CI)
Unplanned extubation	5188	47	0.91 (0.65-1.16)	5756	44	0.76 (0.54-0.99)
Selective intubation*	5188	0	0	5755	6	0.10 (0.02-0.19)
ETT obstruction†	5188	12	0.23 (0.10-0.36)	5755	34	0.59 (0.39-0.79)
Hemoptysis	5188	34	0.66 (0.44-0.88)	5755	45	0.78 (0.55-1.01)
Spo_2 <85%	5188	207	3.99 (3.45-4.53)	5755	236	4.10 (3.58-4.62)
Cardiac arrest	5188	88	1.70 (1.34-2.05)	5754	87	1.51 (1.19-1.83)
Heart rate <30/min	5188	72	1.39 (1.07-1.71)	5755	81	1.41 (1.10-1.71)
SAP <60 mm Hg	5188	148	2.85 (2.39-3.31)	5754	135	2.35 (1.95-2.74)
Pressure sores‡	5188	157	3.03 (2.55-3.50)	5756	208	3.61 (3.12-4.10)
Atelectasis	5188	28	0.54 (0.34-0.74)	5756	28	0.49 (0.31-0.67)
Intracranial hypertension	5188	3	0.06 (0.00-0.12)	5756	9	0.16 (0.05-0.26)
Pneumothorax	5188	28	0.54 (0.34-0.74)	5756	22	0.38 (0.22-0.54)

Abbreviations: CI, confidence interval; ETT, endotracheal tube; SAP, systolic arterial pressure; 95% Spo_2, transcutaneous oxygen saturation of arterial blood.
*P=.01.
†P=.002.
‡P=.005 between supine and prone position groups.

Guérin *et al.* JAMA 2004

Rescue therapies

Inhaled NO

- Endogenous NO (50-100 ppb upper airways)
- Additive effects (PEEP, almitrine, PP, HFO …)
- RV dysfunction

Chollet-Martin *et al.* AJRCCM 96

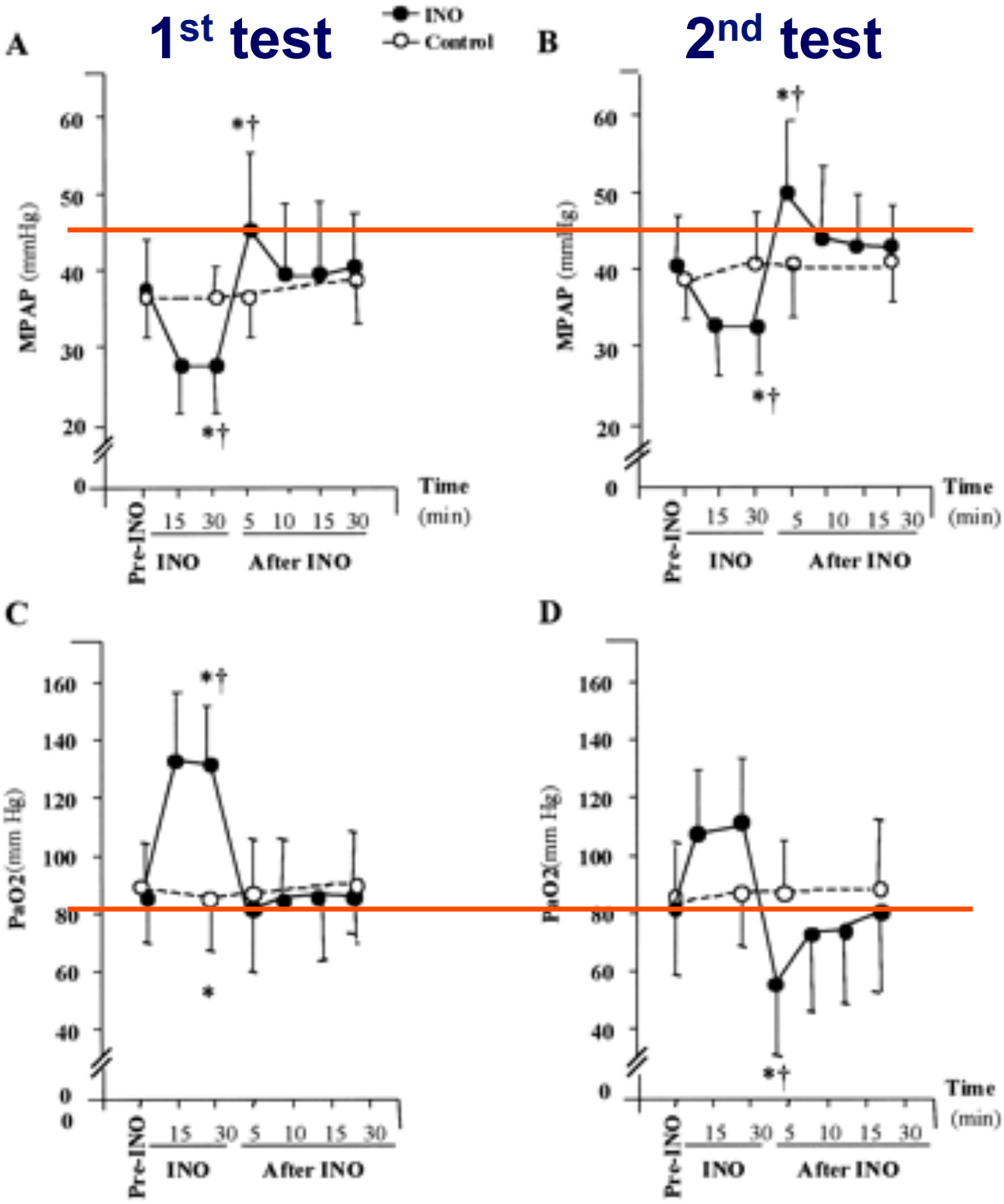
- Anti-inflammatory effects…
- Easy to start…

Rebound effect

*$p < 0.05$ vs pre-INO

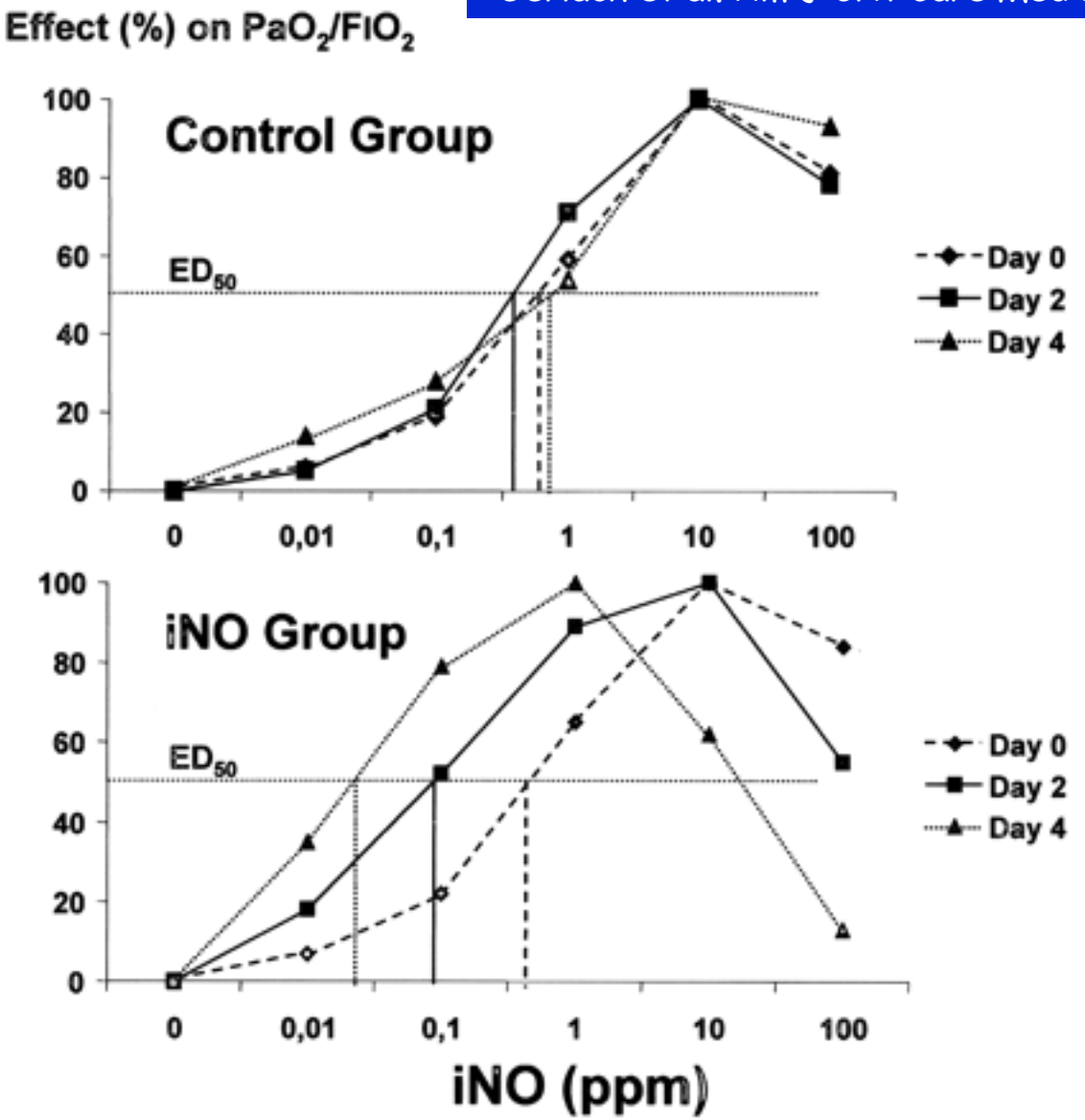
† $p < 0.05$ vs control

Chen *et al.* AJP 2001



Daily re-evaluation of the dose

Gerlach et al. Am J Crit Care Med 2003

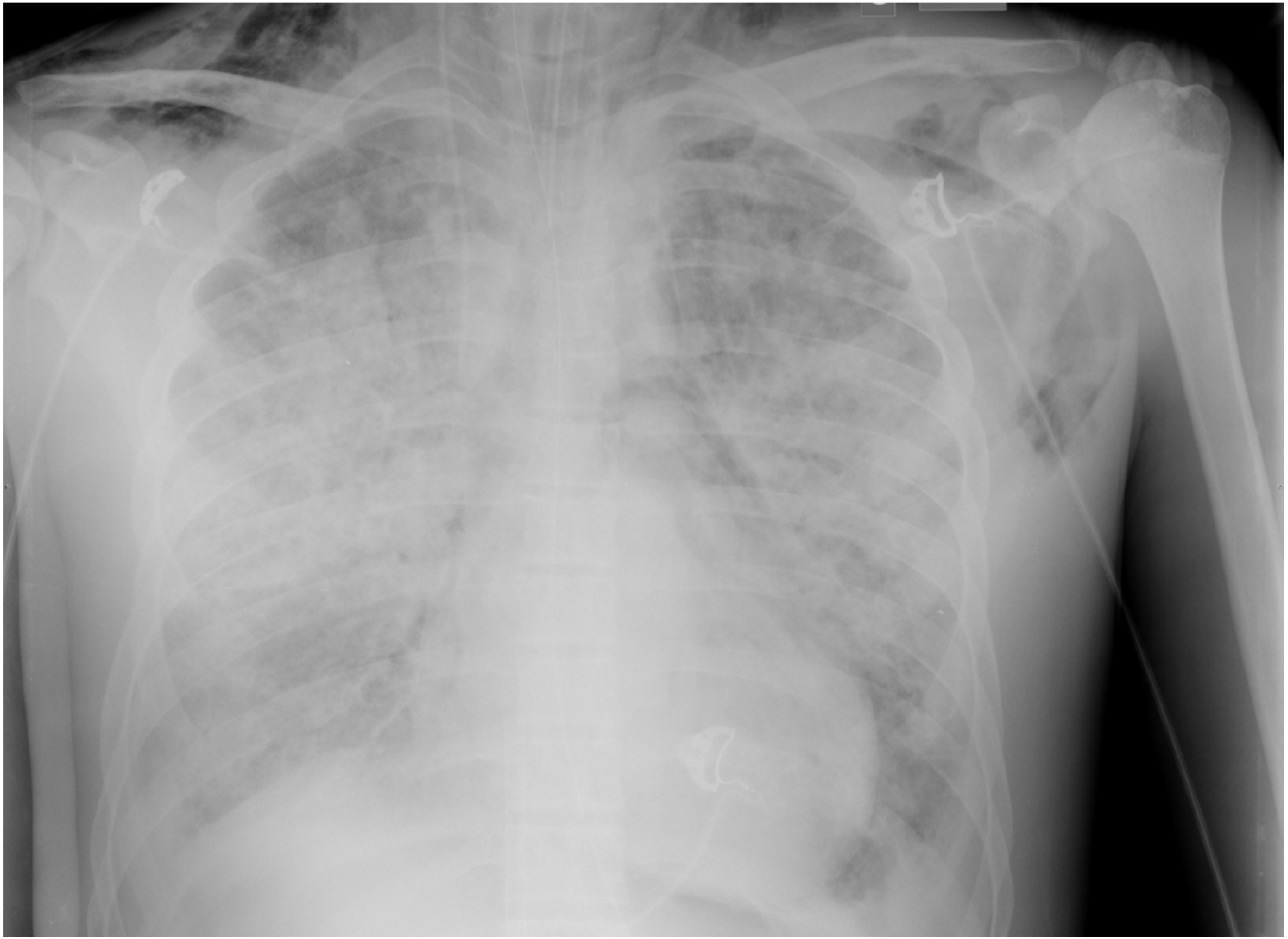


RCTs

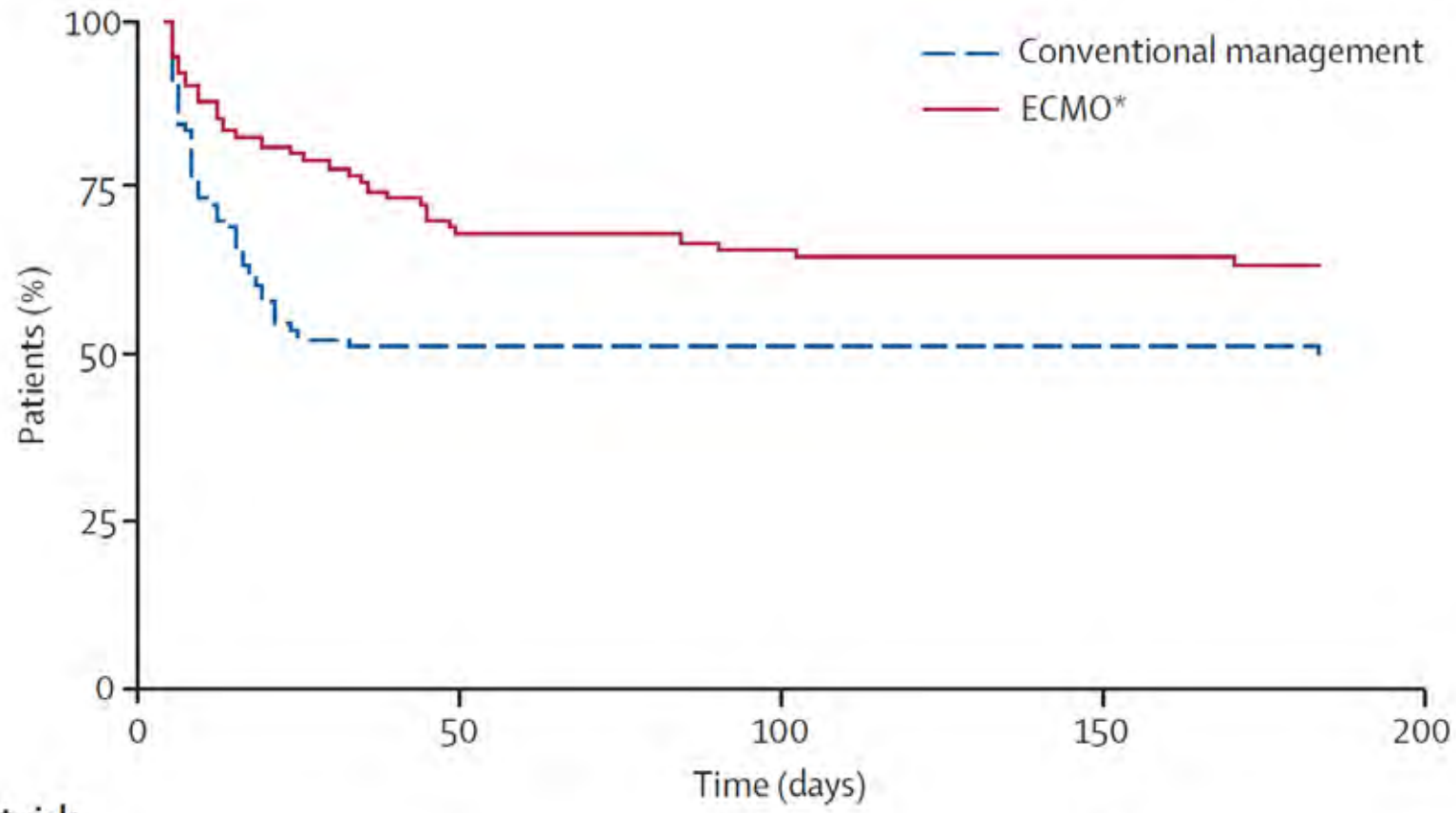
	n	% R	talité
Dellinger CCM 98	177		32/30
Lundin ICM 99		67%	44/41
Payen	203	60%	68/66
Taylor 2004	385	?	23/21

In severe ARDS ventilated according to a lung protective strategy?

Hello boss! I'm sorry… the P/F ratio is still at 60!



Death or dependency et 6 months



Patients at risk					
Conventional management	90	45	44	44	0
ECMO*	90	61	59	58	0

Peek et al. Lancet 2009

ECMO centers

- Hypoxemia
  - PaO2/FiO2<50
  - PEEP>15-20 cmH2O
  - + PP +/- iNO
- Injurious MV
  - PaO2/FiO2 70-100 (FiO2=1)
    - Pplat ≥ 35 cmH2O
    - And/or respiratory acidosis (pH < 7,15)
  - Despite ↘ PEEP
  - Despite ↘ Vt

Non-ECMO centers

- Hypoxemia
  - PaO2/FiO2<70
  - PEEP>15-20 cmH2O
- Injurious MV
  - PaO2/FiO2 70-100 (FiO2=1)
    - Pplat ≥ 35 cmH2O
    - And/or respiratory acidosis (pH < 7,15)
  - Despite ↘ PEEP
  - Despite ↘ Vt

ESERVE score: PRedicting dEath for SEvere ARDS VV-ECMO

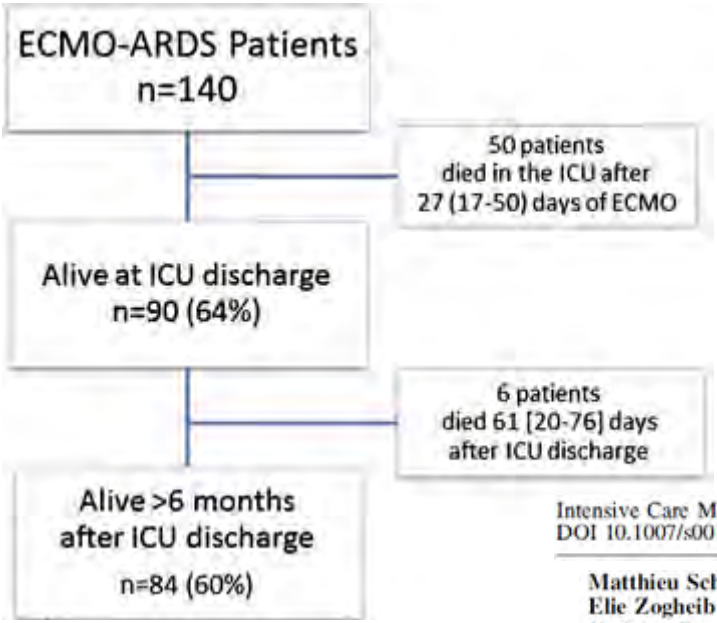


Table 3 Factors available at ECMO institution independently associated with death by 6 months post-ICU discharge

Factor	OR (95 % CI)	*p*-Value
Age	1.08 (1.04–1.12)	<0.001
Body mass index	0.90 (0.84–0.97)	0.004
Immunocompromised[a]	4.33 (1.55–12.12)	0.005
SAPS II[b]	1.04 (1.00–1.08)	0.028
Days of MV	1.07 (1.01–1.14)	0.015
No prone positioning before ECMO	2.93 (1.04–8.25)	0.043
PEEP, cm H_2O	0.84 (0.71–0.99)	0.039
Plateau pressure, cm H_2O	1.18 (1.05–1.32)	0.006

Intensive Care Med (2013) 39:1704–1713
DOI 10.1007/s00134-013-3037-2

SEVEN-DAY PROFILE PUBLICATION

Matthieu Schmidt
Elie Zogheib
Hadrien Rozé
Xavier Repesse
Guillaume Lebreton
Charles-Edouard Luyt
Jean-Louis Trouillet
Nicolas Bréchot
Ania Nieszkowska
Hervé Dupont
Alexandre Ouattara
Pascal Leprince
Jean Chastre
Alain Combes

The PRESERVE mortality risk score and analysis of long-term outcomes after extracorporeal membrane oxygenation for severe acute respiratory distress syndrome

one position is not always used prior ECMO

	Paris/Bordeaux Amiens	ECMOnet	ANZ ECMO	Provence/Alps Corsica	Paris/Sidney Melbourne
N	140	60	68	85	168
Prone pos, %	59	27	20	45	26
iNO, %	91	17	32	60	44
HFOV, %	1	7	5	5	4

Schmidt *et al.* Intensive Care Med 2013

Patroniti *et al.* Intensive Care Med 2011

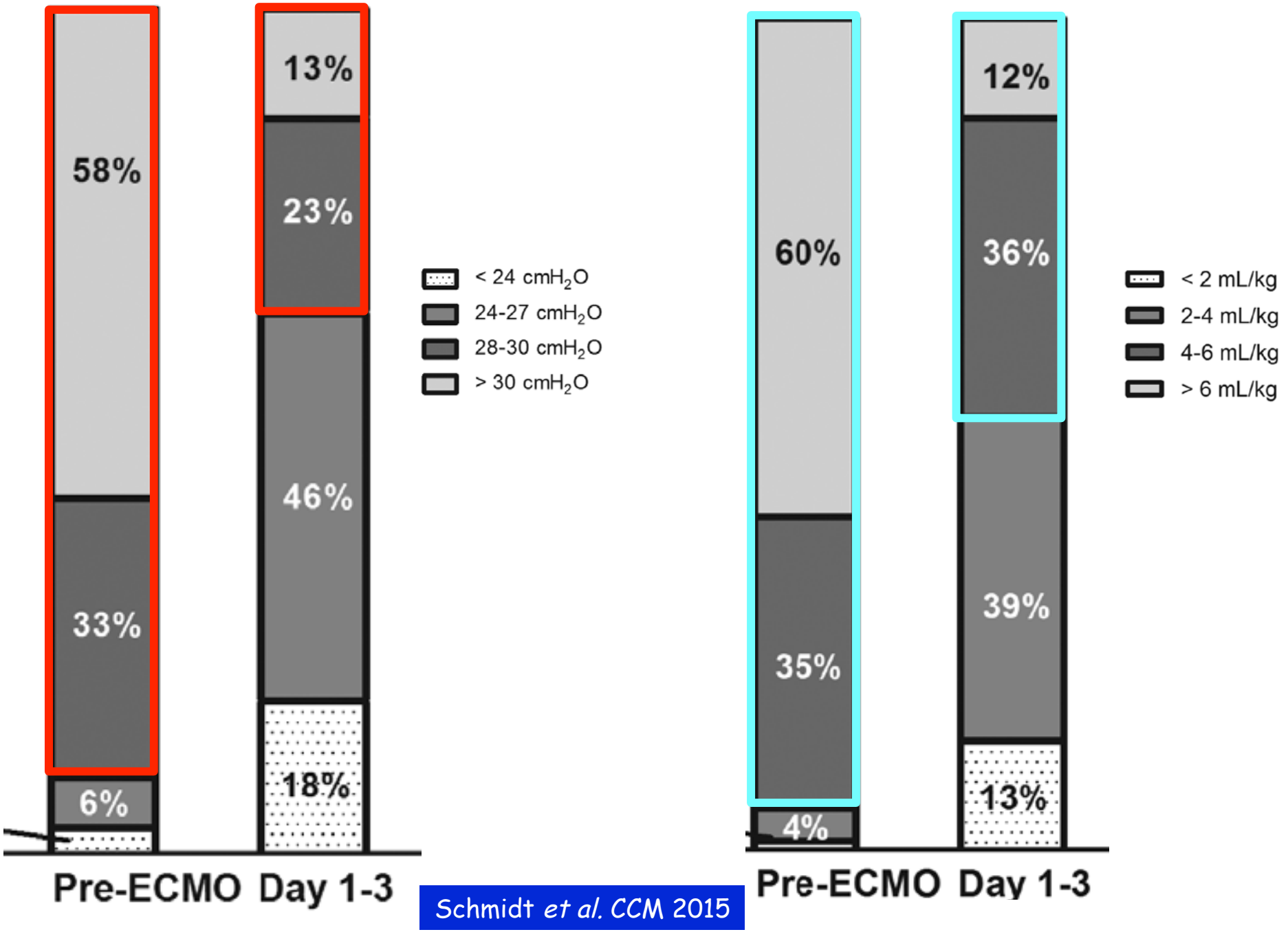
ANZ ECMO JAMA 2009

Roch *et al.* Intensive Care Med 2014

Schmidt *et al.* Crit Care Med 2015

ECMO: key points

- Even in specialized ICUs, indications are rare
- Side effects
- Specificity of MV settings
- Learning curve
- = dedicated specialized ECMO centers



Schmidt *et al. CCM 2015*

Inter-hospital transport under ECMO

UMAC-UMAREC

Unité Mobile d'Assistance Respiratoire Extra-Corporelle

Potentially eligible patients

(In CTC[1], or RH[2] prepared to refer to CTC or ECMO[3] centre)

- severe, but potentially reversible respiratory failure:
  Murray score≥2.5
  or
  uncompensated hypercapnoea with a pH <7.20
- aged 18-65 years
- duration of high pressure and/or high FIO_2 ventilation ≤ 7 days
- no intra-cranial bleeding
- no contra-indication to limited heparinisation
- no contra-indication to continuation of active treatment

Registration

Referring intensivist telephones clinical advisory team

- confirm that the patient is potentially eligible for trial
- confirm beds available (held for at least 2 hours) for
  - ECMO
    and
  - conventional management in CTC

Randomisation

- *potentially eligible patient becomes eligible (i.e. Murray score ≥ 3)*
- *Assent procedure completed.*
- **referring intensivist telephones clinical advisory team**
- provides details or identification and prognostic factors
- clinical advisor 'phones independent central randomisation service for random allocation
- clinical advisor 'phones referring intensivist
  - reveals allocation
- consideration of ECMO — ECMO Centre
- continued conventional treatment — in CTC
- If necessary arranges collection of patient
  - from CTC or RH to ECMO, or
  - from RH to CTC

Outcome measures

Primary

Death or severe disability at six months (defined as death by 6 months or before discharge from hospital at any time to end of data collection, or where the answer to the first two questions of the Euroqol questionnaire (EQ5D) are 'confined to bed' and 'unable to wash or dress yourself').

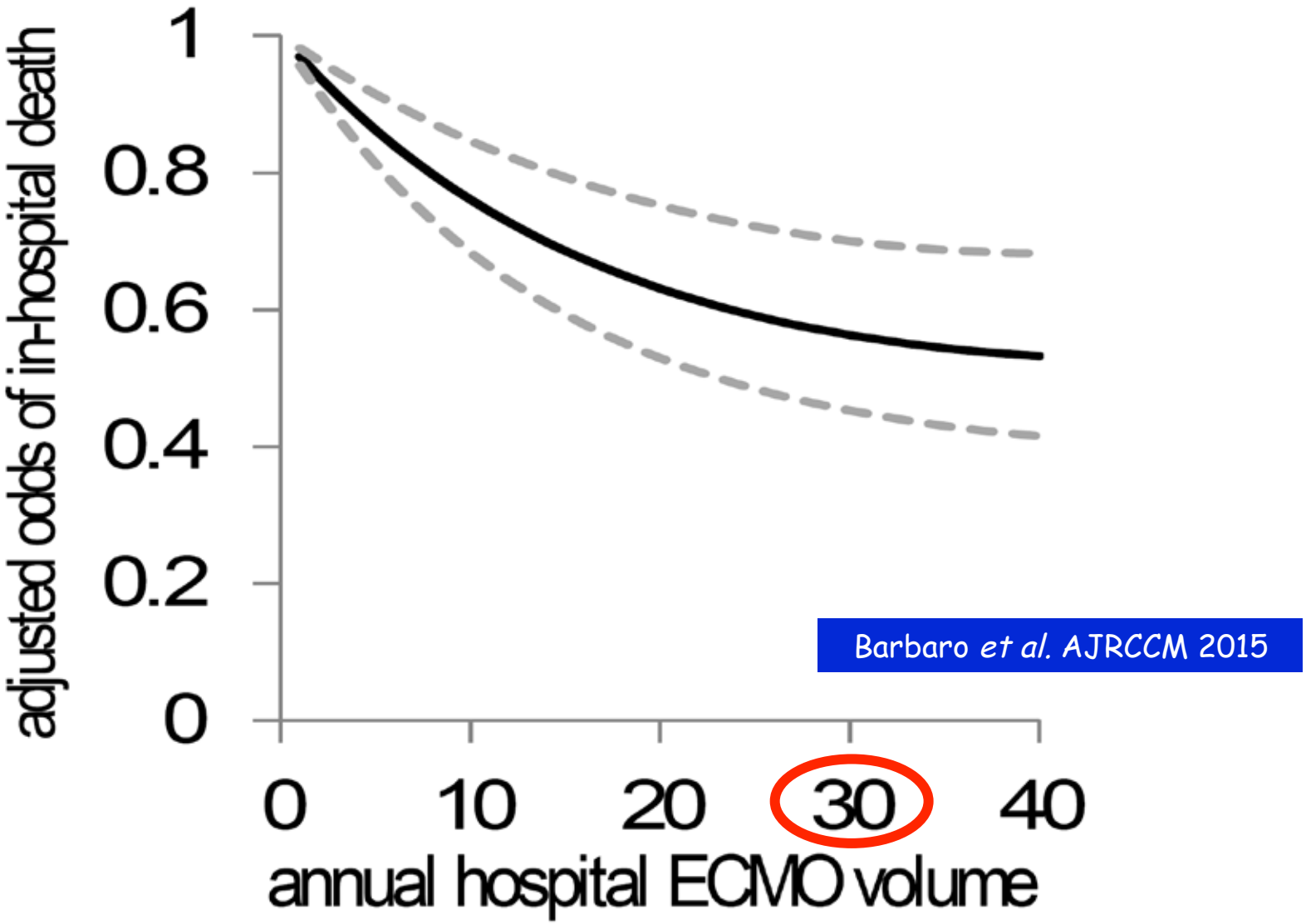
N = 180

Peek et al. Lancet 2009

CESAR

Conventional Ventilation or ECMO for Severe Adult Respiratory Failure

Higher annual hospital ECMO volume is associated with lower mortality



Barbaro *et al.* AJRCCM 2015

deux mots

- ↘ iatrogénie
- ↘ Vt
- ↘ objectifs PaO2 et PaCO2
- SDRA sévère
  - Personnalisation PEEP
  - Limitation pression de plateau
  - Curarisation de courte durée
  - DV
- …

laurent.papazian@ap-hm.fr

Potentially eligible patients

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  or
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N = 180

Peek et al. Lancet 2009

Conventional Ventilation or ECMO for Severe Adult Respiratory Failure

www.jrur.org

10 ANS

Journée RÉANIMATION ET URGENCES RESPIRATOIRES

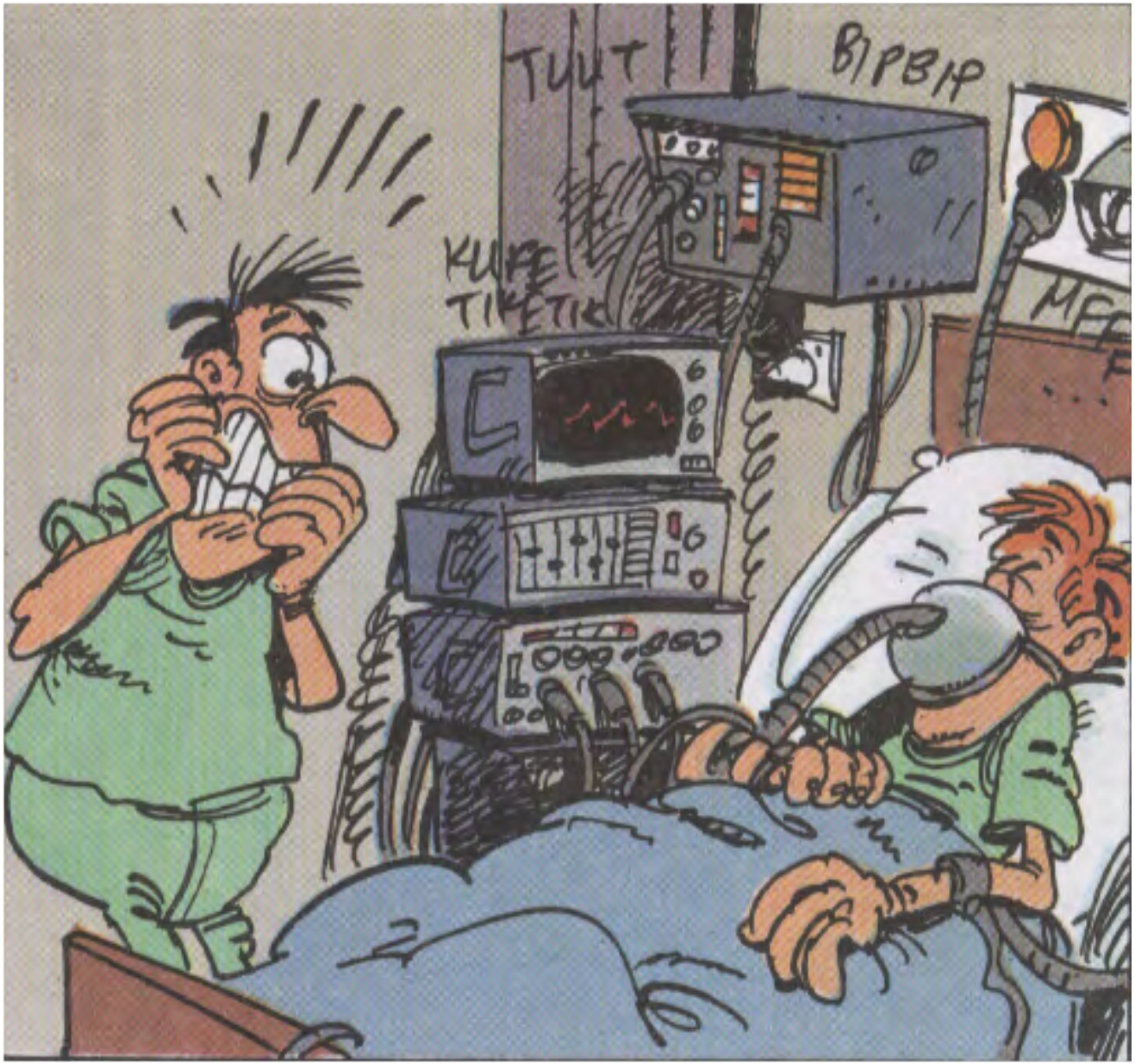
RETENEZ CETTE DATE ! Jeudi 11 Avril 2013 Marseille

LIEU DU CONGRÈS
Mercure Centre
1 rue Neuve Saint-Martin
Marseille

Conférences
Symposium
Ateliers

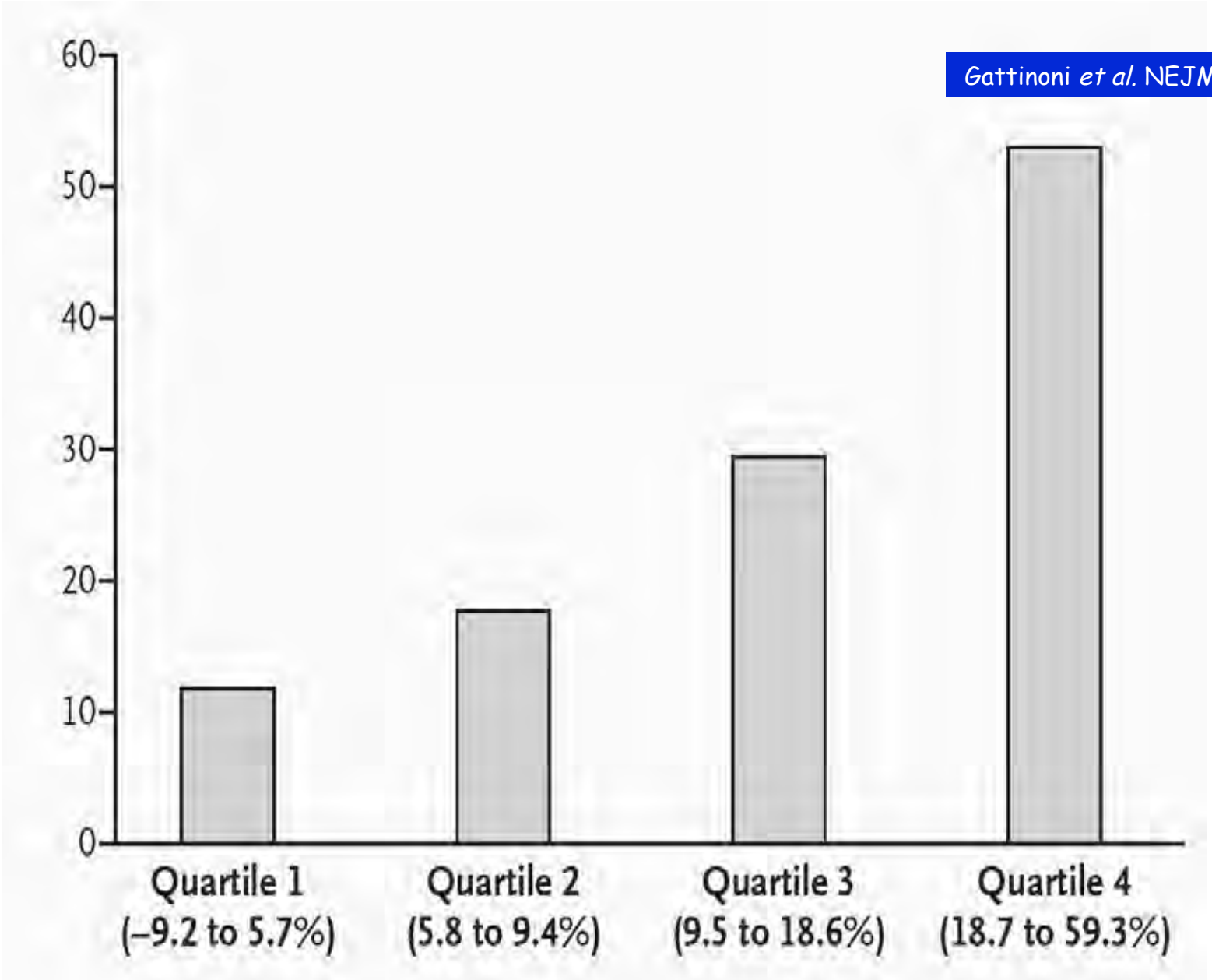
Avec le soutien de la Société de Réanimation de Langue Française

Organisation générale & inscription : Agence AToutT.Com
Tél : 04 42 54 42 60 - jrur@atoutcom.com - www.atoutcom.com


TUUT
BIPBIP

Recrutement = ↘ mortalité ?

Gattinoni *et al.* NEJM 2006



The NEW ENGLAND JOURNAL of MEDICINE

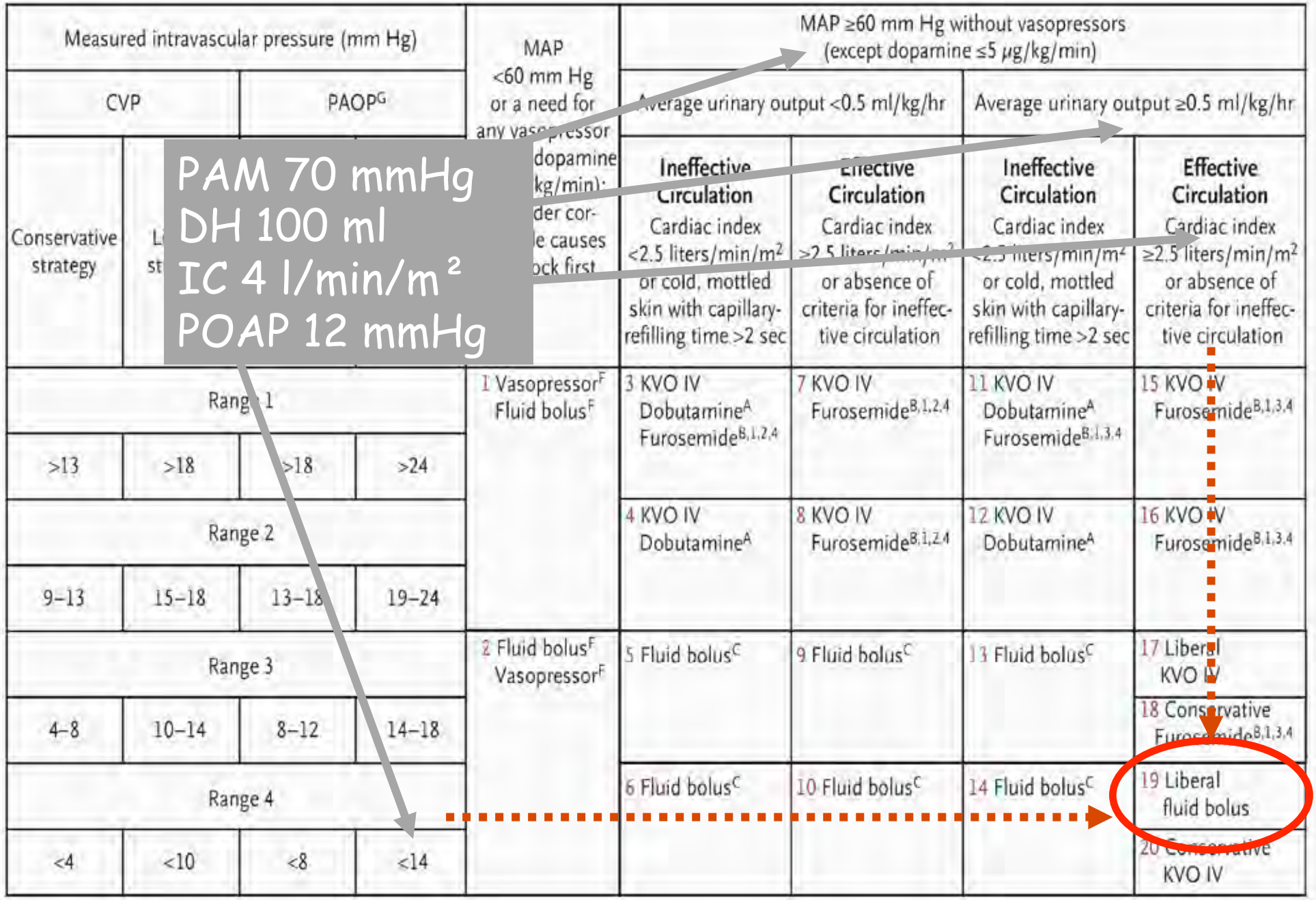
ORIGINAL ARTICLE

Comparison of Two Fluid-Management Strategies in Acute Lung Injury

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

N Engl J Med 2006;354.

Measured intravascular pressure (mm Hg)				MAP <60 mm Hg or a need for any vasopressor (except dopamine ≤5 μg/kg/min); consider correctable causes of shock first	MAP ≥60 mm Hg without vasopressors (except dopamine ≤5 μg/kg/min)			
CVP		PAOP[G]			Average urinary output <0.5 ml/kg/hr		Average urinary output ≥0.5 ml/kg/hr	
Conservative strategy	Liberal strategy	Conservative strategy	Liberal strategy		**Ineffective Circulation** Cardiac index <2.5 liters/min/m² or cold, mottled skin with capillary-refilling time >2 sec	**Effective Circulation** Cardiac index ≥2.5 liters/min/m² or absence of criteria for ineffective circulation	**Ineffective Circulation** Cardiac index <2.5 liters/min/m² or cold, mottled skin with capillary-refilling time >2 sec	**Effective Circulation** Cardiac index ≥2.5 liters/min/m² or absence of criteria for ineffective circulation
Range 1				1 Vasopressor[F] Fluid bolus[F]	3 KVO IV Dobutamine[A] Furosemide[B,1,2,4]	7 KVO IV Furosemide[B,1,2,4]	11 KVO IV Dobutamine[A] Furosemide[B,1,3,4]	15 KVO IV Furosemide[B,1,3,4]
>13	>18	>18	>24					
Range 2					4 KVO IV Dobutamine[A]	8 KVO IV Furosemide[B,1,2,4]	12 KVO IV Dobutamine[A]	16 KVO IV Furosemide[B,1,3,4]
9–13	15–18	13–18	19–24					
Range 3				2 Fluid bolus[F] Vasopressor[F]	5 Fluid bolus[C]	9 Fluid bolus[C]	13 Fluid bolus[C]	17 Liberal KVO IV
4–8	10–14	8–12	14–18					18 Conservative Furosemide[B,1,3,4]
Range 4					6 Fluid bolus[C]	10 Fluid bolus[C]	14 Fluid bolus[C]	19 Liberal fluid bolus
<4	<10	<8	<14					20 Conservative KVO IV



Measured intravascular pressure (mm Hg)				MAP <60 mm Hg or a need for any vasopressor	MAP ≥60 mm Hg without vasopressors (except dopamine ≤5 μg/kg/min)			
CVP		PAOP[G]			Average urinary output <0.5 ml/kg/hr		Average urinary output ≥0.5 ml/kg/hr	
Conservative strategy	Li… st…				**Ineffective Circulation** Cardiac index <2.5 liters/min/m² or cold, mottled skin with capillary-refilling time >2 sec	**Effective Circulation** Cardiac index >2.5 liters/min/m² or absence of criteria for ineffective circulation	**Ineffective Circulation** Cardiac index <2.5 liters/min/m² or cold, mottled skin with capillary-refilling time >2 sec	**Effective Circulation** Cardiac index ≥2.5 liters/min/m² or absence of criteria for ineffective circulation
Range 1				1 Vasopressor[F] Fluid bolus[F]	3 KVO IV Dobutamine[A] Furosemide[B,1,2,4]	7 KVO IV Furosemide[B,1,2,4]	11 KVO IV Dobutamine[A] Furosemide[B,1,3,4]	15 KVO IV Furosemide[B,1,3,4]
>13	>18	>18	>24					
Range 2					4 KVO IV Dobutamine[A]	8 KVO IV Furosemide[B,1,2,4]	12 KVO IV Dobutamine[A]	16 KVO IV Furosemide[B,1,3,4]
9–13	15–18	13–18	19–24					
Range 3				2 Fluid bolus[F] Vasopressor[F]	5 Fluid bolus[C]	9 Fluid bolus[C]	13 Fluid bolus[C]	17 Liberal KVO IV
4–8	10–14	8–12	14–18					18 Conservative Furosemide[B,1,3,4]
Range 4					6 Fluid bolus[C]	10 Fluid bolus[C]	14 Fluid bolus[C]	19 Liberal fluid bolus
<4	<10	<8	<14					20 Conservative KVO IV

NIH NEJM 2006

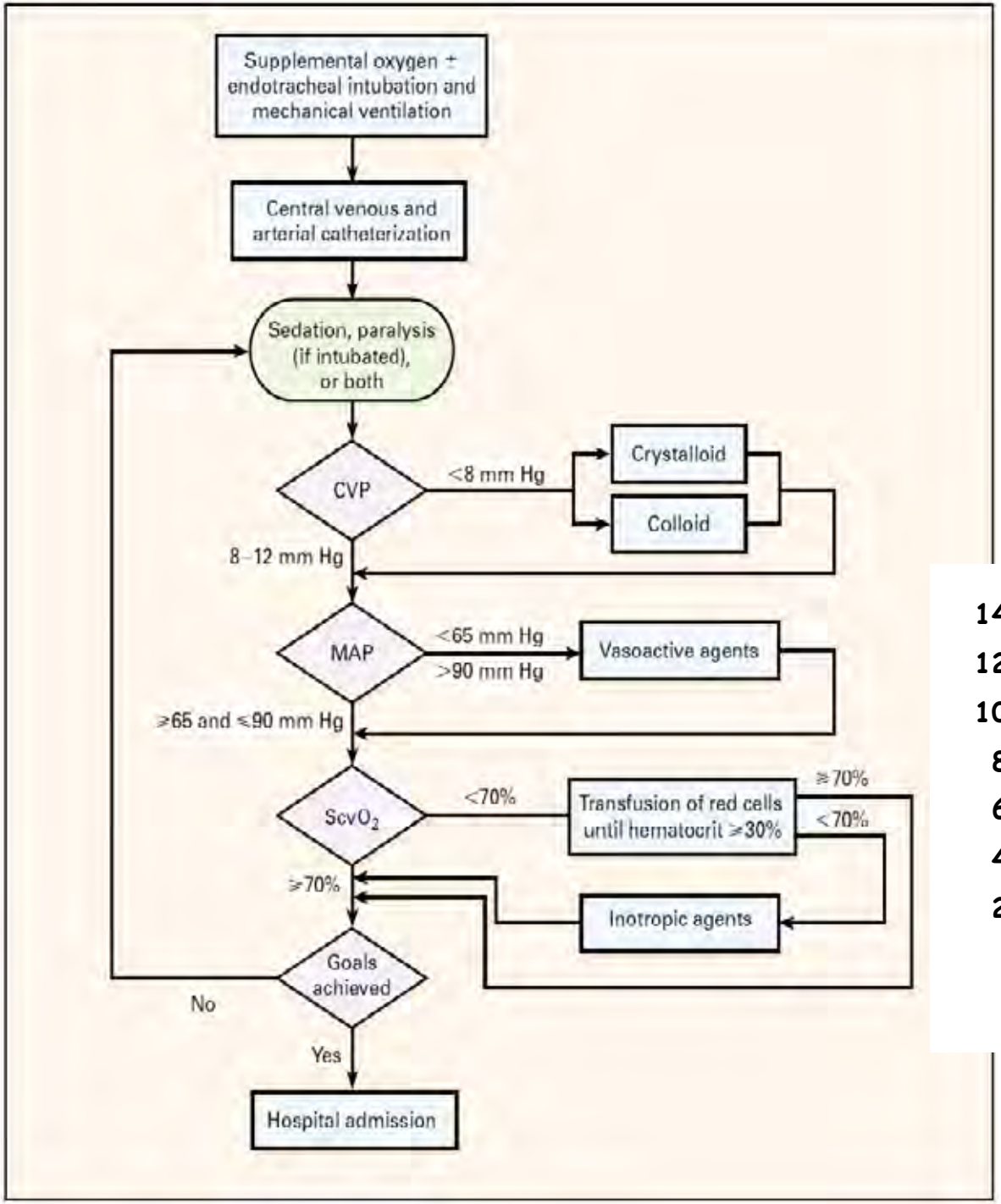
Outcome	Conservative Strategy	Liberal Strategy	P Value
Death at 60 days (%)	25.5	28.4	0.30
Ventilator-free days from day 1 to day 28†	14.6±0.5	12.1±0.5	<0.001
ICU-free days†			
Days 1 to 7	0.9±0.1	0.6±0.1	<0.001
Days 1 to 28	13.4±0.4	11.2±0.4	<0.001
Organ-failure–free days†‡			
Days 1 to 28			
Renal failure	21.5±0.5	21.2±0.5	0.59

EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

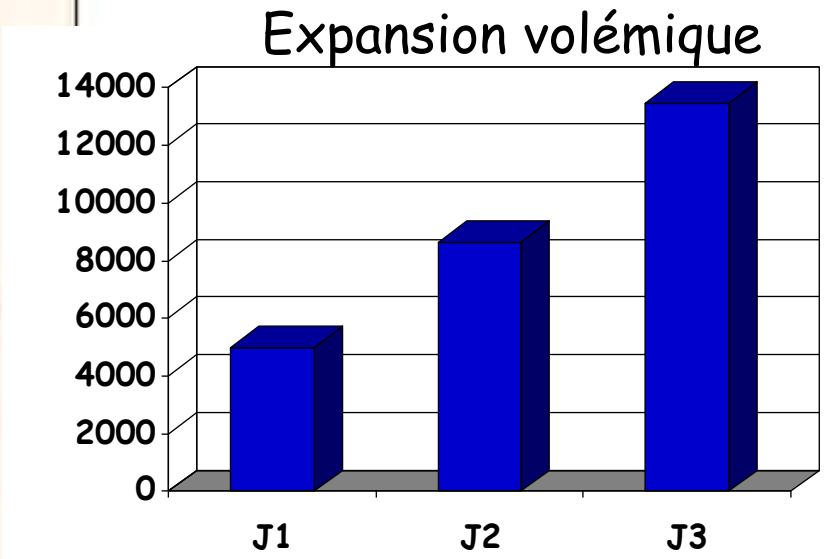
EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D., FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP*

KAPLAN–MEIER ESTIMATES OF MORTALITY AND CAUSES OF IN-HOSPITAL DEATH.*

VARIABLE	STANDARD THERAPY (N=133)	EARLY GOAL-DIRECTED THERAPY (N=130)	RELATIVE RISK (95% CI)	P VALUE
	no. (%)			
In-hospital mortality†				
All patients	59 (46.5)	38 (30.5)	0.58 (0.38–0.87)	0.009
Patients with severe sepsis	19 (30.0)	9 (14.9)	0.46 (0.21–1.03)	0.06
Patients with septic shock	40 (56.8)	29 (42.3)	0.60 (0.36–0.98)	0.04
Patients with sepsis syndrome	44 (45.4)	35 (35.1)	0.66 (0.42–1.04)	0.07
28-Day mortality†	61 (49.2)	40 (33.3)	0.58 (0.39–0.87)	0.01
60-Day mortality†	70 (56.9)	50 (44.3)	0.67 (0.46–0.96)	0.03



Rivers *et al.* NEJM 2001

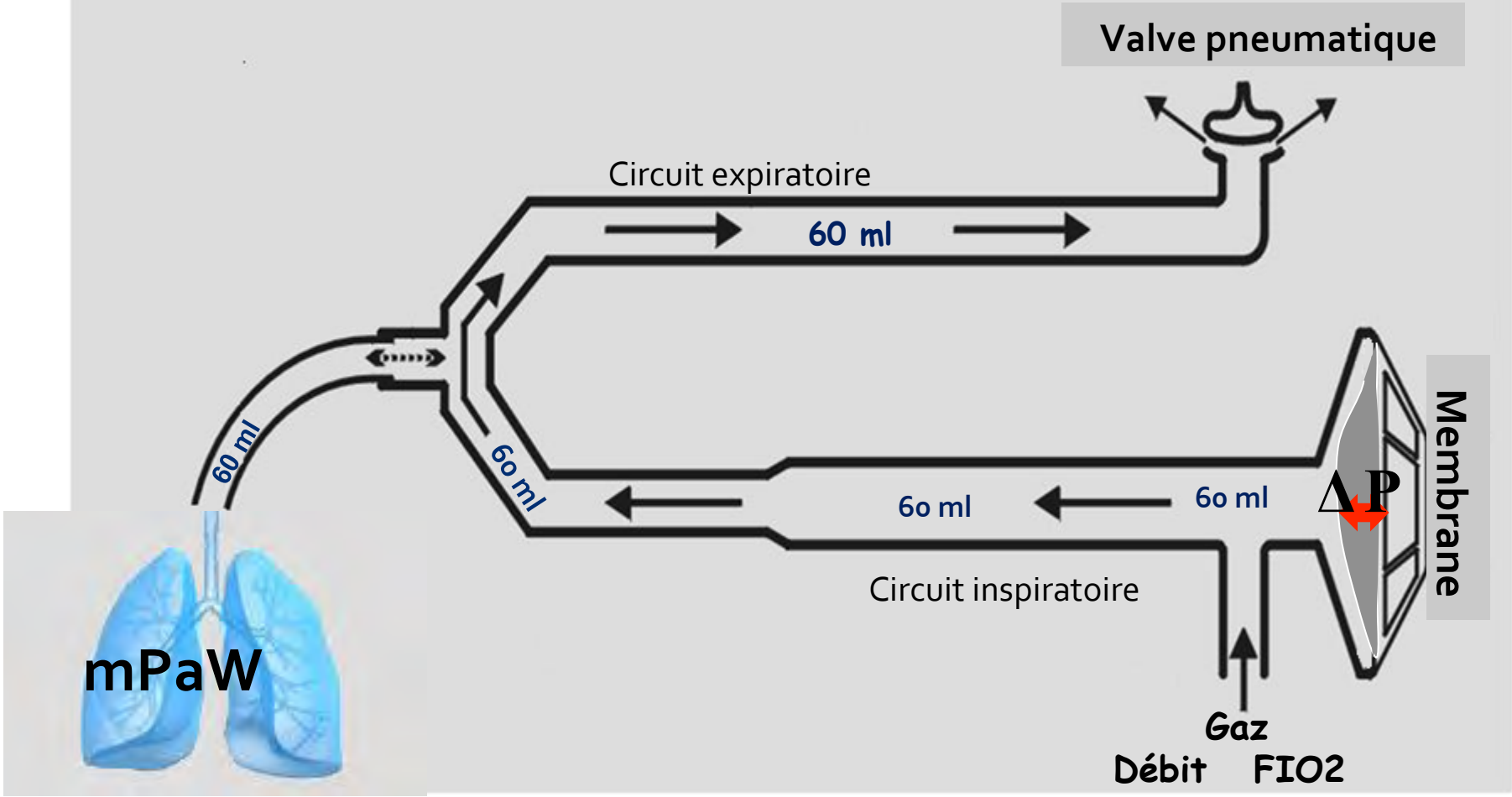


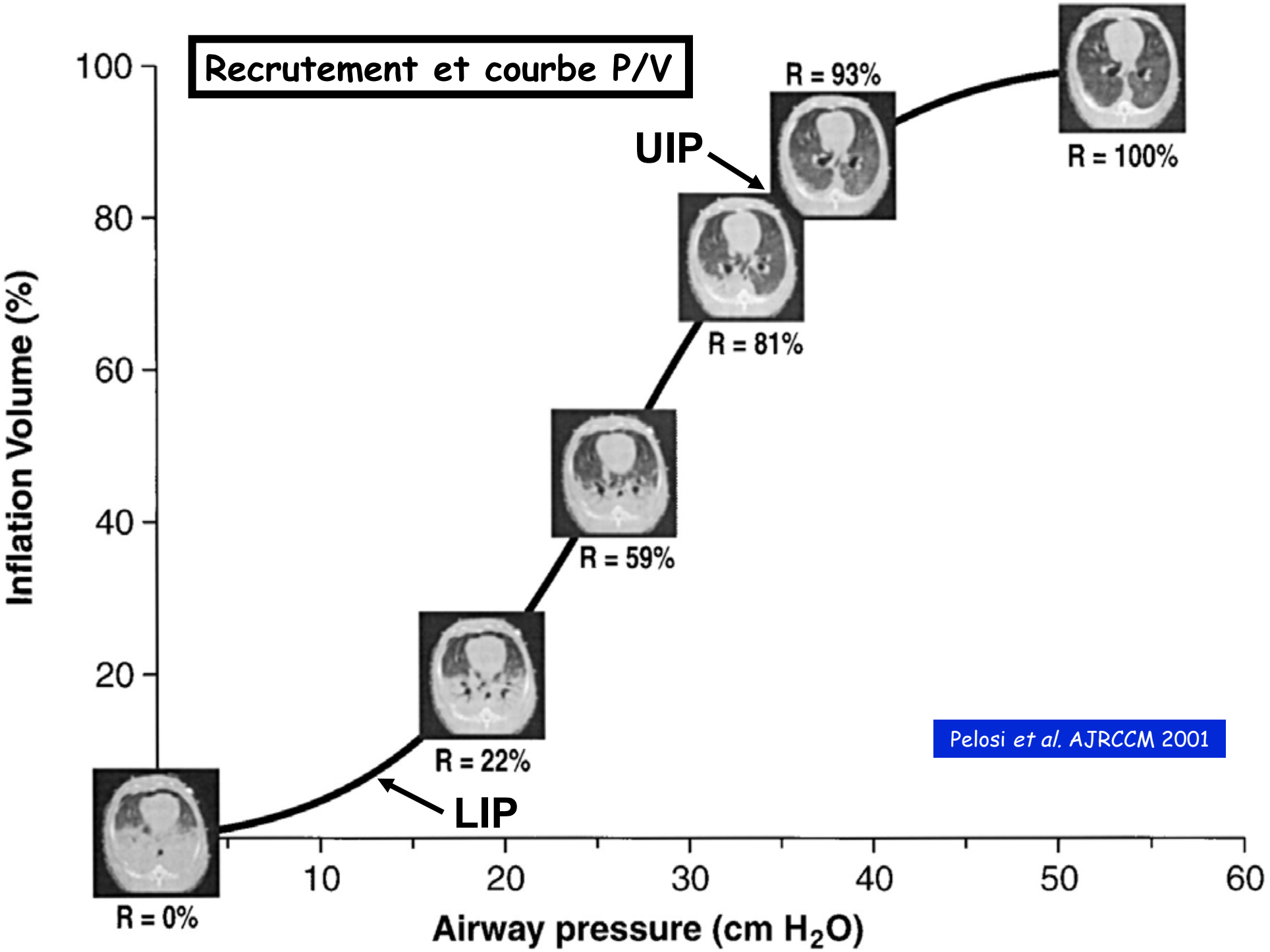
Take-home message

- Limiter la iatrogénie
- Réduction volume courant
- Plusieurs profils de patients
- Approche globale
  - Ajuster la PEEP en fonction de la présentation morphologique
  - Limiter pression de plateau
  - Curariser tôt mais brièvement les plus hypoxémiques
  - Eviter dérecrutement
  - Limiter les objectifs d'oxygénation
- Le reste…

Technique

- **mPaW et FIO2 →** recrutement alvéolaire **→ Oxygénation**
- **↗ΔP et ↘ FR →** ↗ amplitude oscillations **→ Epuration CO2**



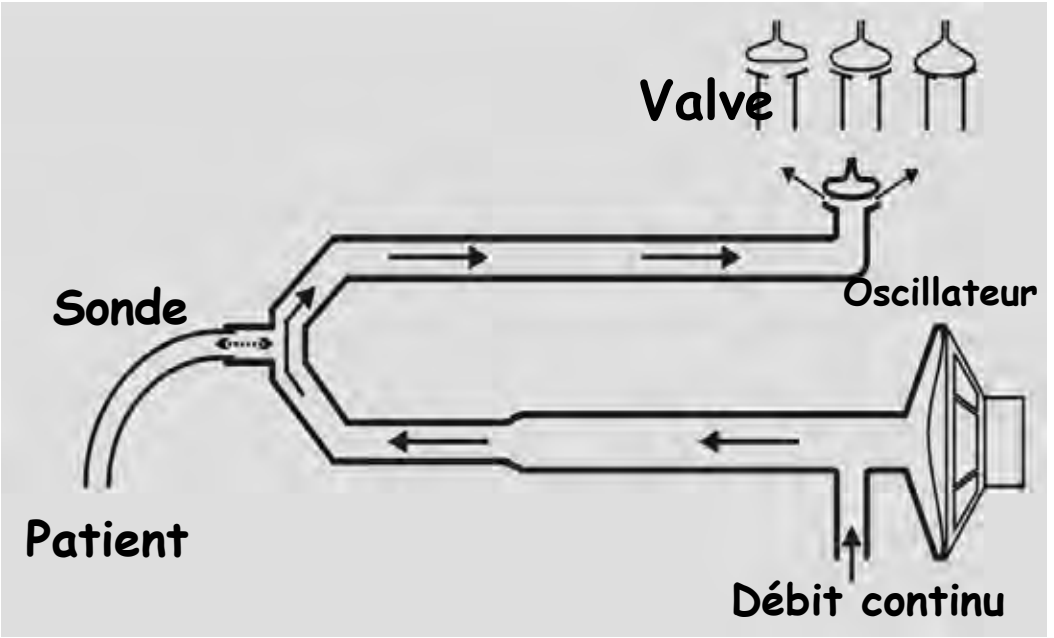

Recrutement et courbe P/V
100
80
60
40
20
Inflation Volume (%)
R = 93%
R = 100%
UIP
R = 81%
R = 59%
R = 22%
LIP
R = 0%
10
20
30
40
50
60
Airway pressure (cm H_2O)
Pelosi *et al.* AJRCCM 2001

Différences entre VC et HFO

	VC	HFO
Fréquence respiratoire, cycles/min	5-150	180-900
Volume courant, ml/kg	3-10	0,5-4
ΔP alvéolaire, cmH2O	10-30	0,1-5

Phase II

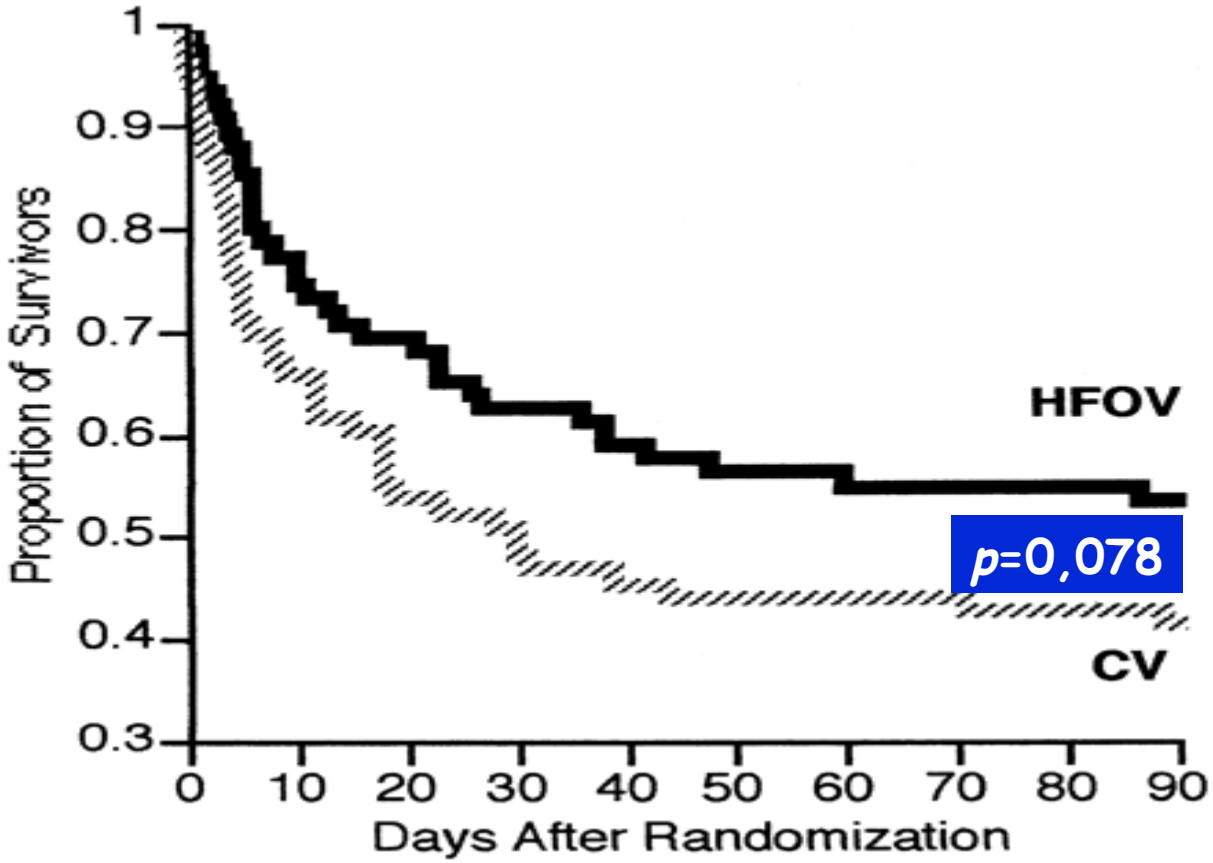
Derdak *et al.* AJRCCM 2002



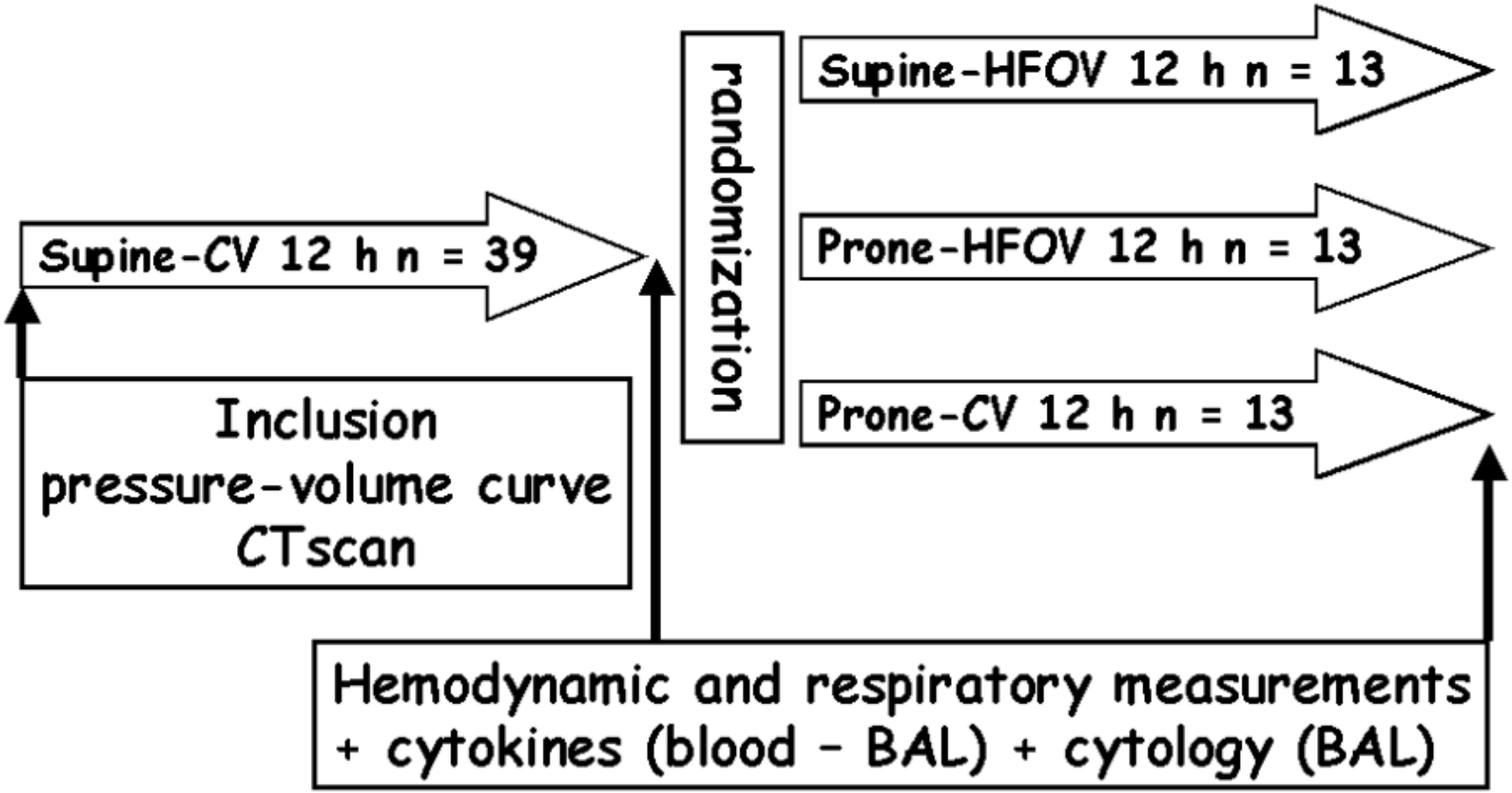
- USA et Canada
- n = 148 en 3 ans
- SDRA < 200 à PEEP 10
- exclusion: FiO2 > 0,8 / 48 h
- randomisation vs VM conventionnelle

Résultats

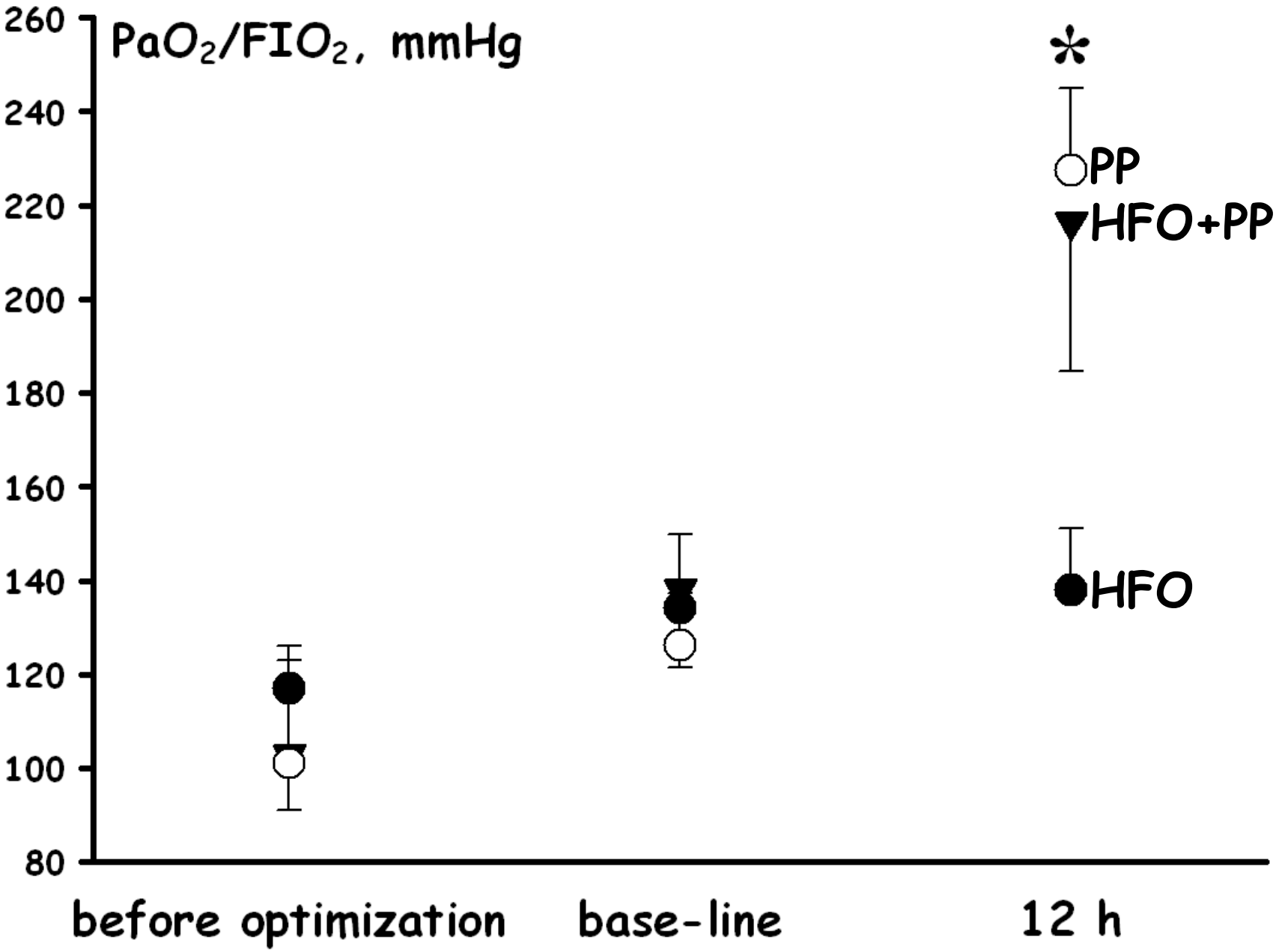
Mortalité	HFO	VMC
J30	*p*=0,057	
6 mois		



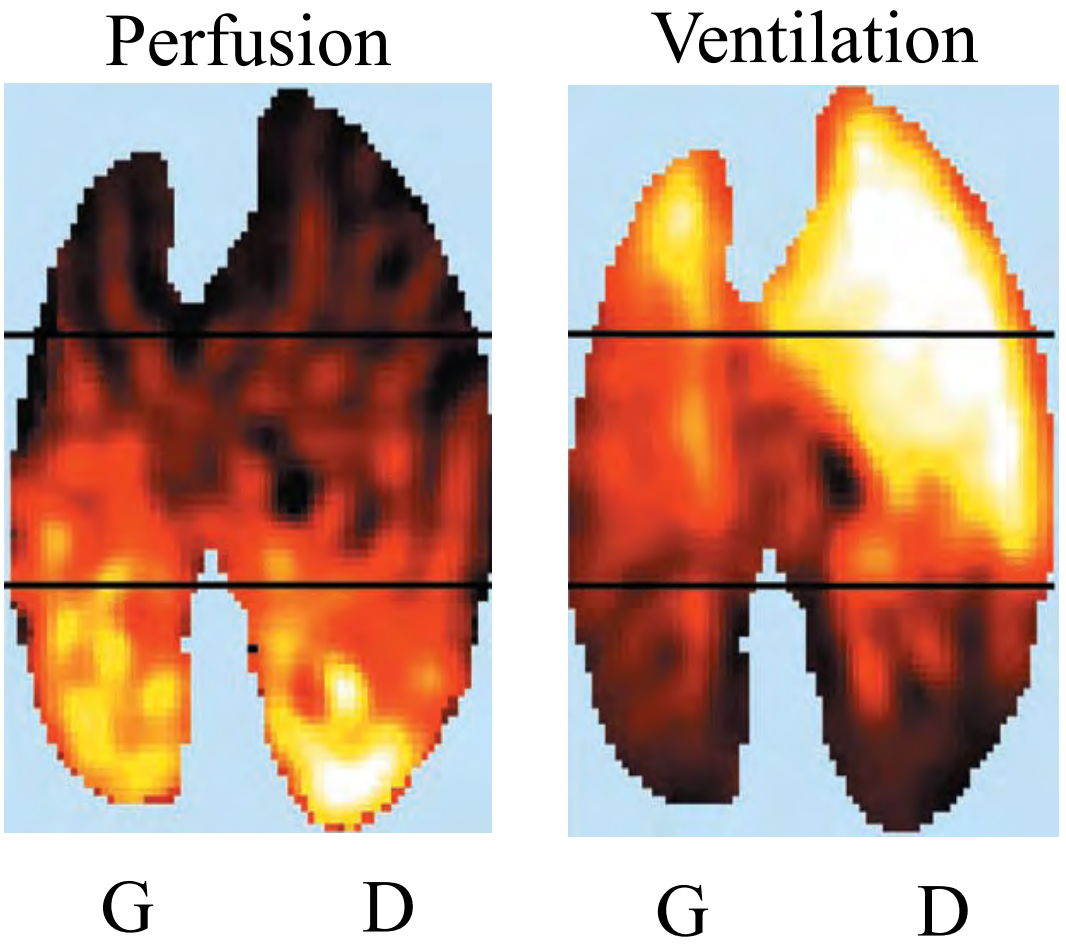
Derdak *et al.* AJRCCM 2002



Papazian *et al.* Crit Care Med 2005

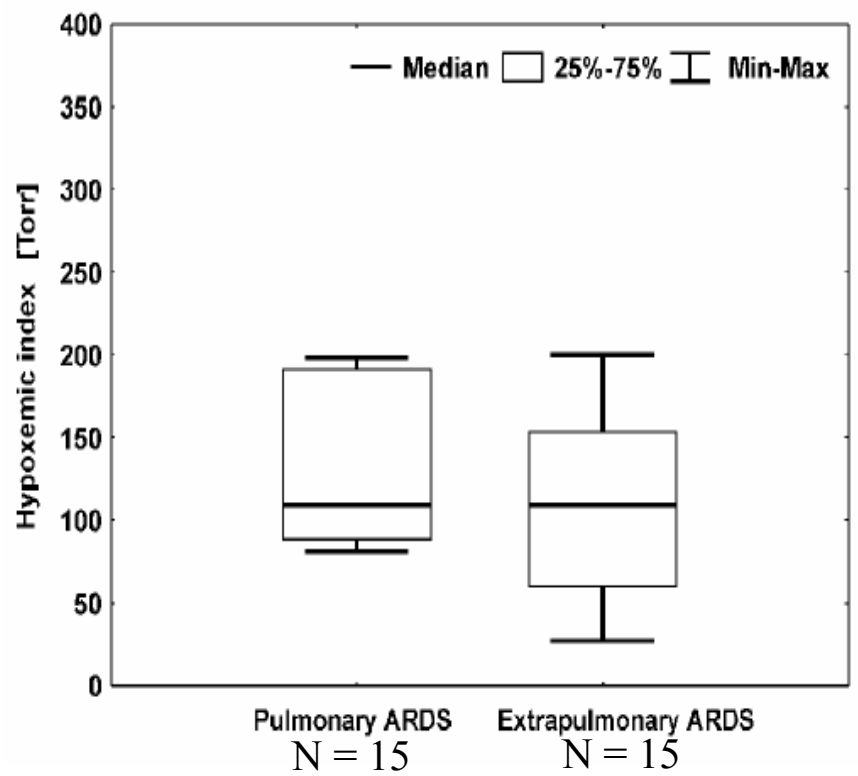

260
240
220
200
180
160
140
120
100
80
PaO2/FIO2, mmHg
*
PP
HFO+PP
HFO
before optimization
base-line
12 h

Hypoxémie au cours de l'HFO

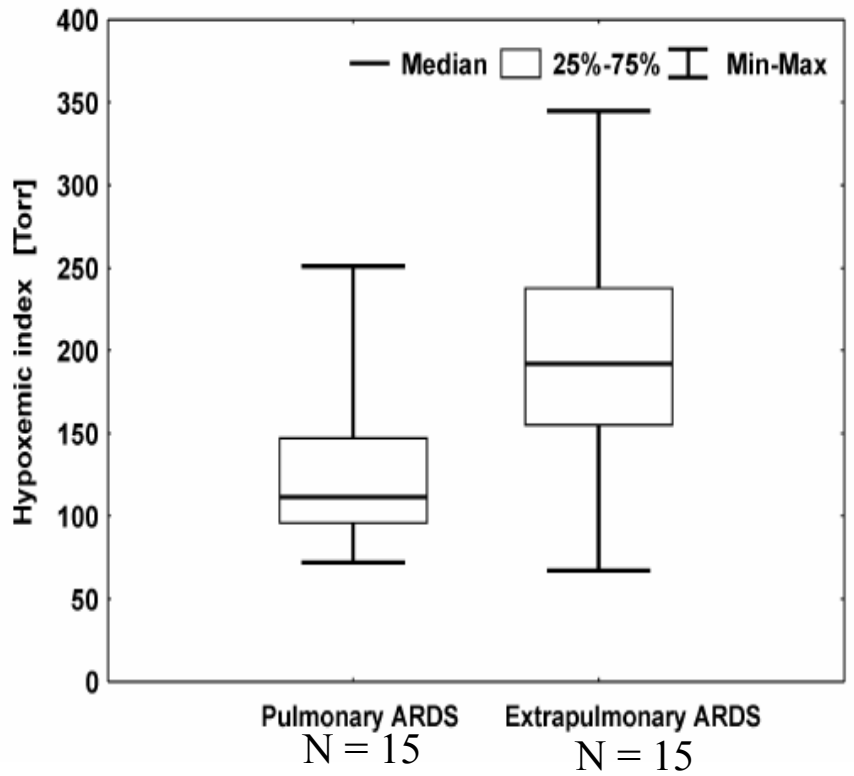


Musch *et al.* Crit Care Med 2004

Importance du type de SDRA



avant HFO

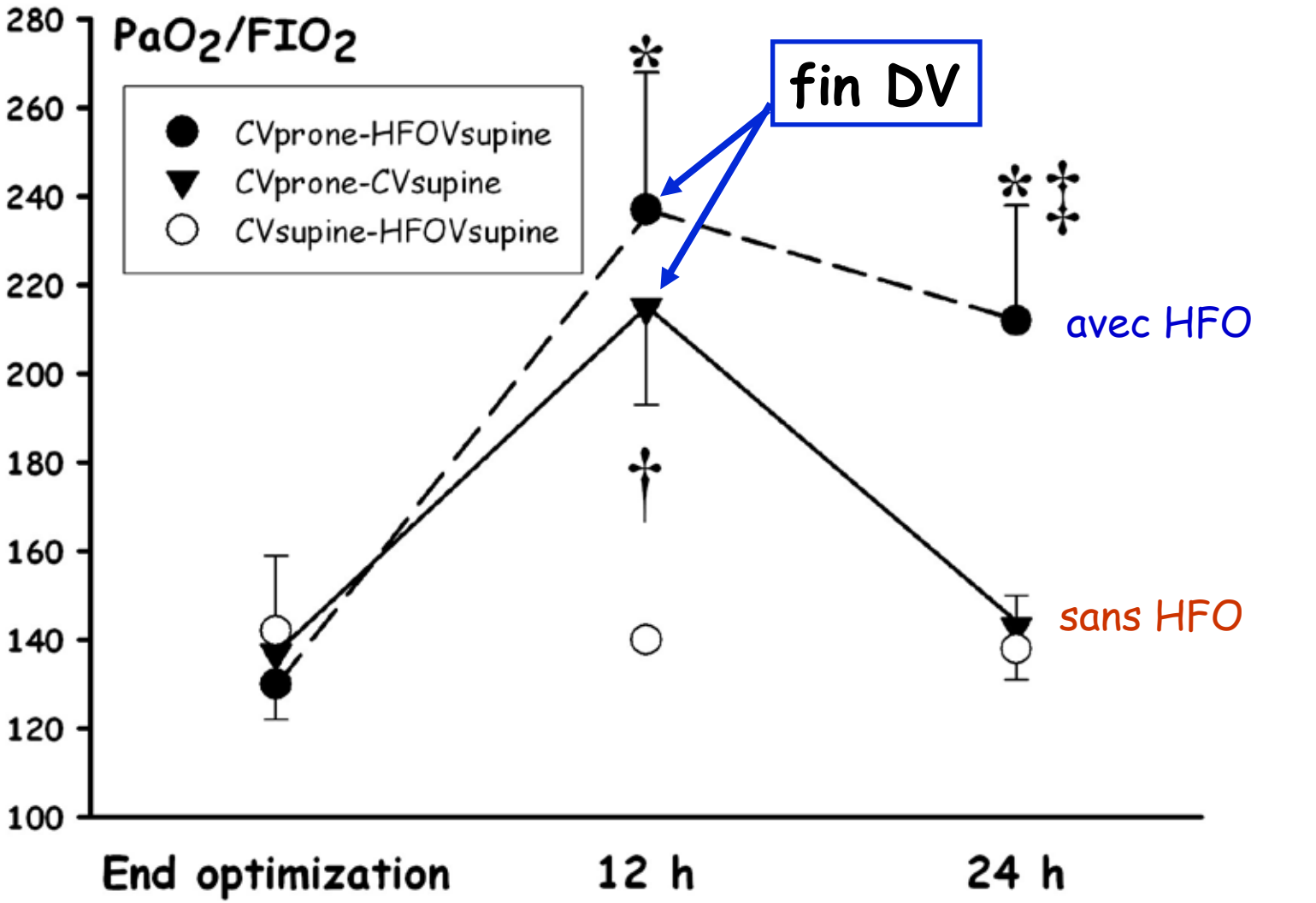


après 6h HFO

Pachl *et al.* Physiol Res 2006

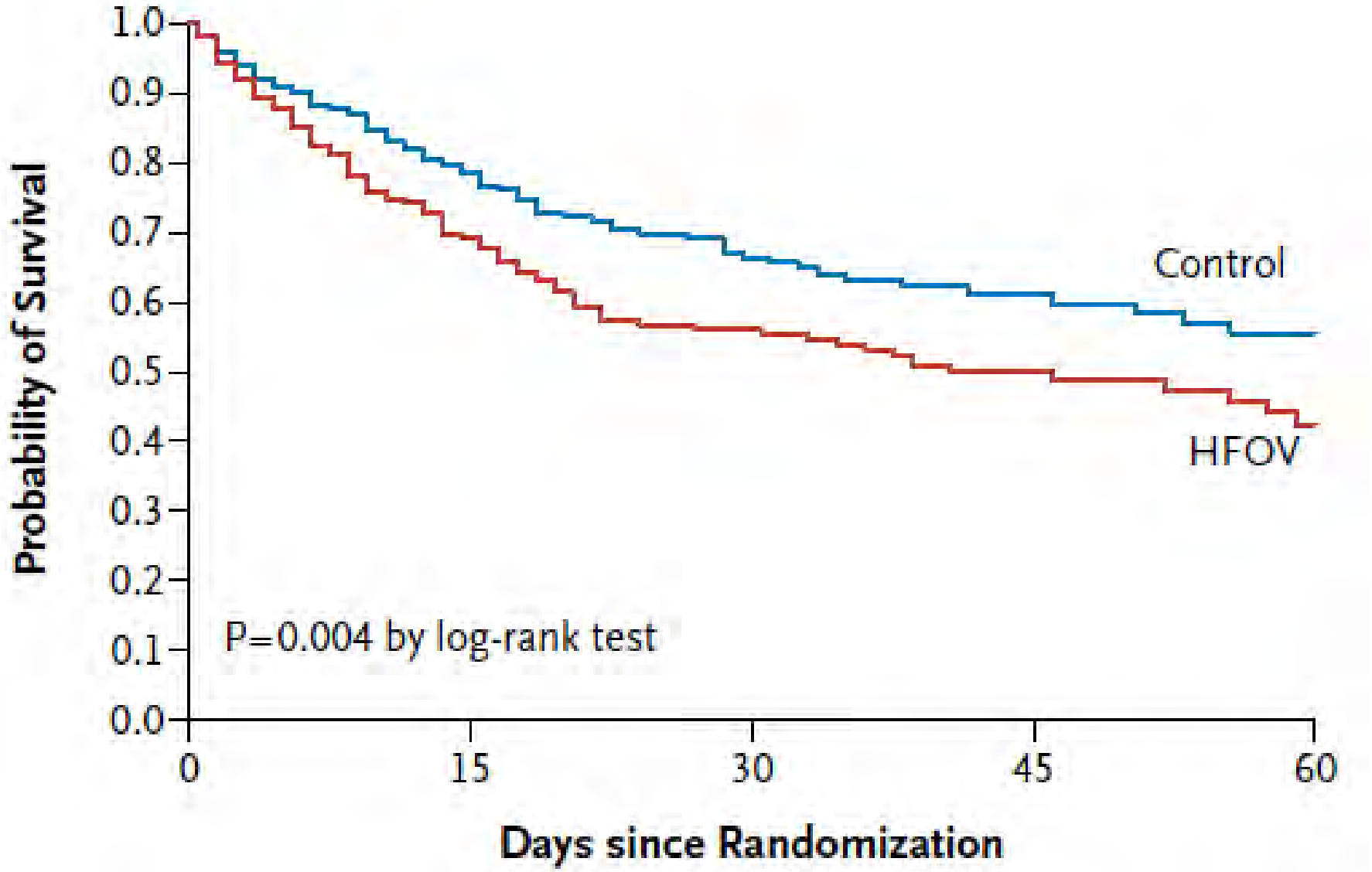
DV et recrutement

Demory et al. CCM 2007



Ferguson *et al.* NEJM 2013

Characteristic	HFOV Group (N=275)	Control Group (N=273)	Patients Eligible but Not Enrolled (N=472)†	P Value‡
Age — yr	55±16	54±16	53±16	0.18
Female sex — no. (%)	108 (39)	120 (44)	198 (42)	0.42
APACHE II score§	29±8	29±7	26±8	<0.001
Duration of hospital stay — days	5.6±8.0	4.9±8.0		
Duration of mechanical ventilation — days	2.5±3.3	1.9±2.3		
Risk factors for ARDS — no. of patients (%)				
Sepsis	128 (47)	130 (48)	193 (41)	0.01
Pneumonia	155 (56)	164 (60)	289 (61)	0.37
Gastric aspiration	49 (18)	44 (16)	51 (11)	0.02
Trauma	10 (4)	5 (2)	24 (5)	0.07
Other	71 (26)	67 (25)	137 (29)	0.34
Tidal volume — ml/kg of predicted body weight	7.2±1.9	7.1±1.8		
Plateau pressure — cm of water	29±6	29±7	27±7	<0.001
Set PEEP — cm of water	13±3	13±4	11±4	<0.001
Minute ventilation — liters/min	11.3±3.1	11.2±3.3		
Oxygenation index	19.6±11.2	19.9±9.3	17.8±10.2	0.002
Pao_2:FIo_2 ratio — mm Hg	121±46	114±38	118±47	0.17
Pao_2 — mm Hg	46±13	47±14	45±14	0.01
Arterial pH	7.32±0.10	7.31±0.10	7.32±0.12	0.06



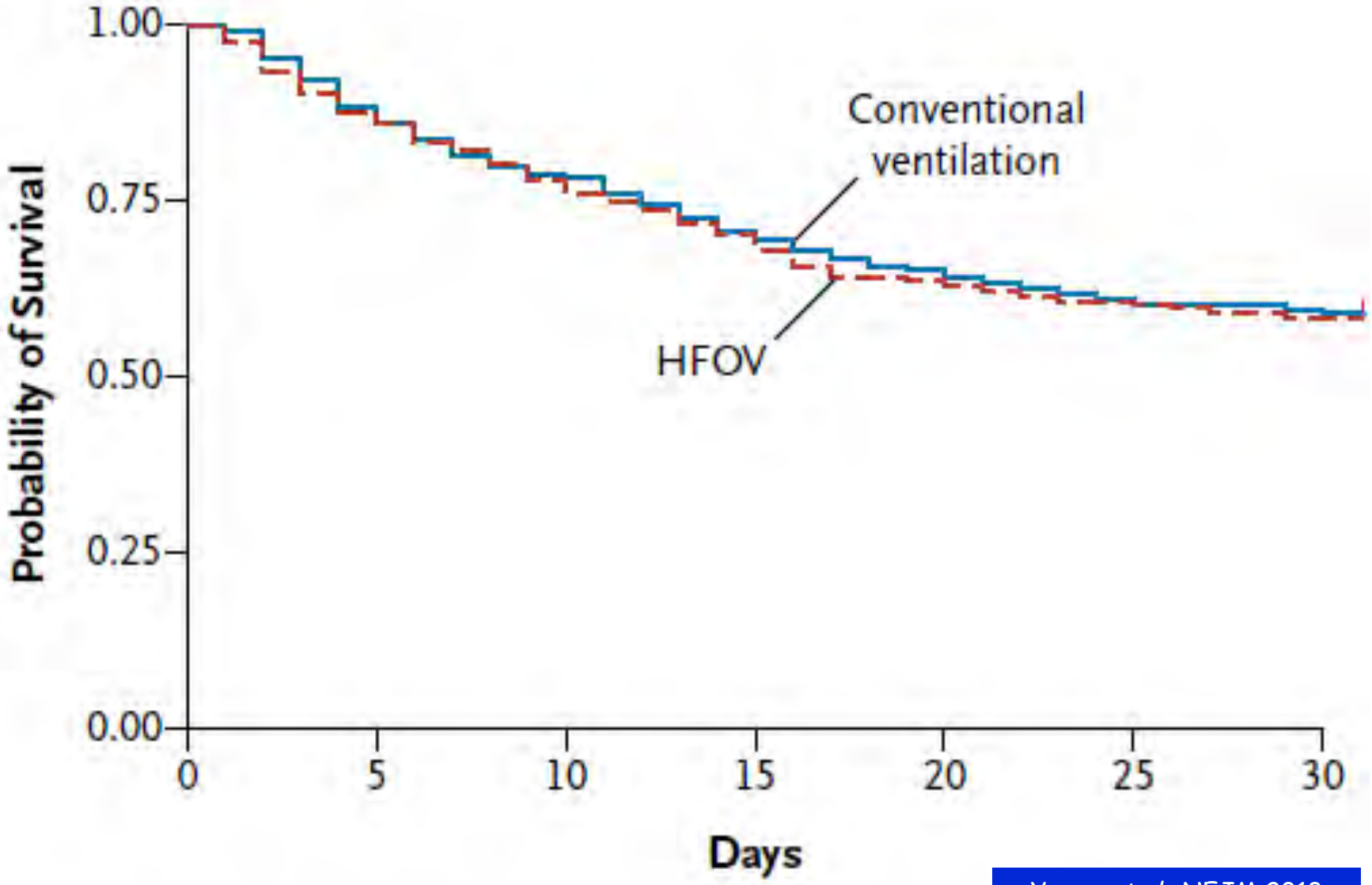
Ferguson *et al.* NEJM 2013

Ferguson *et al.* NEJM 2013

Outcome	HFOV Group (N = 275)	Control Group (N = 273)	Relative Risk (95% CI)	P Value
Death in hospital — no. (%)	129 (47)	96 (35)	1.33 (1.09–1.64)	0.005
Death in intensive care unit — no. (%)	123 (45)	84 (31)	1.45 (1.17–1.81)	0.001
Death before day 28 — no. (%)	111 (40)	78 (29)	1.41 (1.12–1.79)	0.004
New barotrauma — no./total no. (%)*	46/256 (18)	34/259 (13)	1.37 (0.91–2.06)	0.13
New tracheostomy — no./total no. (%)†	59/273 (22)	66/267 (25)	0.87 (0.64–1.19)	0.39
Refractory hypoxemia — no. (%)	19 (7)	38 (14)	0.50 (0.29–0.84)	0.007
Death after refractory hypoxemia — no./total no. (%)	15/19 (79)	25/38 (66)	1.20 (0.87–1.66)	0.31
Refractory acidosis — no. (%)	9 (3)	8 (3)	1.12 (0.44–2.85)	0.82
Refractory barotrauma — no. (%)	2 (<1)	2 (<1)	0.99 (0.14–7.00)	0.99
Use of mechanical ventilation, among survivors — days				0.59
Median	11	10		
Interquartile range	7–19	6–18		
Stay in intensive care, among survivors — days				0.93
Median	15	14		
Interquartile range	9–25	9–26		
Length of hospitalization, among survivors — days				0.74
Median	30	25		
Interquartile range	16–45	15–41		

Characteristic	Conventional Ventilation (N=397)	HFOV (N=398)	All Patients (N=795)
Age — yr	55.9±16.2	54.9±18.8	55.4±16.2
Male sex — no. (%)	239 (60.2)	256 (64.3)	495 (62.3)
APACHE II score†	21.7±6.1	21.8±6.0	21.8±6.1
Probability of in-hospital death (as calculated from APACHE II score)	0.43±0.19	0.44±0.19	0.43±0.19
Pao_2:FIo_2 ratio — mm Hg	113±38	113±37	113±38
Exhaled tidal volume — ml	505±173	541±271	523±228
Exhaled tidal volume — ml/kg of ideal body weight‡	8.3±3.5	8.7±3.5	8.5±3.9
Exhaled minute ventilation — liters/min	10.17±3.46	10.41±3.25	10.29±3.35
Positive end-expiratory pressure — cm of water	11.3±3.3	11.4±3.5	11.4±3.4
Duration of mechanical ventilation before randomization — days	2.1±2.1	2.2±2.3	2.2±2.2
Pulmonary cause of ARDS — no. (%)	304 (76.6)	302 (75.9)	606 (76.2)

Young *et al.* NEJM 2013



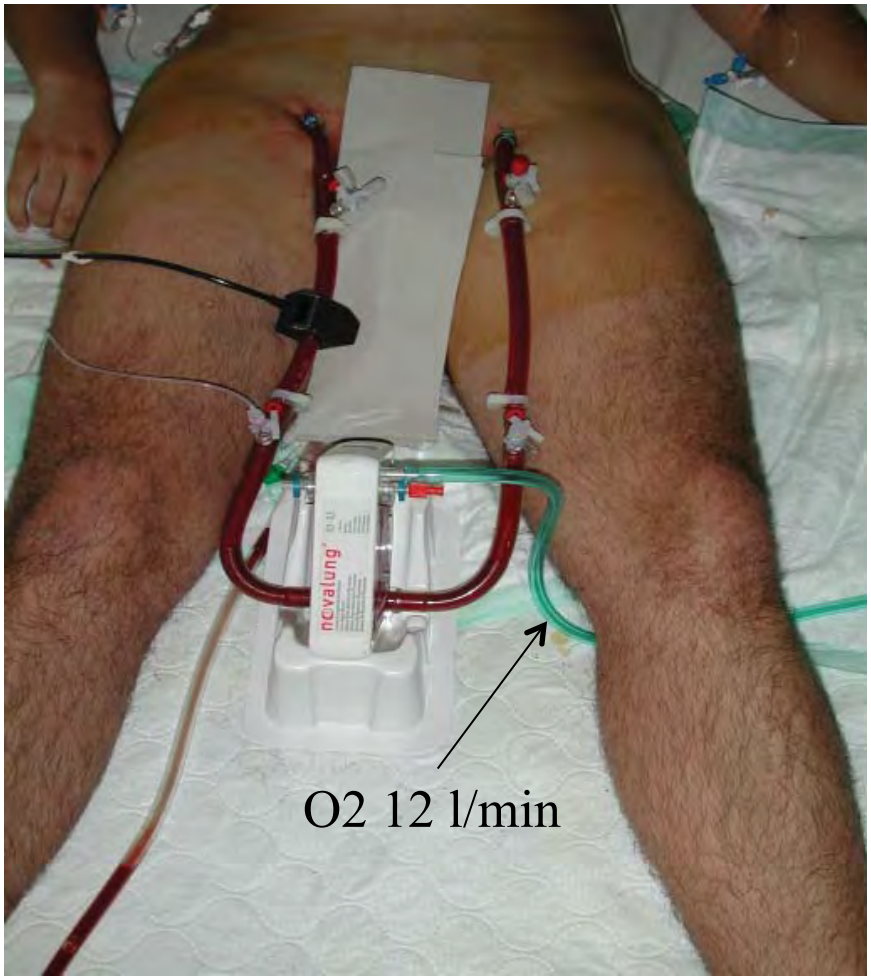
Young *et al.* NEJM 2013

Variable	Day 1		Day 2		Day 3	
	HFOV	Conventional Ventilation	HFOV	Conventional Ventilation	HFOV	Conventional Ventilation
No. of patients	370	392	326	374	240	348
Mean airway pressure (HFOV) or plateau pressure (conventional ventilation) — cm of water	26.9±6.2	30.9±11.0	25.3±5.5	29.5±10.7	25.1±5.4	28.5±11.2
Total respiratory frequency — Hz (HFOV) or breaths/min (conventional ventilation)	7.8±1.8	21.7±8.4	7.5±1.8	22.7±9.0	7.2±1.8	23.3±8.2
Cycle volume (HFOV) or tidal volume (conventional ventilation) — ml (HFOV) or ml/kg of ideal body weight (conventional ventilation)	213±72	8.3±2.9	228±75	8.2±2.5	240±75	8.3±3.0
Positive end-expiratory pressure — cm of water (conventional ventilation only)	NA	11.4±3.6	NA	11.0±3.6	NA	10.5±3.7
Pao_2:FIo_2 ratio — mm Hg	192±77	154±61	212±69	163±66	217±69	166±63
$Paco_2$ — mm Hg	55±17	50±19	56±16	49±13	56±17	48±13
Arterial pH	7.30±0.10	7.35±0.10	7.32±0.09	7.37±0.10	7.34±0.10	7.39±0.09
Medication use — no. (%)†						
Neuromuscular-blocking agent	209 (52.5)	165 (41.6)	147 (36.9)	115 (29.0)	110 (27.6)	77 (19.4)
Vasoactive or inotropic agent	173 (43.5)	177 (44.6)	158 (40.0)	146 (36.8)	126 (31.7)	112 (28.2)
Sedative agent	390 (98.0)	388 (97.7)	371 (93.2)	363 (91.4)	341 (85.7)	335 (84.4)

Young *et al.* NEJM 2013

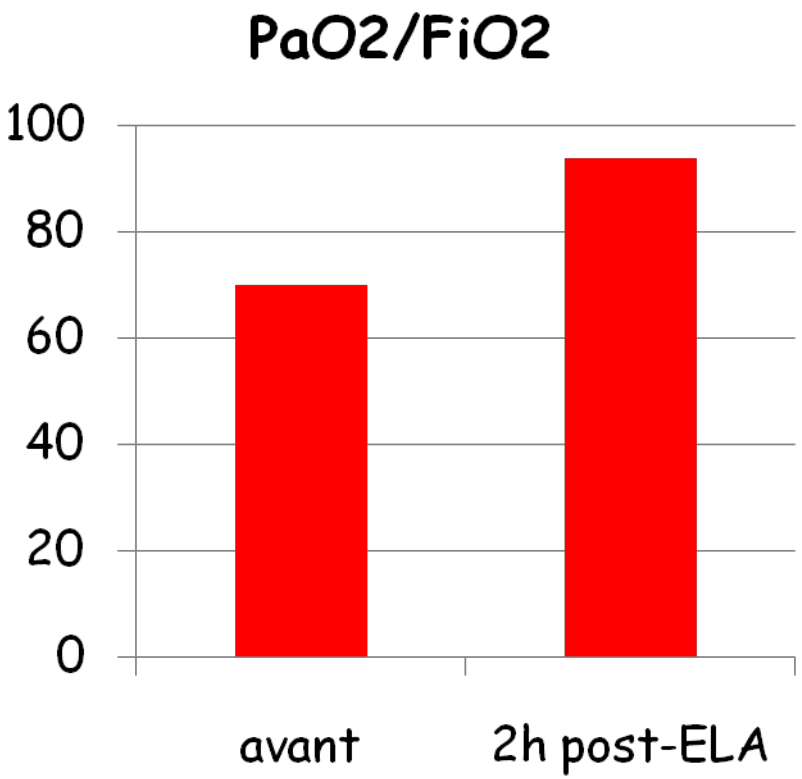
Interventional Lung Assist

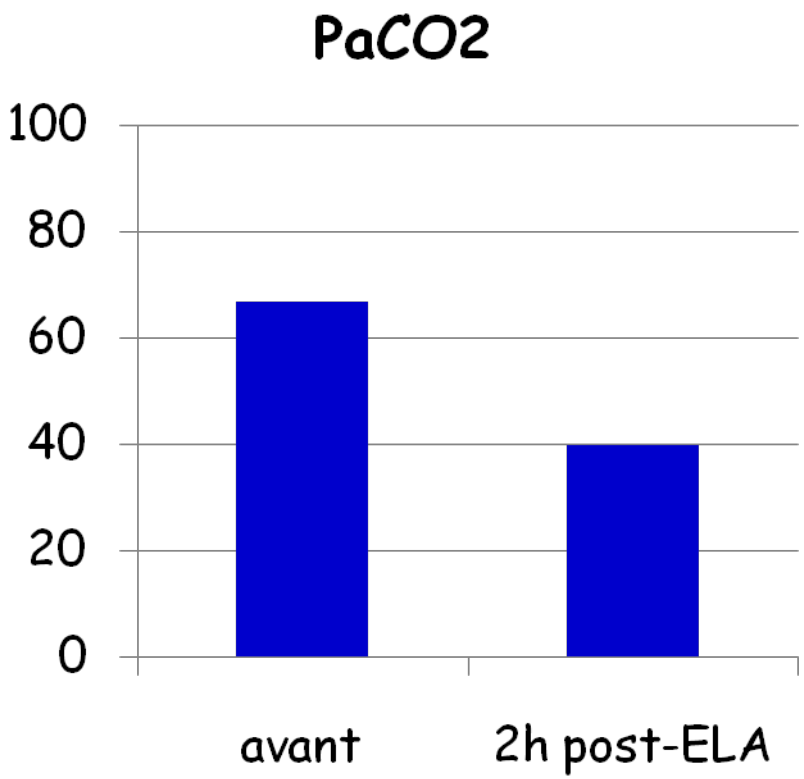
- Novalung® sans pompe
- Canule artérielle
- Canule veineuse + large de 2 Fr
- Membrane en polymethylpentene
- TCA 1,5
- PAM > 70 mmHg
- Efficacité PaCO2 +++
- Efficacité PaO2 +



Efficacité ELA

Müller *et al.* Eur Respir J 2009





"Therefore, according to the current data, interventional lung assist should probably not be used in patients with the most severely impaired oxygenation or in patients with reduced cardiac output."

Müller *et al.* Eur Respir J 2009

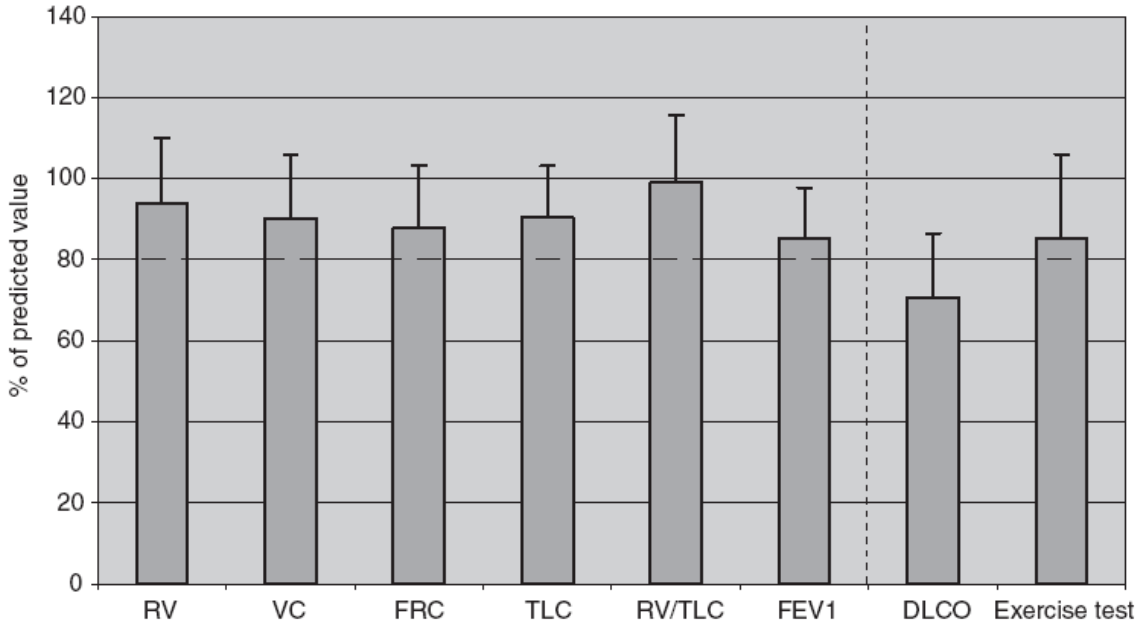
" In haemodynamically unstable patients requiring high doses of vasopressors (noradrenaline 0.4 µg/kg/minute or higher) or in patients with severe hypoxaemic ARDS, a pump-driven ECMO is still the rescue measure of choice."

Zimmermann *et al.* Crit Care 2009

Que sont-ils devenus ?

- 12-50 mois après ECMO
- Reprise activité: 76%
- TDM
  - Opacités réticulées: 76%
  - Opacités en verre dépoli: 24%
  - Normal: 14%
  - Etendue des anomalies: 10% du parenchyme

Linden *et al.* Acta Anaesthesiol Scand 2009



"Optimisation"

- Facteurs de mauvais pronostic à l'inclusion
  - analyse univariée
    - $PaCO_2$
    - DVA avant arrivée
    - Nb défaillances viscérales
    - SAPS II
    - réponse à l'optimisation

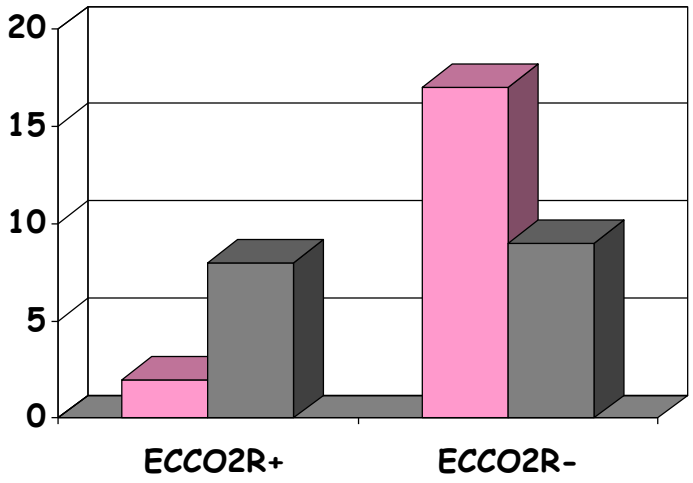
Guinard et al. Chest 97

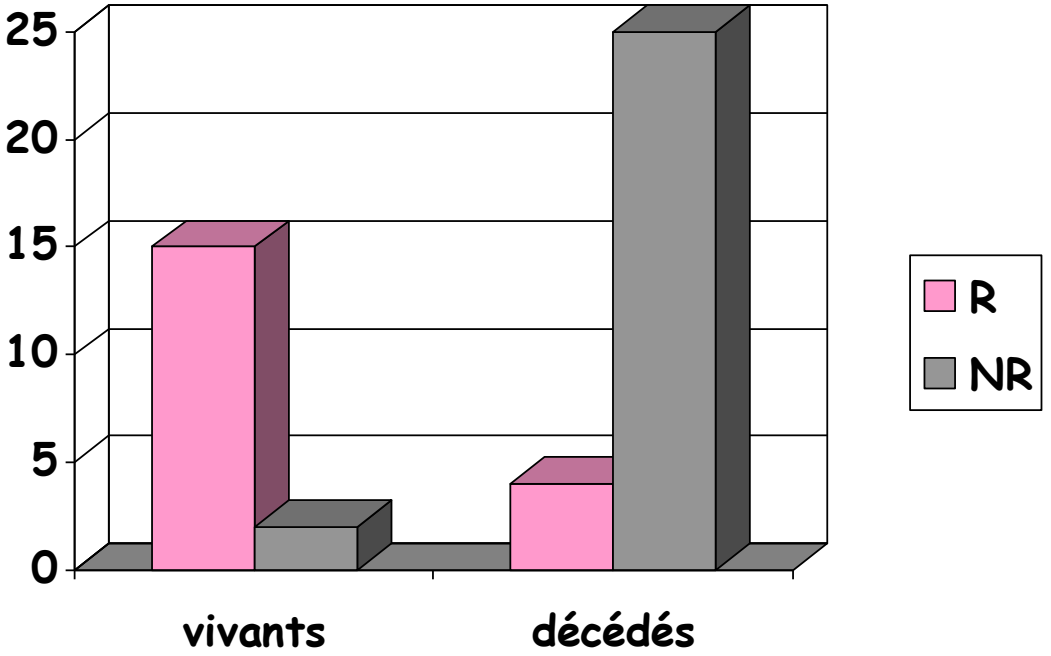
  - analyse multivariée
    - SAPS II
    - réponse à l'optimisation

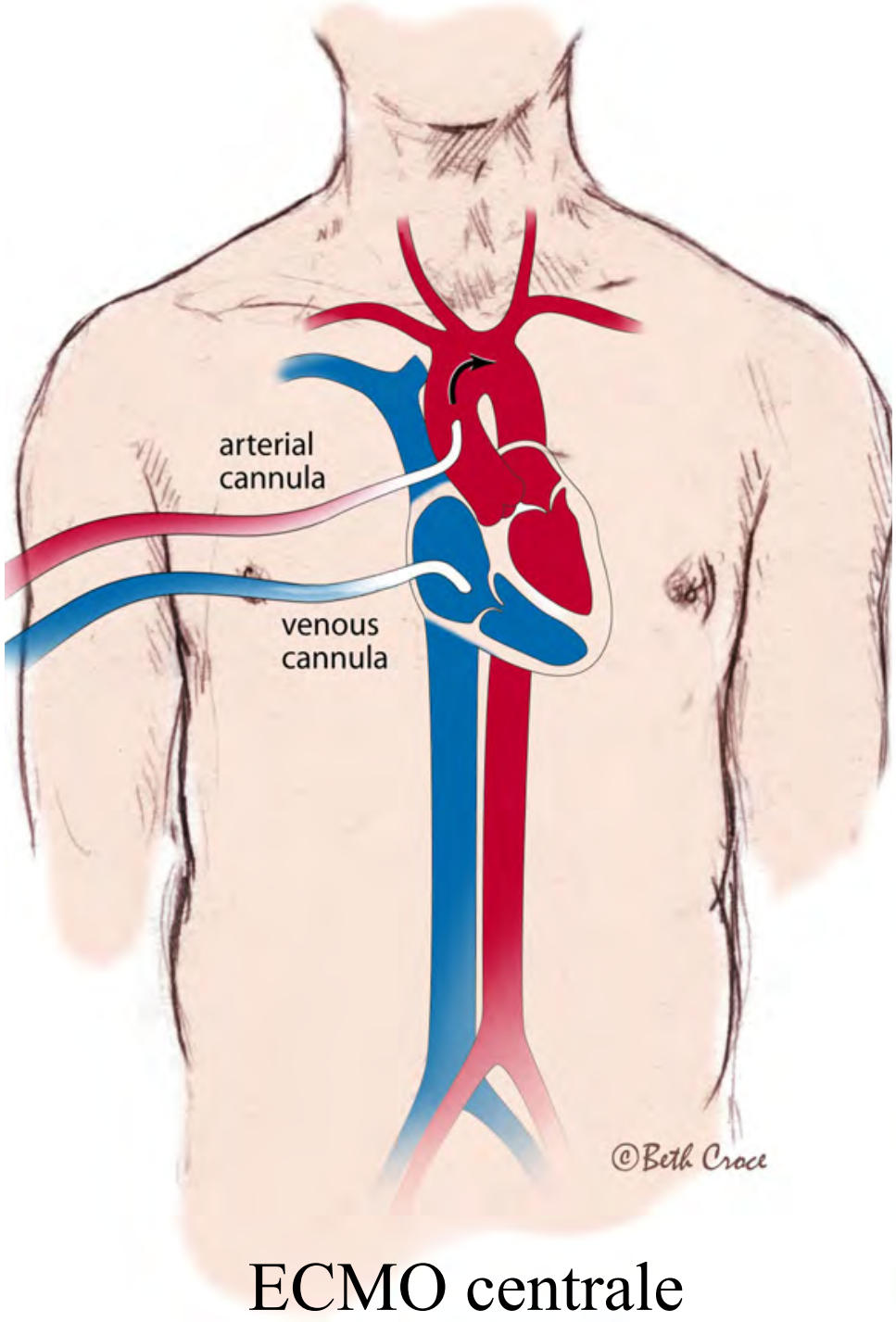
"Optimisation"

Guinard et al. Chest 97

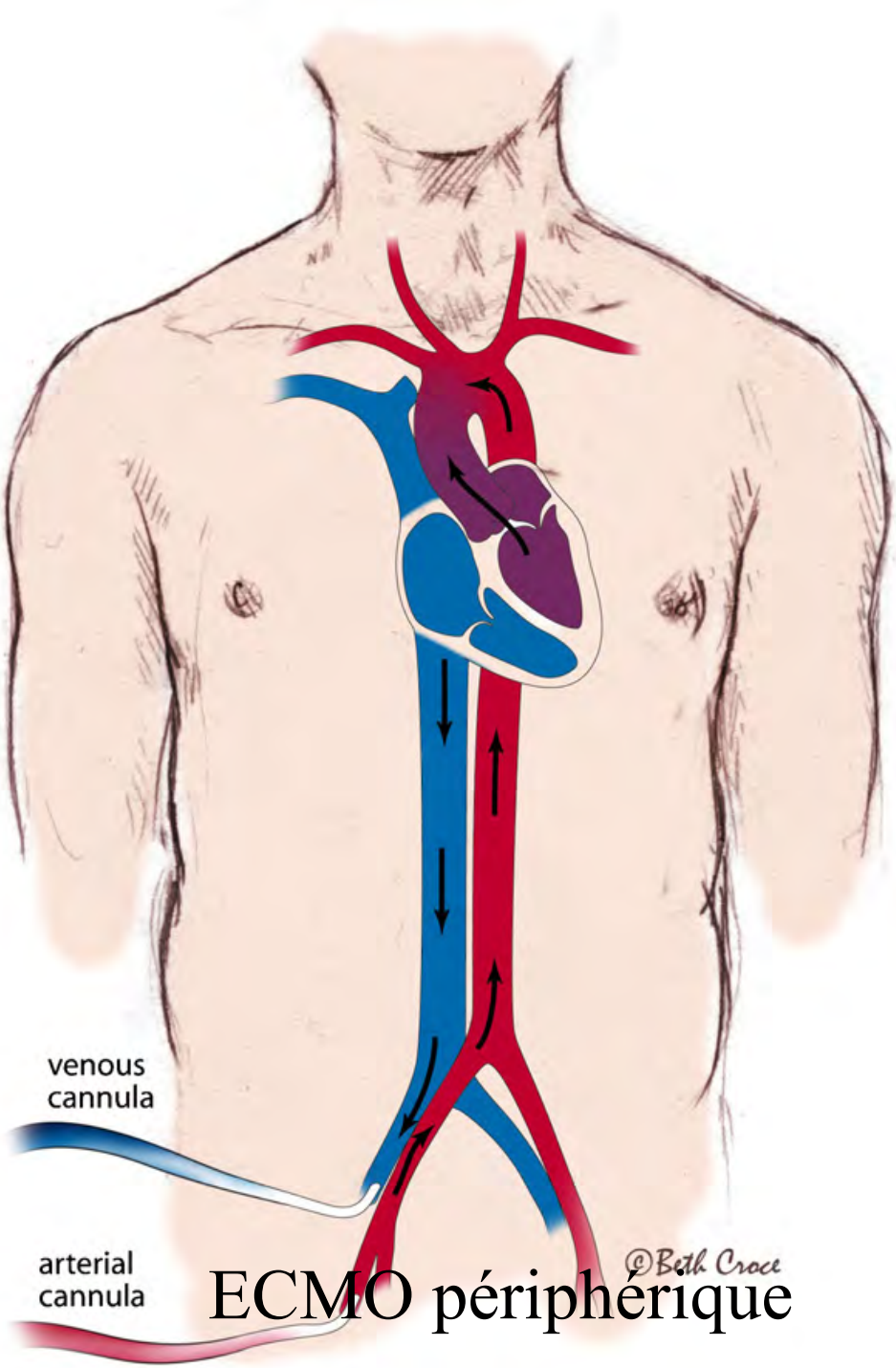
- NR : ↗ Nb de défaillances viscérales p < 0,05





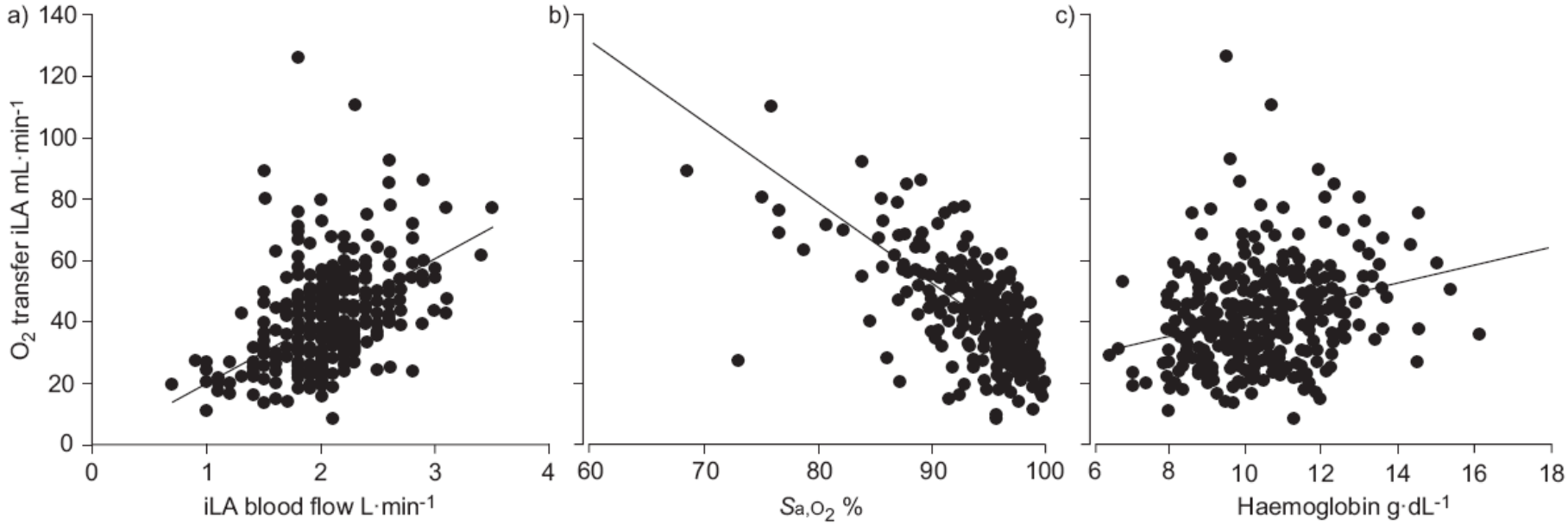


ECMO centrale



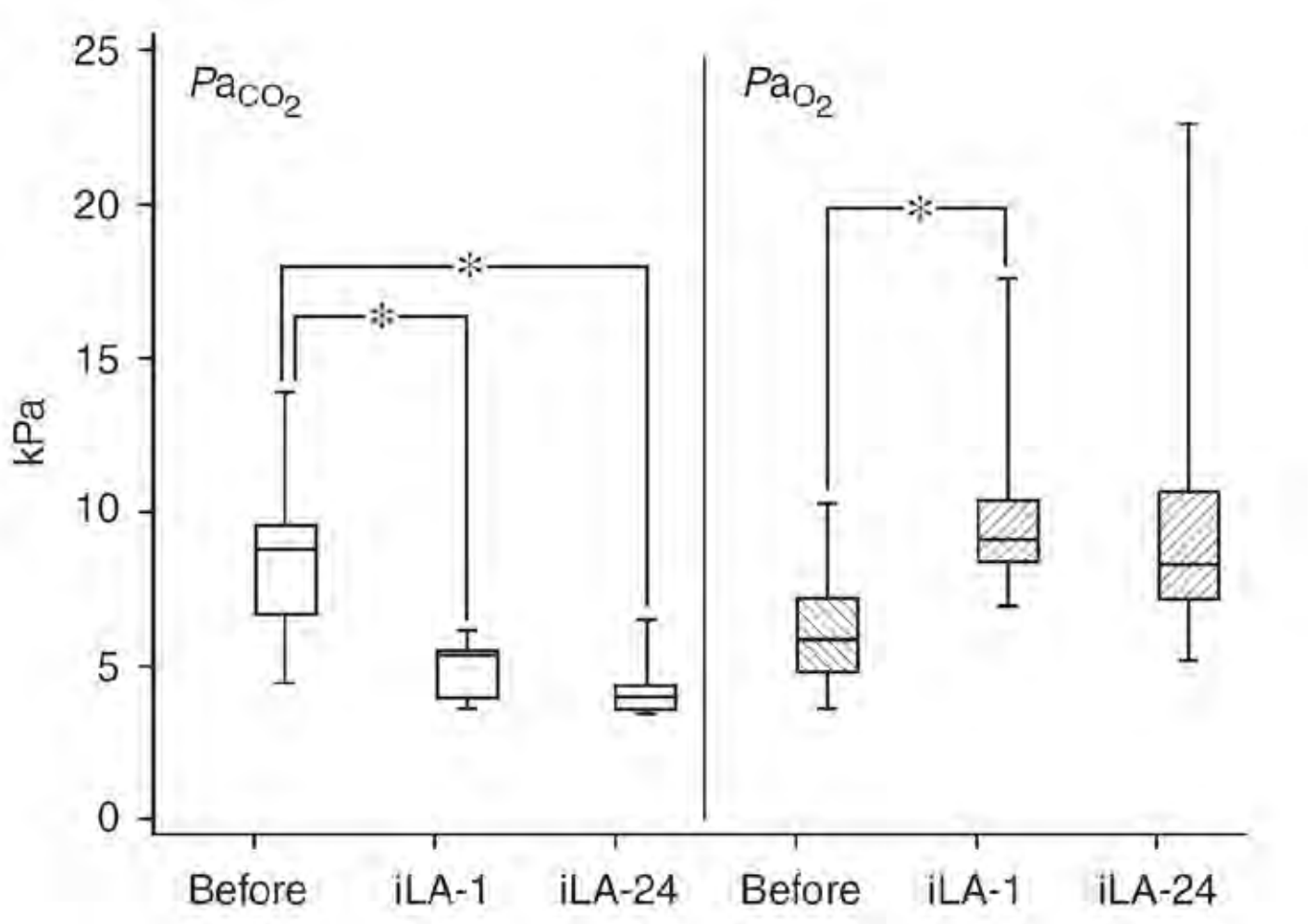
ECMO périphérique

Déterminants de l'efficacité sur l'oxygénation



Efficacité ILA

Zimmermann *et al.* Br J Anaest 2006



Patients à haut risque hémorragique

	Age	Mechanism and Severity of Trauma	CPR	Interventions before ECLS	ISS	SOFA	PaO_2	$PaCO_2$
1	47	Car driver collision 1. Bilateral hemothoraces 2. Liver laceration grade III 3. Spleen laceration grade III 4. Occult colon perforation 5. Pelvic fracture 6. Right radioulnar open fracture 7. Subarachnoid hemorrhage 8. Rhabdomyolysis 9. Cardiac contusion	Y	1. Splenectomy and hepatorrhaphy 2. Wedge resection of RLL 3. Repair of diaphragmatic hernia	50	16	56	68
2	25	Pedestrian crushed by truck 1. Bilateral hemopneumothorax 2. Liver laceration grade III 3. Stable pelvic fracture 4. Urethra injury 5. Renal contusion	N	1. Right bi-lobectomy 2. Hepatorrhaphy	43	13	64	82
3	18	Car driver collision 1. Right hemopneumothorax and bilateral lung contusion 2. Bronchial hemorrhage 3. Liver laceration grade IV 4. Cardiac contusion 5. Tear drop fracture of atlas	N	1. Bronchoscopy 2. One-lung ventilation 3. Pulmonary artery embolization	50	7	43	58
4	38	Motorcyclist collision 1. Main bronchial disruption and tension hemopneumothorax 2. Brain contusion with intracranial hemorrhage. 3. Multiple ribs fracture 4. Right femoral shaft fracture 5. Right zygomatic fracture	N	1. Bronchoscopy 2. High frequency jet ventilation 3. Tube thoracostomy	43	8	48	49
5	45	Motorcyclist collision 1. Right hemopneumothorax 2. Cardiac contusion 3. Right clavicle fracture 4. Right humerus fracture 5. Left tibial open fracture 6. Alcoholic liver cirrhosis, child A	N	Tube thoracostomy	35	16	47	45
6	35	Motorcyclist collision 1. Right hemothorax with pulmonary destruction 2. Left traumatic pneumothorax 3. Multiple rib fractures 4. Cardiac contusion	N	1. Right lung, bi-lobectomy 2. Pericardiotomy drainage for tamponade	45	8	42	78
7	43	Motorcyclist collision 1. Bilateral hemothorax 2. Pneumomediastinum 3. Multiple rib fracture (flail chest) 4. Femoral fracture, open type II 5. Brain contusion, unconscious for 6 h	N	1. Tube thoracostomy 2. External fixation of right femoral shaft fracture	50	13	52	86
8	37	Chest stabbing 1. Right lower lobe laceration with massive hemothorax 2. Hypothermia (34.1 °C) 3. Metabolic acidosis 4. Brain concussion	Y	Wedge resection of RLL	42	16	31	80
9	28	Car driver collision 1. Traumatic aortic pseudoaneurysm 2. Bilateral hemopneumothorax 3. Liver laceration grade 3 with hemoperitoneum 4. Duodenal and colon contusion with mesocolon tear 5. Fracture of left zygoma and maxillary sinus. 6. Fracture of transverse process of L1 and L2 7. Fracture of left acetabulum and patella 8. Cardiac contusion	N	1. Laparotomy 2. Trans-arterial embolization of hepatic artery 3. Hemi-arch aortic replacement	43	11	58	52

Huang *et al.* Resuscitation 2009

Interventions durant AREC

	Indication	Trauma to ECLS (h)	Entry criteria	ECLS Mode	ECLS Flow (L/min)	IABP Use	Procedures during ECLS (h s/p ECLS deployment)
1	ECPR	47	F	VA	4.5	N	Repair of colon perforation (4)
2	Hypercapnia	384	S	VV	4	N	None
3	Hypoxemia	33	F	VV	4.4	N	Bronchoscope for blood clot evacuation (168)
4	Hypoxemia	10	F	VV	4.3	N	External fixation of femoral fracture (10)
5	Hypoxemia	48	S	VV	5.2	N	Chest wall necrotizing fasciitis debridement (201)
6	Hypoxemia	6	F	VV	4.4	N	Explore laparotomy (12)
7	Hypoxemia	21	F	VV	5.3	N	None
8	ECPR	4	F	VA	4.4	Y	Explore thoractomy for hemothorax twice (12 and 53)
9	Hypoxemia	175	S	VV	5.2	N	None

Modification paramètres de VM

Zimmermann *et al.* Crit Care 2009

	Pre-iLA	2 hours after insertion
PaO_2/FiO_2	75 (62 to 130)	102 (70 to 127) *
$PaCO_2$ (mmHg)	73 (61 to 86)	44 (36 to 54) **
Arterial pH	7.23 (7.16 to 7.30)	7.38 (7.32 to 7.46) **
MAP (mmHg)	73 (65 to 80)	83 (75 to 91) **
Noradrenaline (µg/kg/minute)	0.16 (0.04 to 0.35)	0.11 (0.03 to 0.28)
iLA-flow (L/minute)	-	1.8 (1.6 to 2.0)
FiO_2	1 (0.8 to 1.0)	0.8 (0.7 to 1.0) **
MV (L/minute)	11.5 (9.3 to 12.5)	8.6 (6.4 to 10.5) **
V_T ml/IBW	6.6 (5.3 to 7.2)	5.0 (4.0 to 6.4) **
RR (breaths/minute)	25 (22 to 27)	23 (20 to 30)
P_{plat} (cmH_2O)	35 (31 to 38)	34 (30 to 37)
PEEP (cmH_2O)	17 (14 to 20)	15 (11 to 19) *

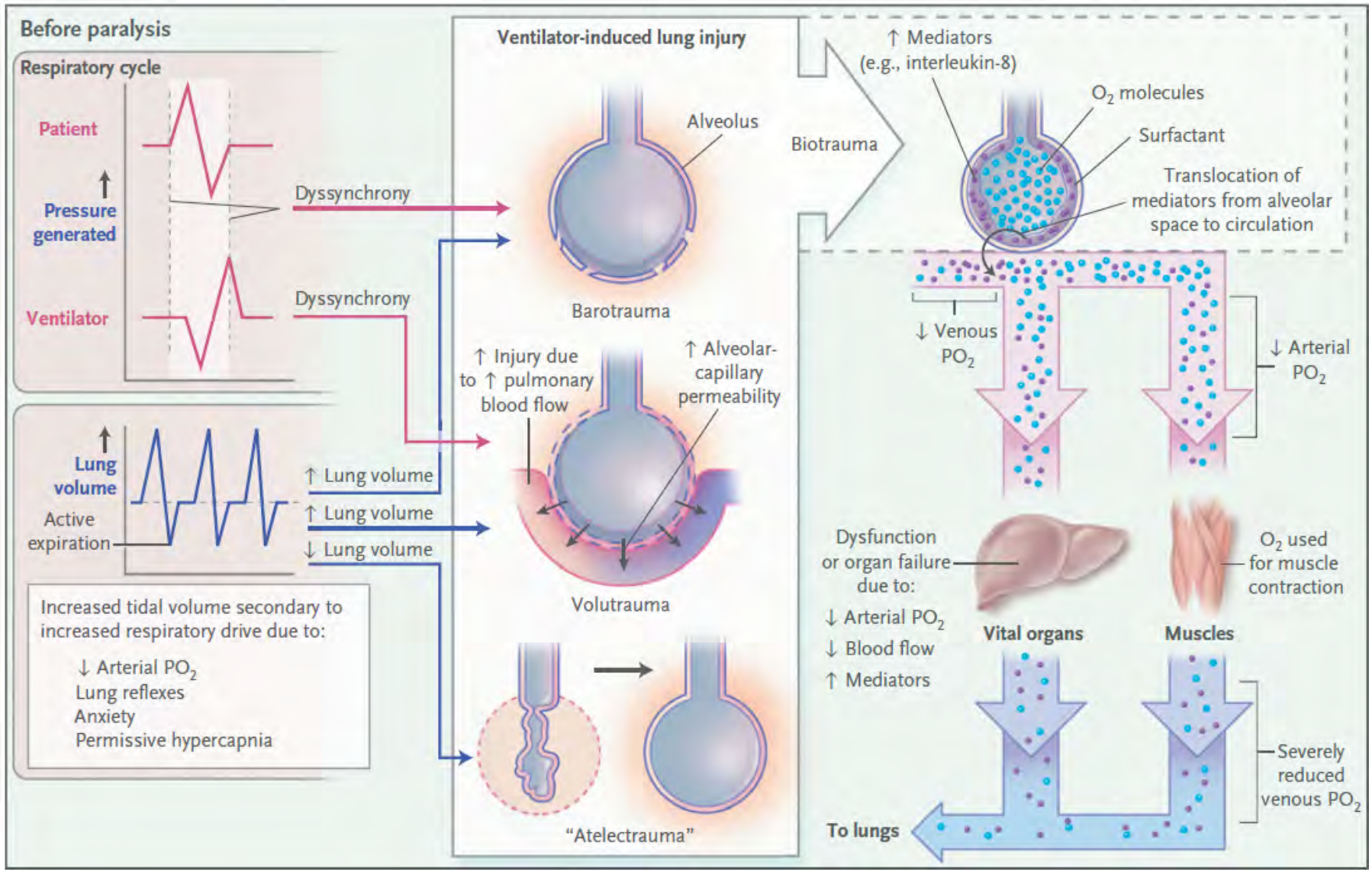
Le petit manuel du parfait ARDSologue

- Limiter la iatrogénie
- Réduction volume courant
- Plusieurs profils de patients
- Approche globale
  - Ajuster la PEEP en fonction de la présentation morphologique
  - Limiter pression de plateau
  - Curariser tôt mais brièvement
  - Eviter dérecrutement
  - Limiter les objectifs d'oxygénation
- Le reste…

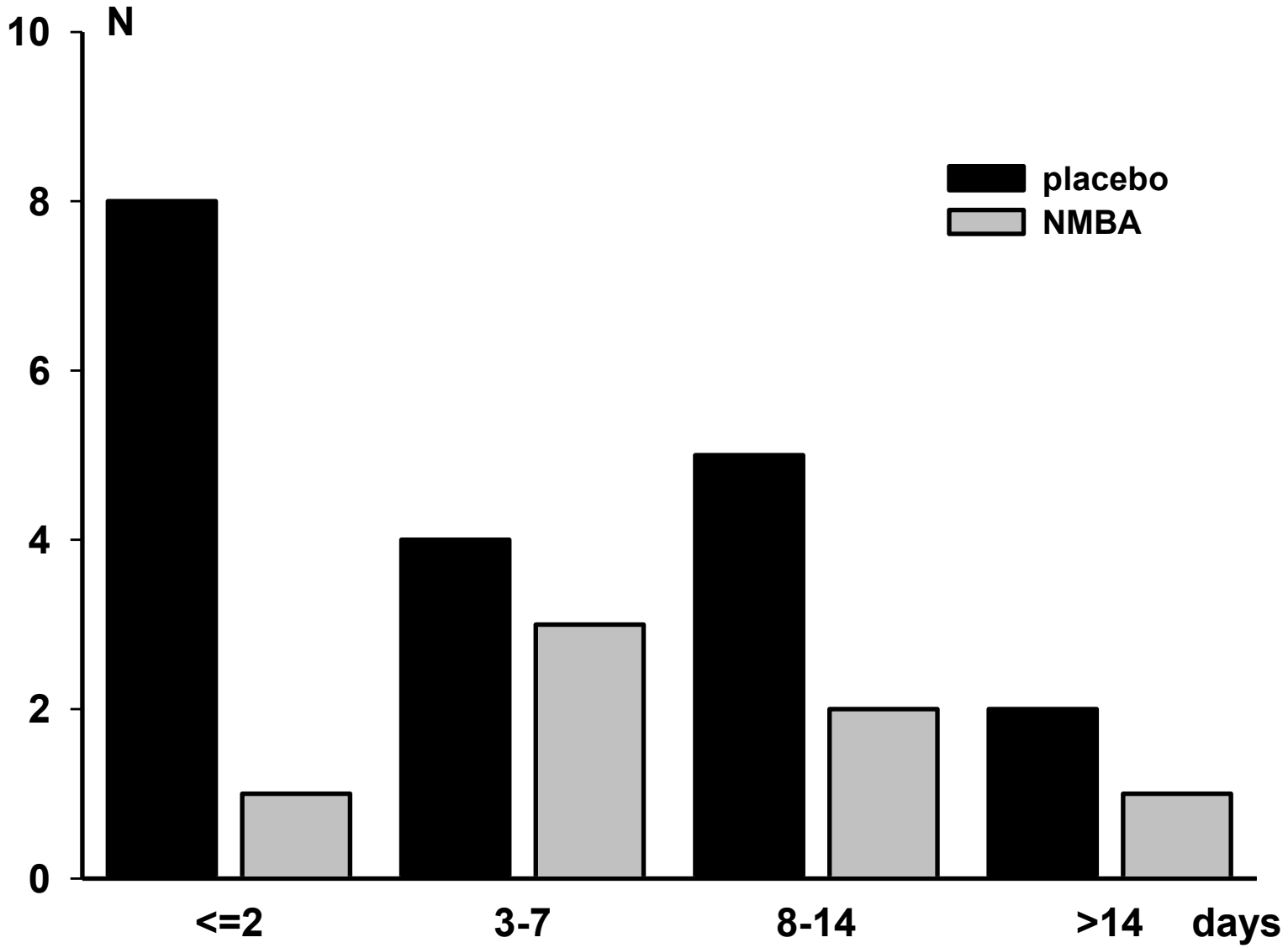
Mechanisms potentially involved

Neuromuscular Blocking Agents in ARDS

Arthur S. Slutsky, M.D.

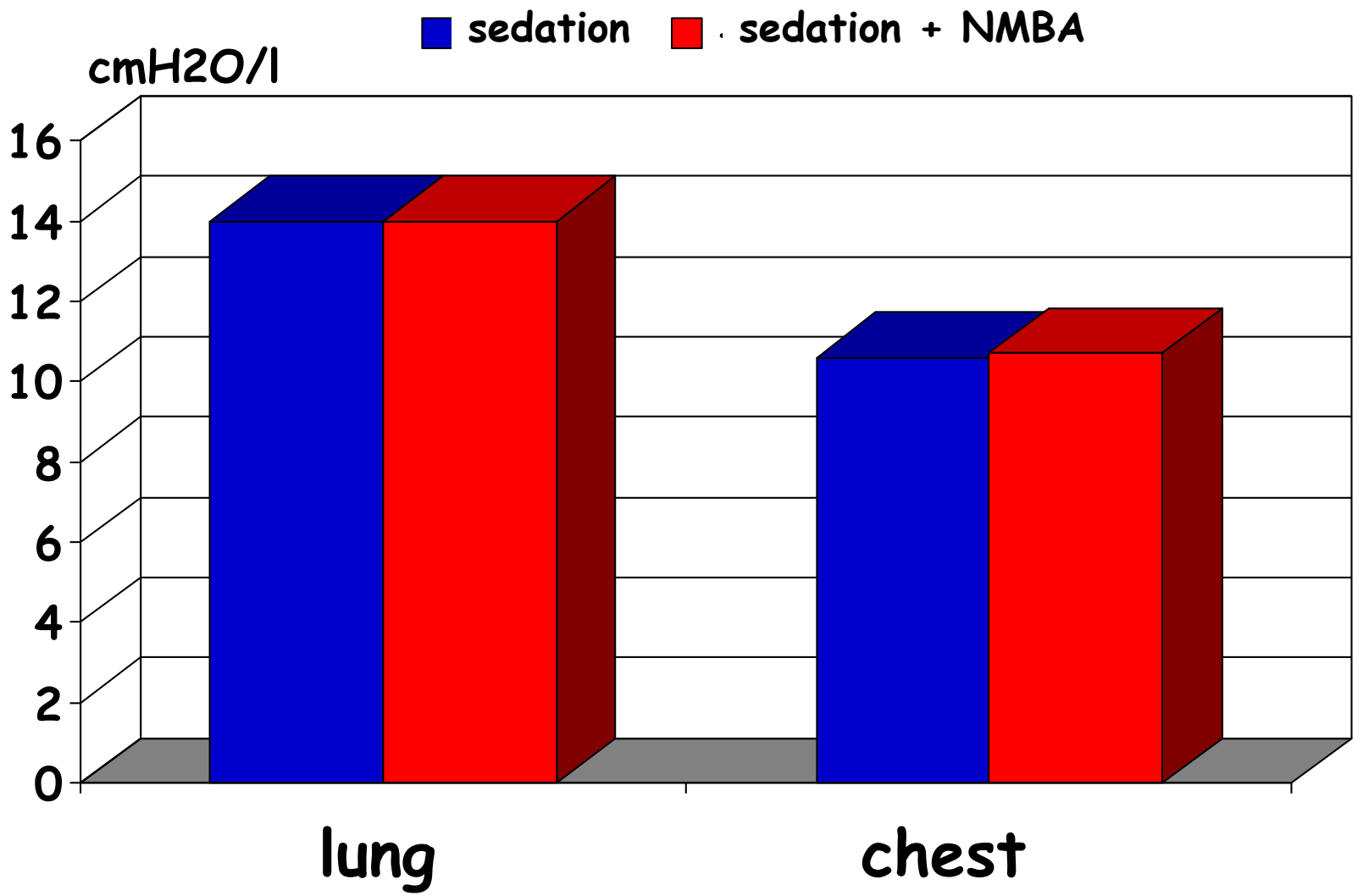


Time from inclusion to pneumothorax

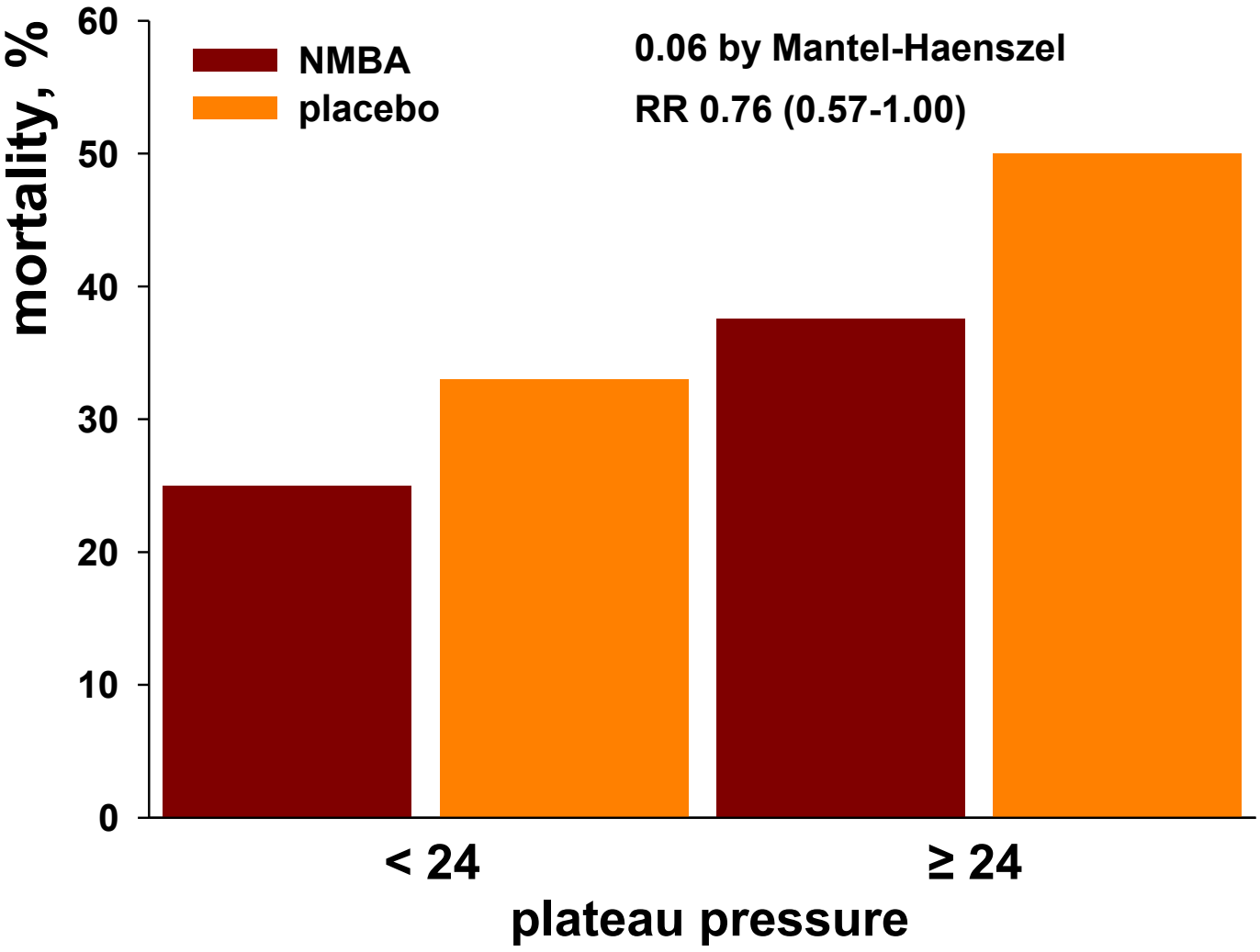


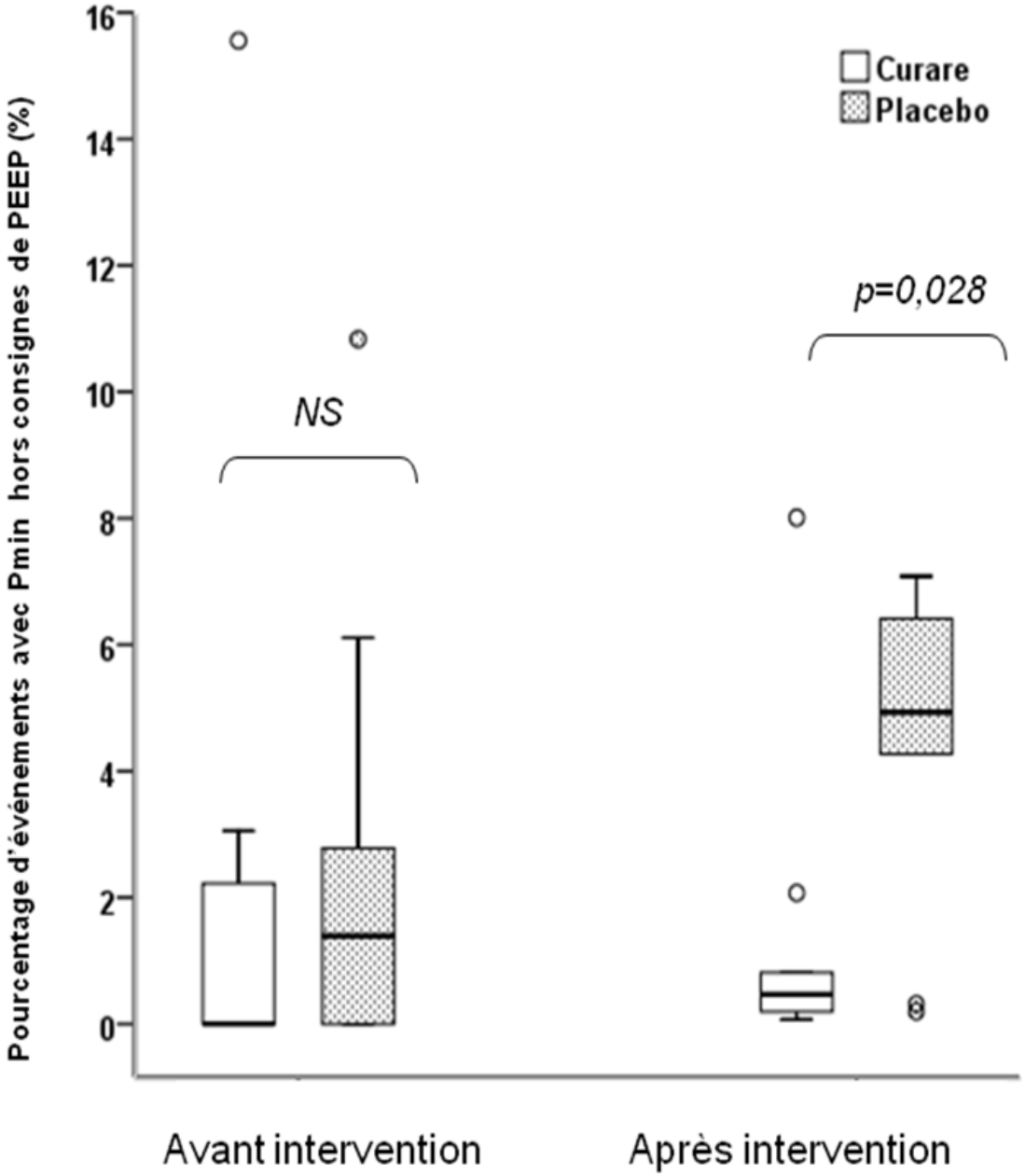
Elastance, sedation and NMBA

Conti et al. ICM 95



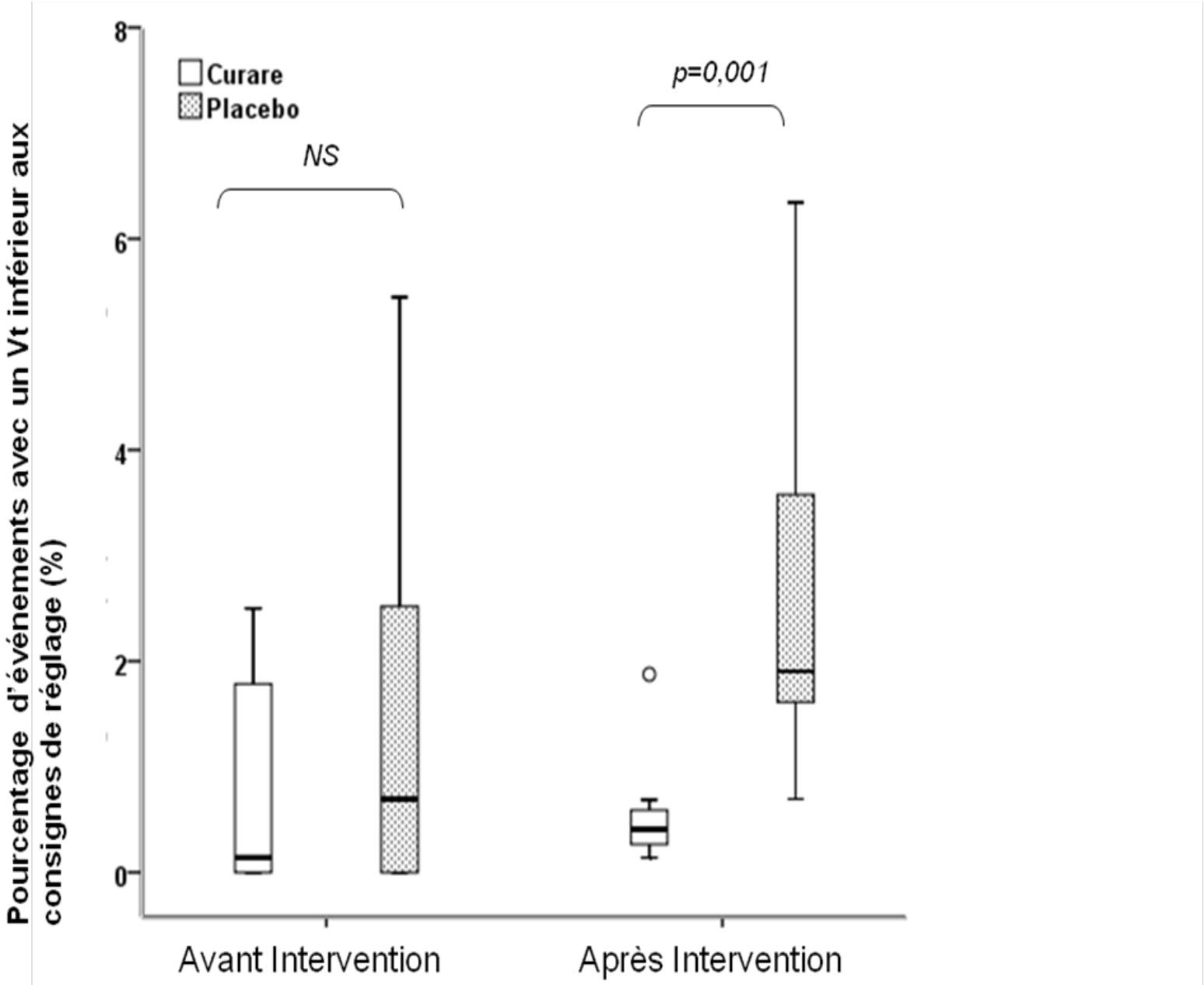
Mortality d90 and plateau pressure on inclusion





Befort *et al.* SRLF 2011

Pourcentage d'événements avec Pmin hors consigne de PEEP réglée sur le ventilateur



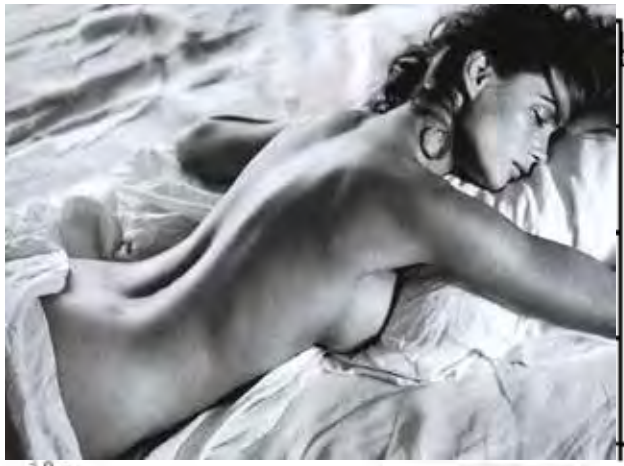
Pourcentage d'événements avec des volumes courants mesurés inférieurs à la consigne de réglage du volume courant sur le ventilateur

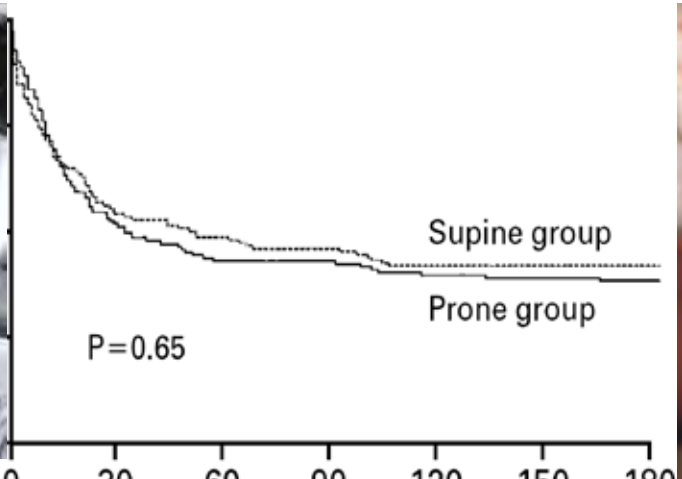
Protéine C activée

24 mg/kg/h for 96 h et placebo

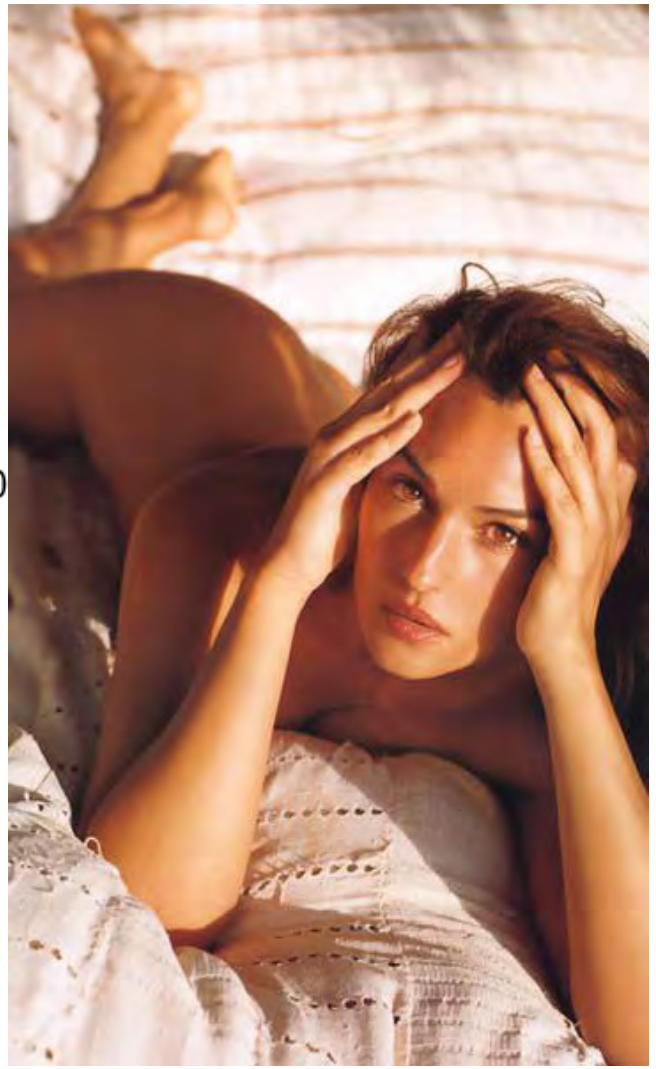
	Placebo ($n = 38$)	APC ($n = 37$)	P Value
Ventilator-free days, median (IQR)	19 (0–24)	19 (14–22)	0.78
Death by Day 60, n (%)	5 (13.5)	5 (13.5)	1.00
Ventilator-free days among survivors, median (IQR)	21 (5–25)	20 (16–23)	0.36
Organ failure–free days, median (IQR)	23 (14–27)	23 (16–27)	0.46
Cardiovascular failure, median (IQR)	25 (20–28)	26 (23–28)	0.30
Coagulation failure, median (IQR)	28 (28–28)	28 (28–28)	0.57
Renal failure, median (IQR)	28 (18.5–28)	28 (28–28)	0.41
Hepatic failure, median (IQR)	28 (27–28)	28 (28–28)	0.36

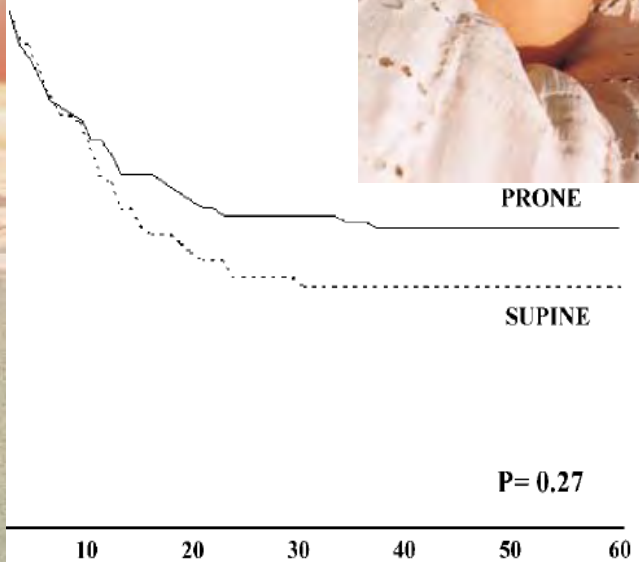
Liu *et al.* AJRCCM 2008




Supine group
Prone group
P=0.65
0
30
60
90
120
150
180


Supine Position
Prone Position
Cumulative Probability of Survival
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3




PRONE
SUPINE
P= 0.27
10
20
30
40
50
60

BTTF

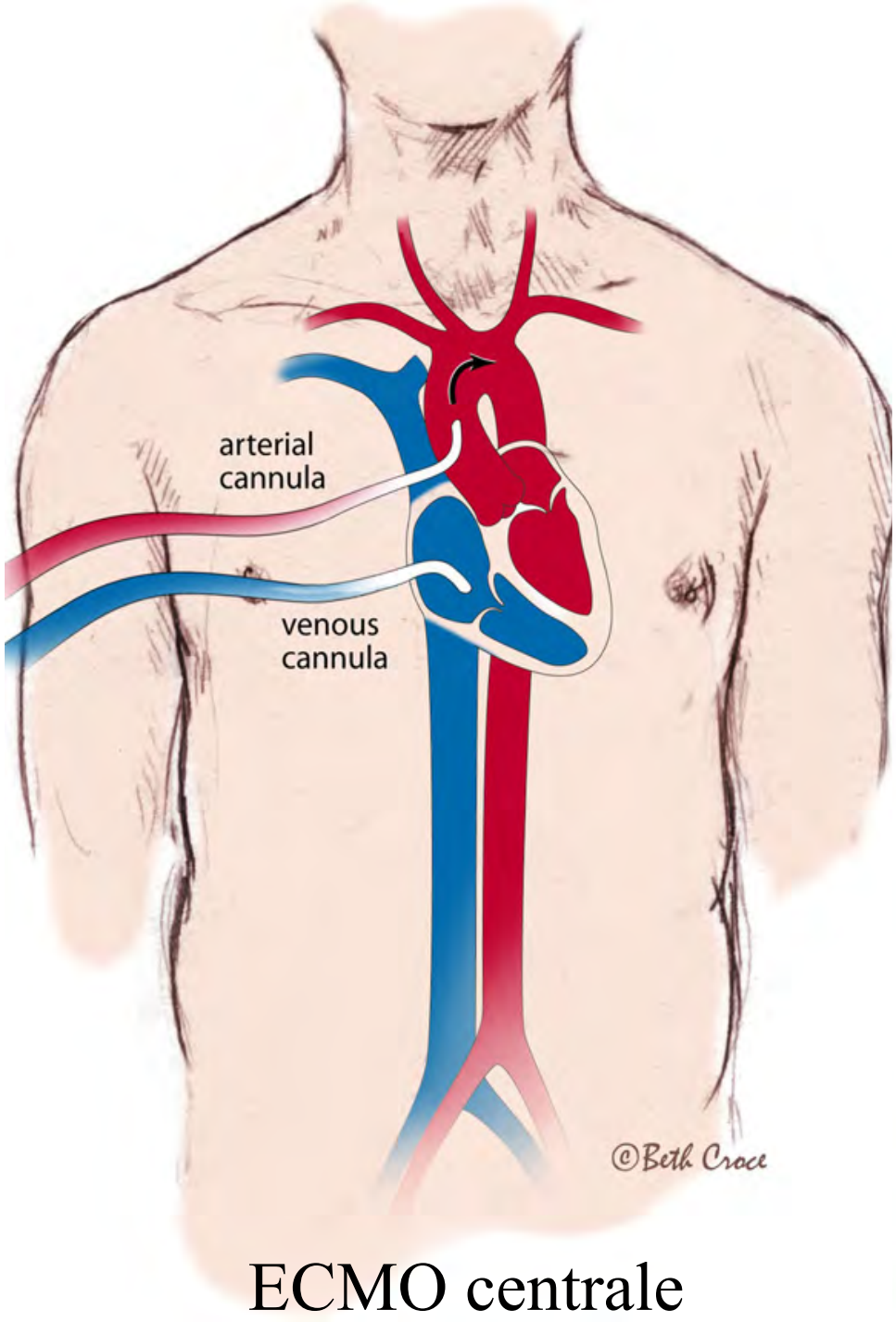

STEVEN SPIELBERG Présente
RETOUR VERS LE FUTUR
Un film de ROBERT ZEMECKIS
Jamais à temps
à l'école,
Jamais à temps
à la maison,
Un jour
il se retrouve
complètement
hors du temps...
"RETOUR VERS LE FUTUR" MICHAEL J. FOX
CHRISTOPHER LLOYD · LEA THOMPSON · CRISPIN GLOVER
ROBERT ZEMECKIS & BOB GALE ALAN SILVESTRI BOB GALE NEIL CANTON
STEVEN SPIELBERG, KATHLEEN KENNEDY FRANK MARSHALL
ROBERT ZEMECKIS
UN FILM UNIVERSAL DISTRIBUE PAR CINEMA INTERNATIONAL CORPORATION

- **103 services participants**
- **Plus de10 000 patients screenés (60 services)**
- **557 admis en réa. atteints de grippe A / H1N1**
- **420 patients ventilés (75%)**
- **328 SDRA**

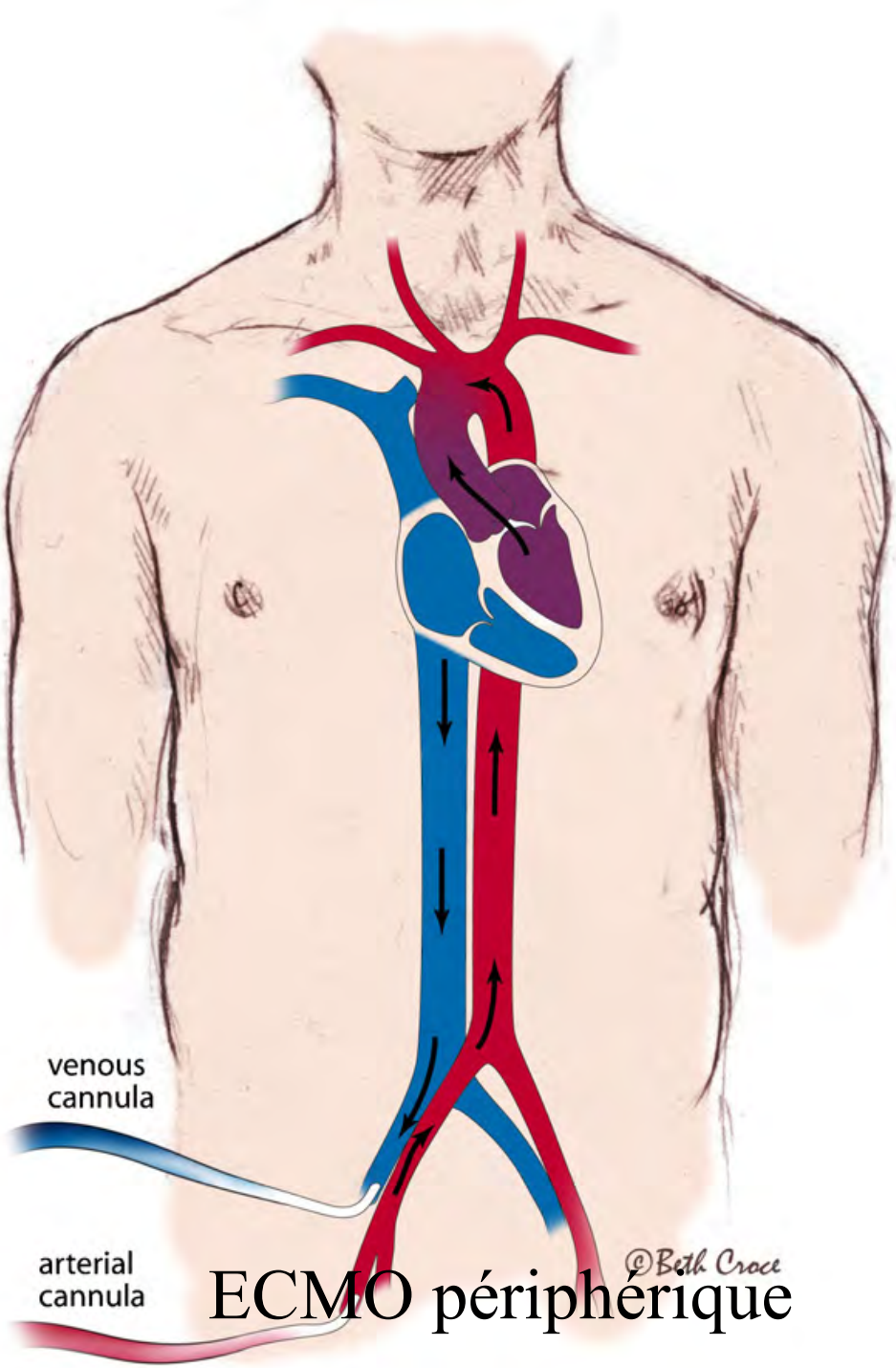
Cas enregistrés au 15 Mars 2010

Prise en charge et pronostic

% des admissions réa	ANZIC NEJM 2009	Canada JAMA 2009	Mexico JAMA 2009	REVA
VM	64,6	76	75,9	74,5
ECMO	11,6	4,2	0	11,4
Décès	16,9	17,3	41	19



ECMO centrale

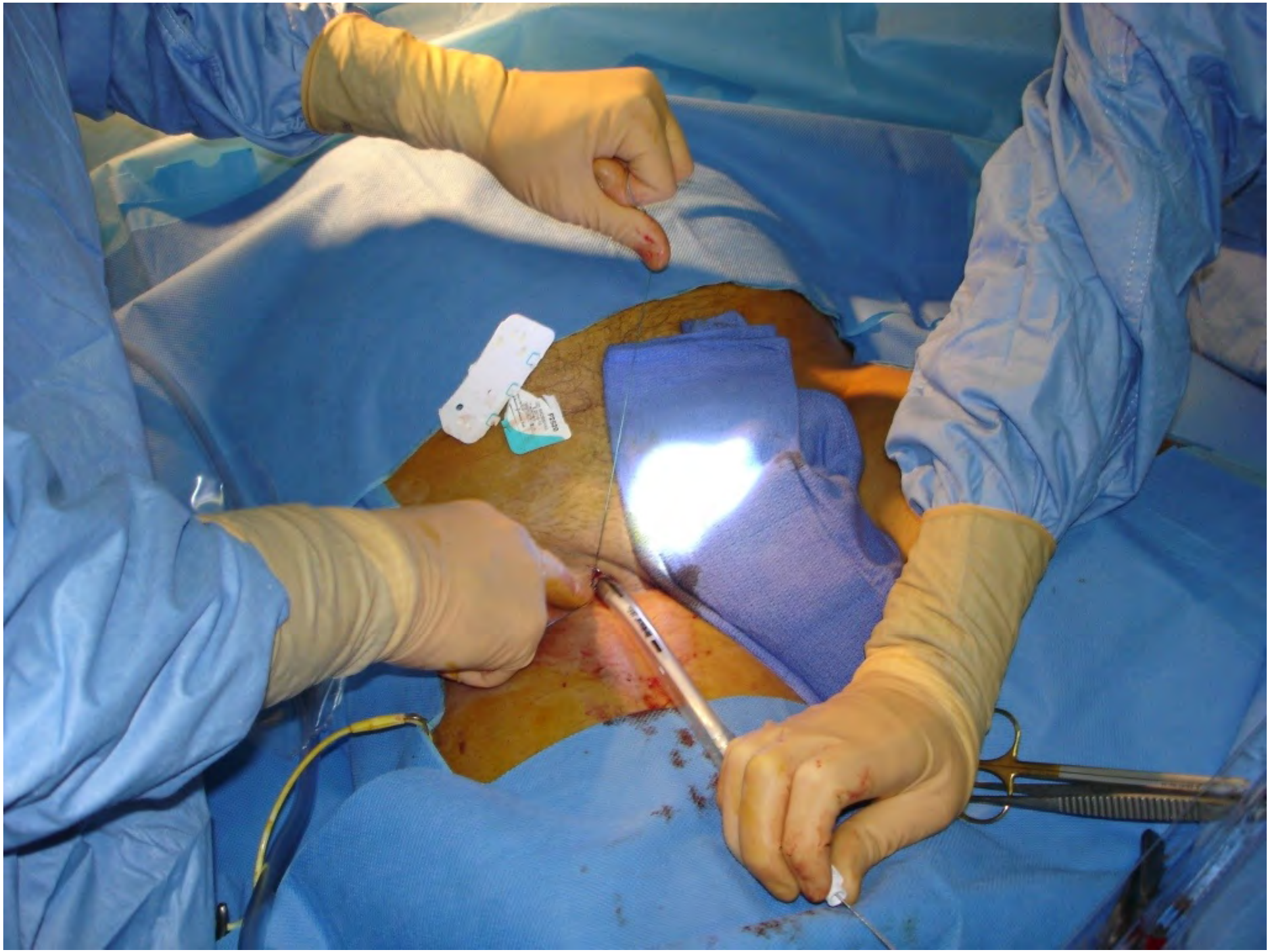


ECMO périphérique

ECMO

Collaboration multidisciplinaire

- Équipe chirurgie cardiaque disponible 24/24h



Complications

- Thrombopénie
- Hémolyse
- Activation
  - C
  - GB

Aspects pratiques

- TCA 1,5
- Objectif: 40-50% du débit cardiaque
- 2 abords veineux afférents si
  - Hyperdébit
  - Hypoxémie très sévère

ECMO

Sevrage

Diminution des paramètres de CEC

↘ Débit, vitesse de pompe, FIO2, balayage

Reprise ventilation mécanique

↗ FR, Vt , ↘ PEEP, ↗ ↘ FIO2

Retrait des canules

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 (doi:10.1001/jama.2009.1535)

- **Étude observationnelle sur 3 mois**
- **201 patients Grippés sur 15 Réanimations**
- **2,6 ECMO/ million d'habitant**
- **Critères de mise sous ECMO: non connus**

ANZ ECMO JAMA 2009

Table 1. Comparison of Patients With Influenza A Who Received ECMO and Those Who Received Mechanical Ventilation But Without ECMO at ECMO Centers[a]

Parameter	ECMO (n = 61)	Mechanical Ventilation But Without ECMO (n = 133)	*P* Value
Age, median (IQR), y	36 (27-45)	44 (31-54)	.02
Male sex	29 (48)	63 (47)	.54
BMI, median (IQR)	29 (23-36)	29 (24-37)	.92
Chronic lung disease	18 (30)	35 (26)	.64
APACHE III comorbidity[b]	5 (8)	30 (23)	.02
Pregnancy or postpartum	10 (16)	12 (9)	.21
Diabetes mellitus	9 (15)	23 (17)	.64
H1N1 positive	56 (92)	107 (80)	.05
At ICU admission			
Mechanical ventilation	53 (87)	117 (88)	.80
Vasopressor	35 (57)	46 (34)	.02
Renal replacement therapy	5 (8)	9 (7)	.95
Duration or length of stay, median (IQR), d			
Mechanical ventilation	18 (9-27)	8 (4-14)	.001
ICU	22 (13-32)	12 (7-18)	.001
Hospital	28 (15-43)	20 (13-31)	.07
Mortality			
in ICU	14 (23)	12 (9)	.01
in hospital	14 (23)	17 (13)	.06

ANZ ECMO JAMA 2009

Assistance respiratoire extra-corporelle

- **Inclusion:**

Zapol *et al.* JAMA 79

  - Fast entry criteria= PaO2 < 50 > 2h

  avec FiO2 1.0 et PEEP > 5

  - Slow entry criteria= PaO2 < 50 > 12h

  avec FiO2>0.6 et PEEP > 5 ; maximal therapy > 48h

- **Exclusion:**
  - durée de la VM > 7j
  - CI aux anticoagulants,
  - lésions cérébrales irréversibles,
  - pathologie pulmonaire chronique sévère,
  - immunosuppression,
  - maladie terminale,
  - défaillance multi viscérale

US NIH Zapol *JAMA 79*

- étude contrôlée multicentrique
- 90 patients randomisés entre VM conventionnelle +/- ECMO
- Mortalité 92 vs 90%

Morris *AJRCCM 1994*

- VM (pression contrôlée) Vs VM + ECMO (ECCO2-R)
- ETUDE INTERROMPUE après analyse intermédiaire sur 40 patients
- Pas de différence significative sur la survie (42% vs 33%)

En 1974… US NIH Zapol *JAMA*

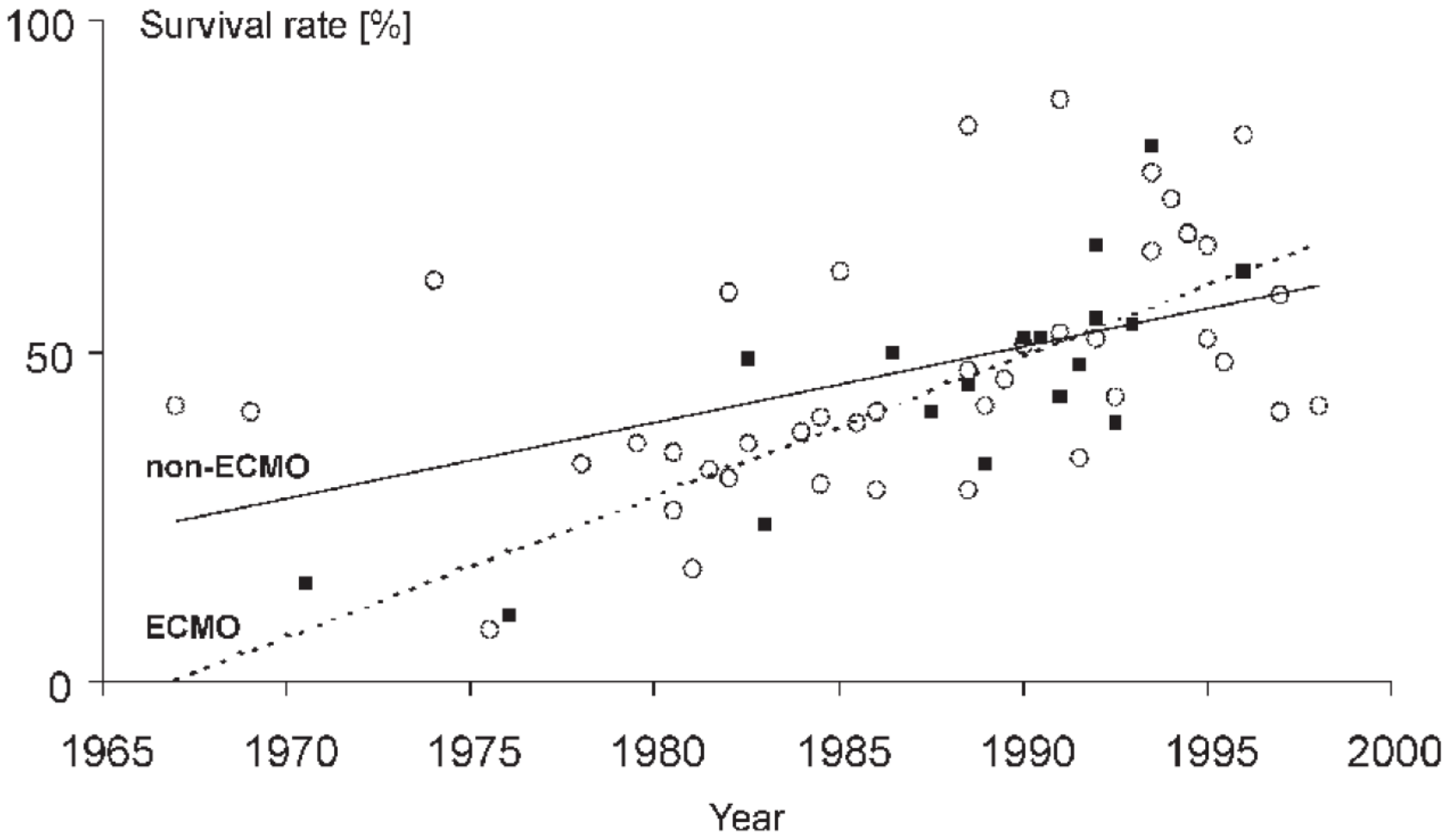
- étude contrôlée multicentrique
- 90 patients randomisés entre VM conventionnelle +/- ECMO
- Mortalité 92 vs 90%

- mais: mortalité ds le groupe contrôle élevée (malades trop graves?)
- Plusieurs centres inexpérimentés
- Remplissage excessif, Vt élevé, anticoagulation+++
- Veino-Artériel
- Durée de VM prolongée avant ECMO

En 1994, Morris *AJRCCM*

- VM (pression contrôlée) Vs VM + ECMO (ECCO2-R)
- ETUDE INTERROMPUE après analyse intermédiaire sur 40 patients
- Pas de différence significative sur la survie (42% vs 33%)
- Mais mode ventilatoire non uniforme ds le groupe ECMO, Pplat élevée
- Haut niveau de survie ds le groupe contrôle
- Faible débit de l'ECMO
- Beaucoup de complications hémorragiques (inexpérience ?)

Survie: modification // évolutions technologiques



Type de membrane

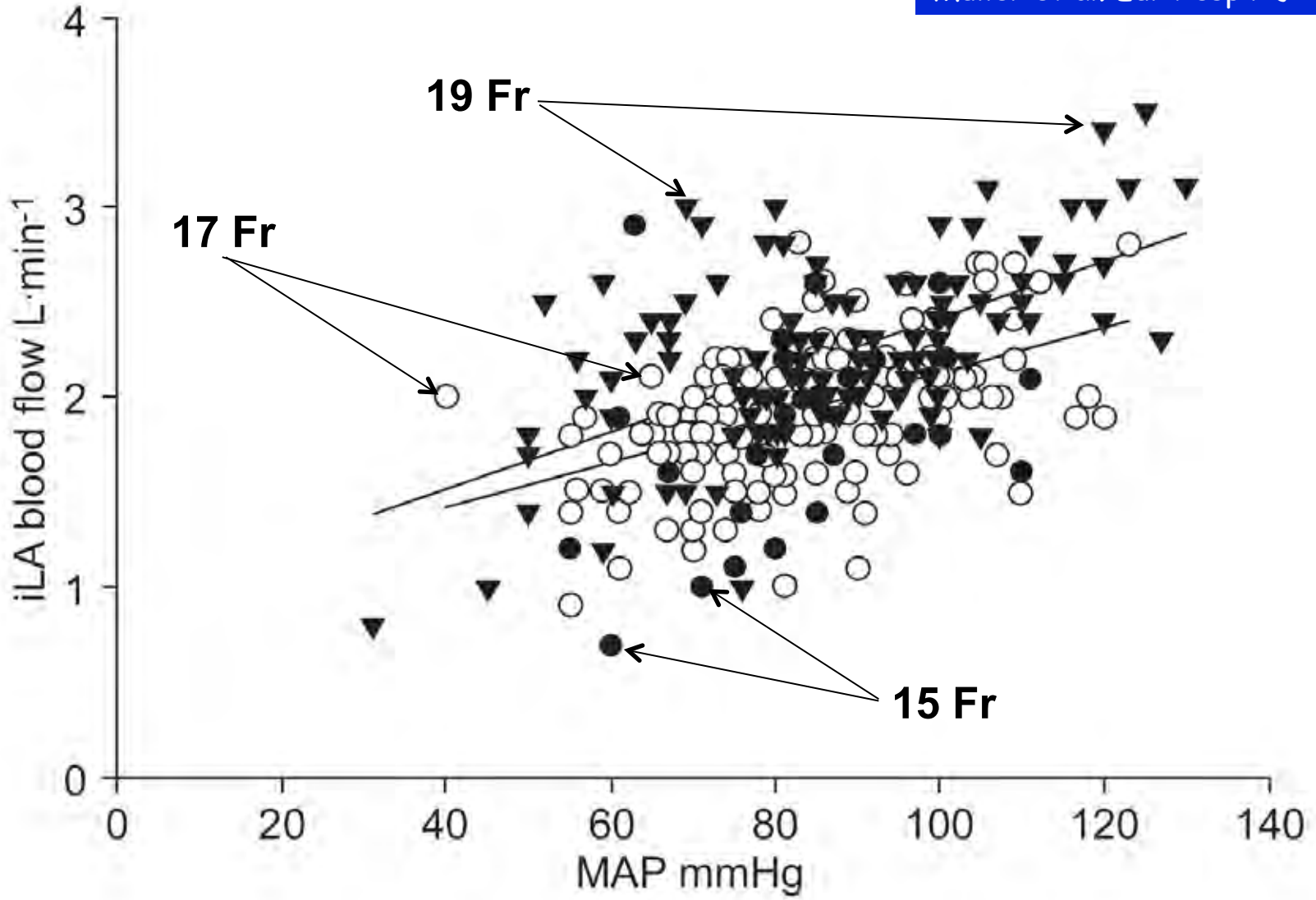
- Silicone: + résistantes
- Fibres microporeuses (polypropylène): + performantes et mieux tolérées
  - Fuite plasma
  - Changements quotidiens
- Microfibres microporeuses en polymethylpentene
  - Quadrox D
  - MEDOS
  - Novalung
  - Dideco

Progrès techniques

- Surfaces pré-héparinées
- Canules percutanées

Relation PAM, diamètre canule - débit

Müller *et al.* Eur Respir J 2009



Critères d'inclusion

PaO_2/FIO_2 ratio, < 100 on FIO_2 of 1.0, or $P(A\text{-}a)O_2$ of > 600 mm Hg, or Murray lung score of ≥ 3.0,[35] or uncompensated hypercapnea with a pH of < 7.20
Age < 65 yr
Receipt of mechanical ventilation for < 7 d
No known contraindication to limited anticoagulation
Patients who are not moribund and do not have contraindication to full intensive therapy

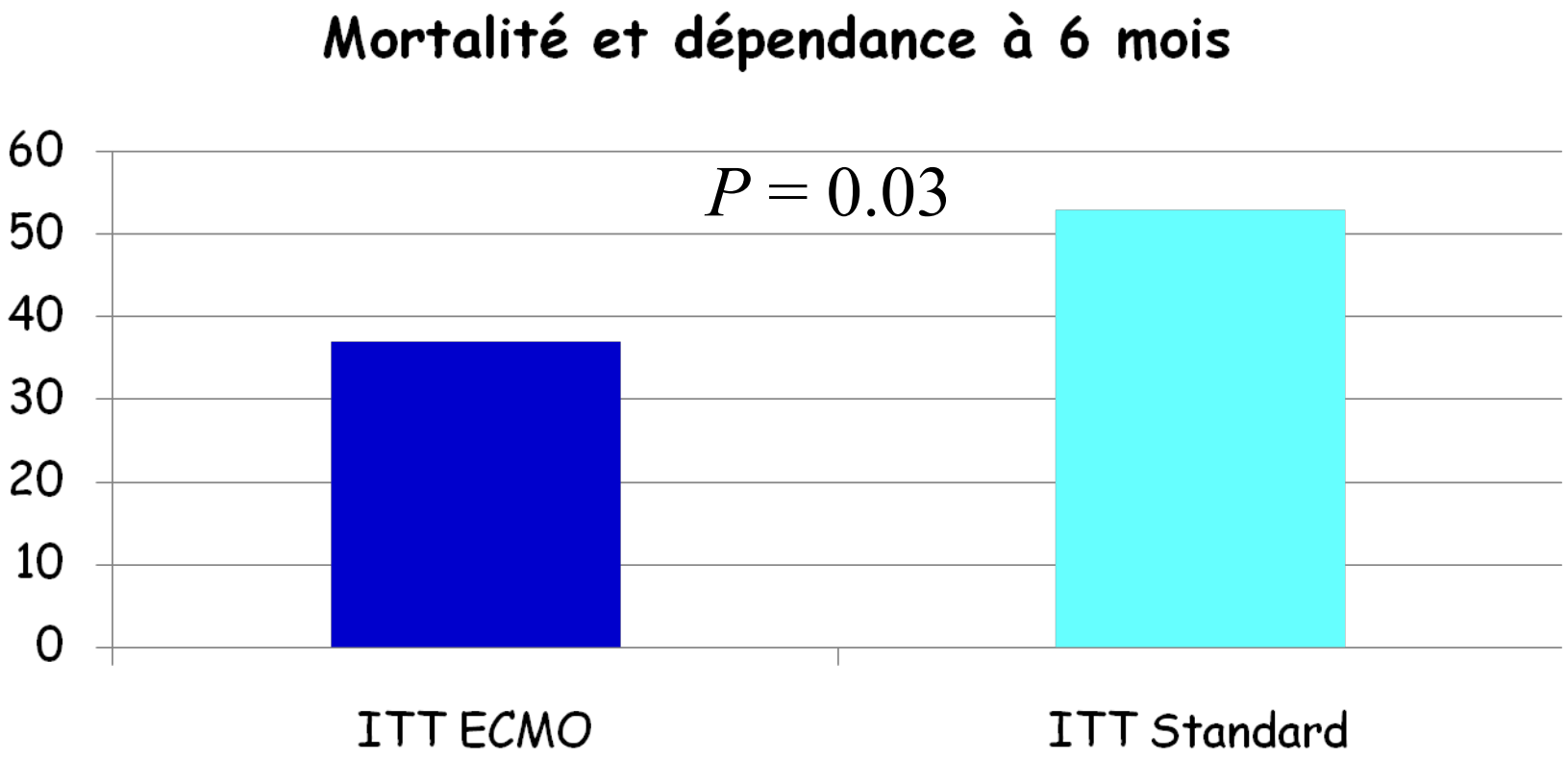
*$P(A\text{-}a)O_2$ = alveolar-arterial gradient.

CESAR
Conventional Ventilation or ECMO for Severe Adult Respiratory Failure

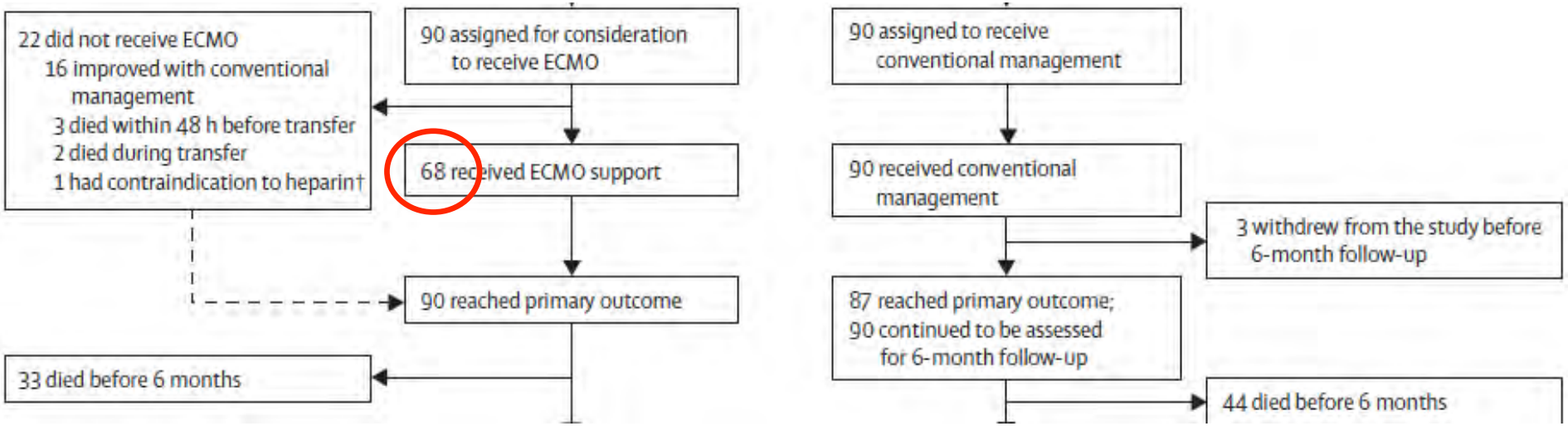
	ECMO	CONV
Age (ans)	40	40
PNEUMONIE (n)	56	53
TRAUMA (n)	5	7
DUREE VM (HEURES)	35	37
PAO2	85	87
LIS	3.5	3.4
APACHE II	20	20
HFO (n)	6	13
NO (n)	9	6
DV (n)	32	38

CESAR
Conventional Ventilation or ECMO for Severe Adult Respiratory Failure

Résultat



CESAR
Conventional Ventilation or ECMO for Severe Adult Respiratory Failure


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†
90 assigned for consideration to receive ECMO
68 received ECMO support
90 reached primary outcome
33 died before 6 months
90 assigned to receive conventional management
90 received conventional management
3 withdrew from the study before 6-month follow-up
87 reached primary outcome;
90 continued to be assessed for 6-month follow-up
44 died before 6 months

Pronostic

	Survivors (n = 132)		Nonsurvivors (n = 123)		
	Mean ± SD	Range	Mean ± SD	Range	*P* Value
Age, y	37.2 ± 13.1	17–68	39.7 ± 13.2	17–69	NS
Male/female, %	56.1/43.9		40.7/59.3		0.02
Weight, kg	82.2 ± 21.9	39–156	82.7 ± 23.9	36–150	NS
Duration of ECLS, h	180.2 ± 136.1	23–735	261.6 ± 238.6	3–1358	0.0009
PaO_2/FiO_2 ratio	56.6 ± 15.5	26–129	53.1 ± 16.1	28–123	NS
Shunt (Qs/Qt)	0.54 ± 0.17	—	0.56 ± 0.21	—	NS
A-aDO_2 gradient, mm Hg	612 ± 19	538–651	611 ± 22	523–658	NS
Pre-ECLS ventilator days	3.2 ± 2.6	0–16	4.5 ± 3.7	0–22	0.002

Hemmila *et al.* Ann Surg 2004

Les principaux critères d'ECMO

- **L'hypoxémie profonde :**
  - PaO2/FiO2 < 70 sous FiO2 1 depuis 2h au moins
  - avec PEEP d'au moins 10 cmH2O
- **Une ventilation protectrice impossible:**
  - PaO2/FiO2 entre 70 et 100 (à FiO2 = 1)
  - avec Pplat > 35 cmH2O
  - ou la présence d'une acidose respiratoire sévère (pH < 7,15 malgré une fréquence respiratoire à 35/min)
- **SOFA extra-respiratoire < 9**

Extracorporeal Membrane Oxygenation for severe Influenza A (H1N1) Acute Respiratory Distress Syndrome: a prospective observational comparative study

- **Équipe UMAC-UMAREC**
- **Opérationnelle depuis le 01 Nov 2009**
- **Inclusion des patients du 01/11/09 à la fin de l'épidémie le 20 Janv 2010**
- **Tous H1N1 confirmé**

2.6 ECMO/ million d'habitant => soit en PACA 11 ECMO

Table 2 Severity of illness in the 6 h preceding ECMO or in the 6 h following initiation of mechanical ventilation in patients without ECMO

	ECMO ($n = 9$)	Without ECMO ($n = 9$)	p value
Ventilation parameters, median (IQR)			
Lowest PaO_2/FiO_2 ratio (mmHg)	52 (50–60)	96 (89–143)	<0.001
Highest PEEP (cmH_2O)	12 (11–14)	10 (10–13)	NS
Highest Pplat (cmH_2O)	31 (30–35)	26 (25–29)	<0.05
Lowest pH	7.17 (7.04–7.25)	7.36 (7.3–7.37)	<0.001
Highest $PaCO_2$ (mmHg)	85 (69–91)	45 (44–53)	<0.001
Lung Injury Score, median (IQR)	3.6 (3.3–3.7)	3 (2.5–3.5)	<0.01
SOFA, median (IQR)	9 (8–10)	7 (6–8)	<0.01

p value, by Mann–Whitney U test

PEEP positive end-expiratory pressure, *Pplat* plateau pressure, *SOFA* Sequential Organ Failure Assessment

Roch et al. Intensive Care Med 2010

	ECMO ($n = 9$)	Without ECMO ($n = 9$)
Age, median (IQR), years	49 (26–57)	54 (43–60)
Male sex	3 (33)	4 (44)
BMI, median (IQR), kg/m^2	30 (25–30)	30 (24–35)
Time from onset of flu symptoms to ICU admission, median (IQR), days	4 (2–6)	3 (1–5)
SAPS II at ICU admission, median (IQR)	47 (30–52)	37 (33–48)
Lactate[a], median (IQR), mmol/l	4.9 (1.9–12.6)	1.7 (1.5–2.4)*
Pregnancy or postpartum	1 (11)	0
Diabetes mellitus	1 (11)	2 (22)
COPD	0	2 (22)
Congestive heart failure	1 (11)	0
Immunosuppressant medications	1 (11)	0
Cancer	2 (22)	2 (22)
At ICU admission		
Mechanical ventilation	7 (78)	3 (33)
Vasopressor	6 (67)	2 (22)
Renal replacement therapy	3 (33)	1 (11)

	ECMO ($n = 9$)	Without ECMO ($n = 9$)
Mortality		
ICU	5 (56)	5 (56)
Hospital	5 (56)	5 (56)
Corticosteroids for ARDS	5 (56)	3 (33)
Cause of death		
Intractable respiratory failure	2 (22)	1 (11)
Multiorgan failure	3 (33)	4 (44)

Les leçons à tirer (point de vue du réanimateur)

- Bon entrainement
- Très grande hétérogénéité inter- et intra-villes
- Réemergence d'une vieille technique d'assistance ventilatoire (AREC)
  - Non-dénuée de risques
  - Peu d'indications annuelles
  - Activité non reconnue par les tutelles donc mal valorisée
  - Urgence à encadrer le déploiement anarchique
- Spécifique à certaines villes: mise en place d'une UMAREC
  - Non valorisée
  - A organiser en fonction d'un Territoire de Santé
- Mauvaise compliance des paramédicaux à la vaccination

Transport inter-hospitalier sous ECMO

UMAREC

Unité Mobile d'Assistance Respiratoire Extra-Corporelle

SAMU

Chirurgie cardiaque

Réanimation

Centres ECMO

- **Hypoxémie réfractaire**
  - PaO2/FiO2 < 50, persistante*
  - FiO2 > 80 % + PEP (≤ 20 cmH2O)
  - Pplat = 32 cmH2O
  - + décubitus ventral +/- NOi
- **Ventilation non-protectrice**

(Pression de plateau ≥ 35 cmH2O)

  - Malgré PEP réduite à 5 cmH2O
  - VT réduit à sa valeur minimale
  - compatible avec un pH ≥ 7,15

Centres pouvant faire appel à une UMAREC

- **Hypoxémie profonde**
  - PaO2/FiO2 < 70 sous FiO2 1 depuis 2h au moins
  - avec une PEEP d'au moins 10 cmH2O
- **Une ventilation protectrice impossible**
  - PaO2/FiO2 entre 70 et 100 (à FiO2 = 1)
    - avec une Pplat > 35 cmH2O
    - ou la présence d'une acidose respiratoire sévère (pH < 7,15 malgré une fréquence respiratoire à 35/min).

•: Caractère persistant doit tenir compte de l'évolutivité (qq h pour les formes très évolutives à 48 h en cas de stabilité)

"Optimisation"

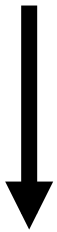
- 36 patients (4,5 ans) : LIS > 2,5 et critères ECMO
- stratégie
  - TDM
  - diurétiques ou HF
  - "↘ Qs pulmonaire"
  - mode ventilatoire

    (Vt, PIM et Pmoy le plus bas possible avec recrutement alvéolaire correct)
  - ± hypercapnie
  - TGI
  - ↘ shunt
    - » PEEP, i/e
    - » NO 15 ppm
    - » DV
    - » almitrine

Guinard et al. Chest 97

"Optimisation"

- R : PaO_2/FiO_2 > 100 pendant au moins 6 h
- NR
  - PaO_2/FiO_2 < 100
  - $PaCO_2$ non-maitrisable
  - détérioration mécanique ventilatoire

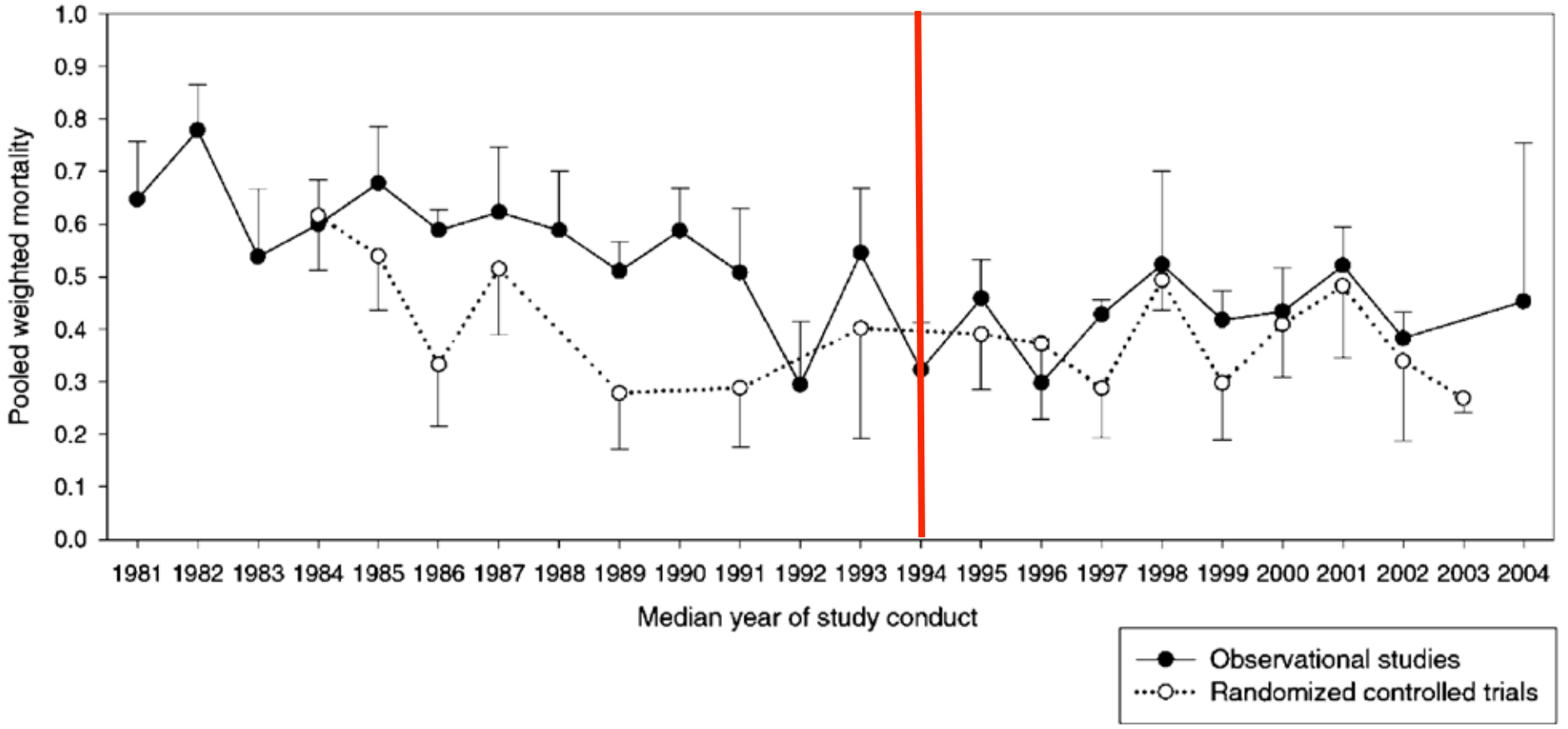


ECCO2R

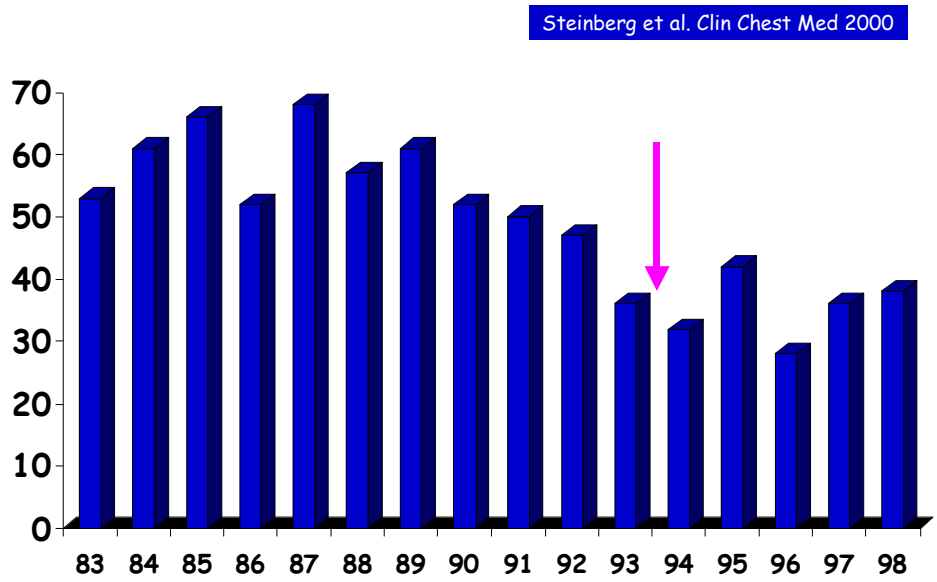
Guinard et al. Chest 97

Evolution mortalité

Phua et al. AJRCCM 2009



Mortalité hospitalière



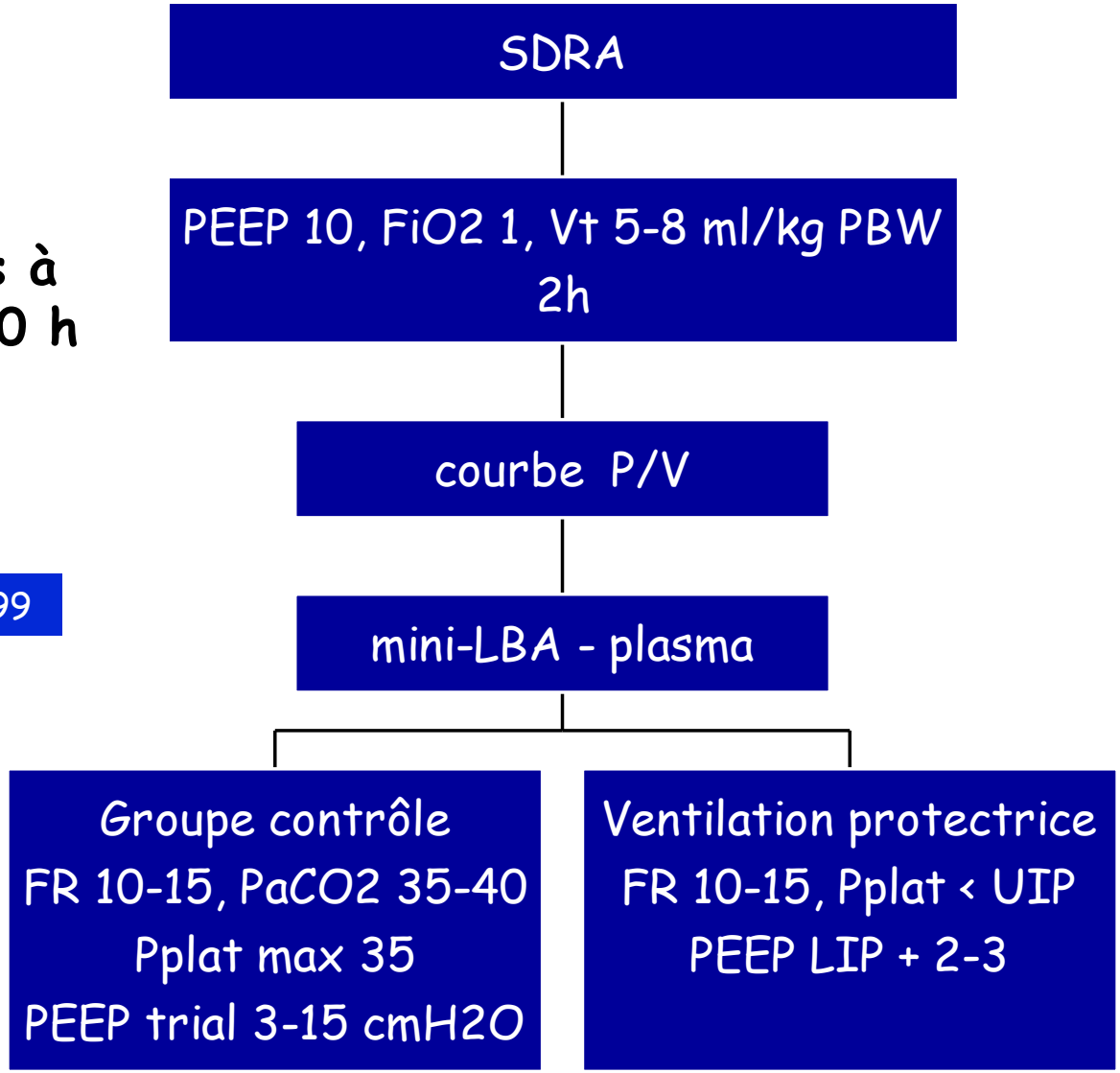
« Par ma foi ! il y a plus de quarante ans que je fais de la protection du poumon sans que j'en susse rien, et je vous suis le plus obligé du monde de m'avoir appris cela. »

Adapted from: Molière – Le bourgeois gentilhomme

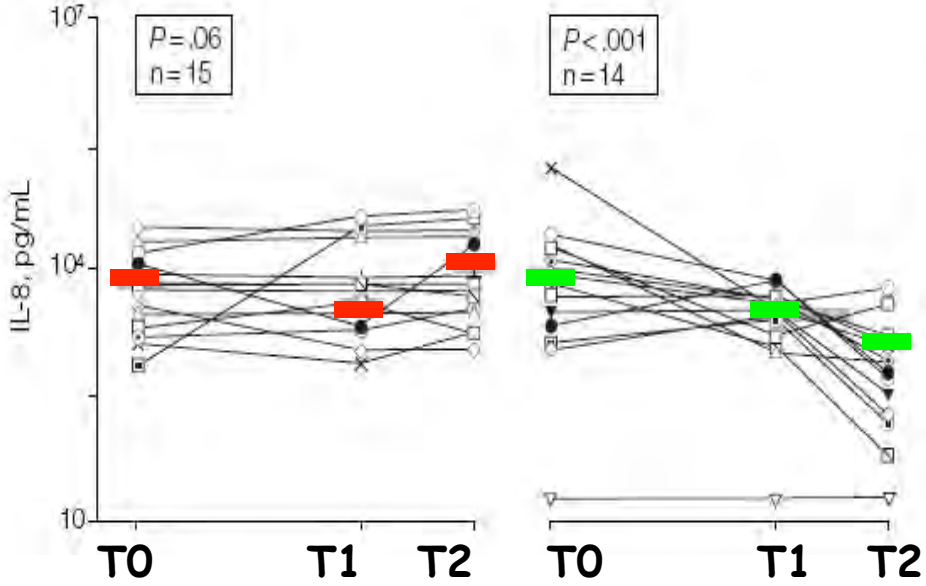
entilation protectrice au cours du SDRA

- **37 patients**
- **Mesures répétées à 24-30 h et 36-40 h**

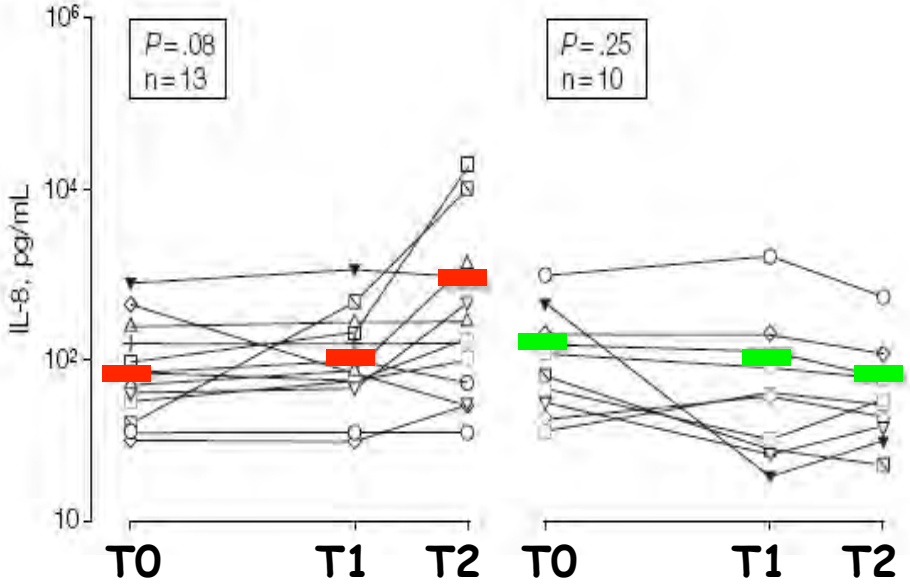
Ranieri *et al.* JAMA 99

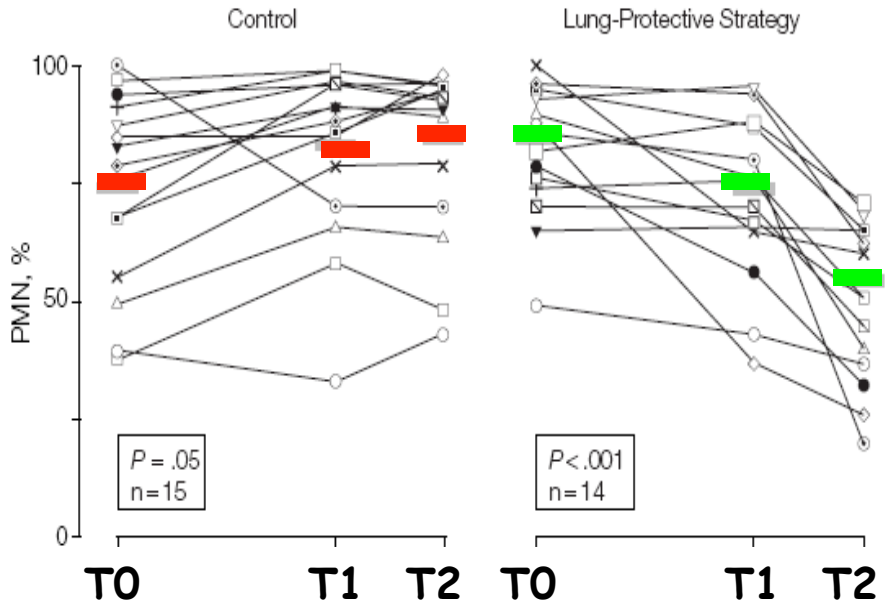


LBA



plasma





Ranieri *et al.* JAMA 99

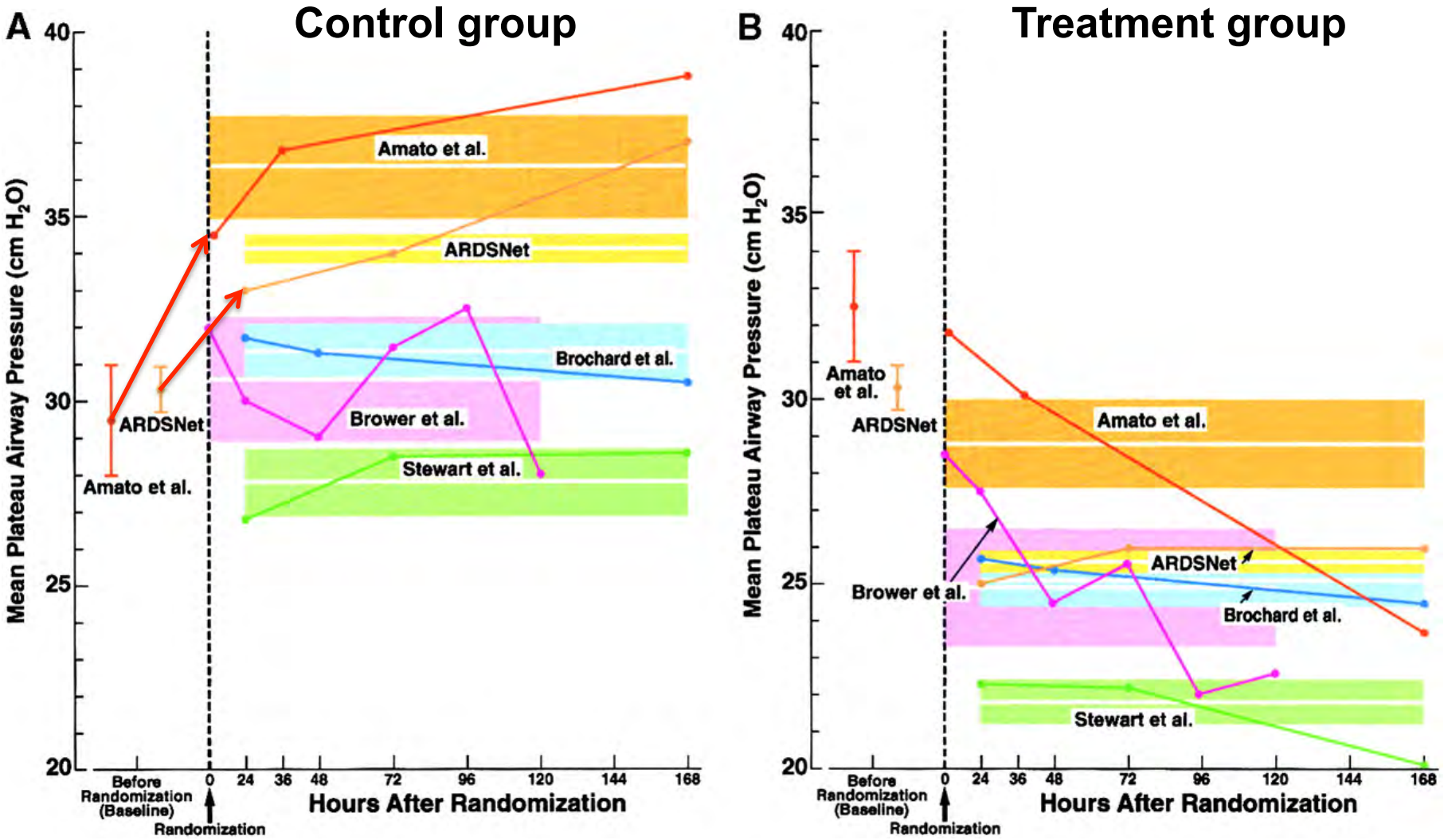
Décompartementalisation





	PLV	cont	PLV	cont	PLV	cont	PLV	cont	PLV	cont
n	60	60	26	26	58	58	29	24	400	400
Vt	7.0	10.7	7.5	10.2	7.1	10.5	6.0	12.0	6.2	11.8
PEEP	8.6	7.2	9.5	8.3	10.7	10.7	16.4	8.7	9.4	8.6
Pplat	22	27	28	31	26	32	30	37	25	33

Eichacker et al. AJRCCM 2003



Esteban et al. JAMA 2002

Table 3. Ventilator Modes and Monitored Variables on Days 1, 3, and 7 of Mechanical Ventilation in Patients With an Exacerbation of Chronic Obstructive Pulmonary Disease (COPD) or Acute Respiratory Distress Syndrome (ARDS)*

	COPD			ARDS		
	Day 1 (n = 522)	Day 3 (n = 283)	Day 7 (n = 85)	Day 1 (n = 231)	Day 3 (n = 174)	Day 7 (n = 82)
Ventilator modes, No. (%)						
A/C	344 (65.9)	180 (63.6)	57 (67.1)	155 (67.0)	111 (63.8)	50 (61.0)
SIMV/PS	50 (9.6)	32 (11.3)	9 (10.6)	24 (10.4)	20 (11.5)	8 (9.8)
PS	40 (7.6)	24 (8.5)	10 (11.8)	3 (1.4)	6 (3.4)	3 (3.7)
PCV	20 (3.9)	11 (3.9)	2 (2.4)	24 (10.4)	23 (13.2)	13 (15.9)
SIMV	24 (4.6)	10 (3.5)	2 (2.4)	10 (4.2)	4 (2.3)	2 (2.4)
Other	39 (8.5)	26 (9.2)	1 (1.2)		10 (5.7)	6 (7.3)
Monitored variables, mean (SD) [median {IQR}]						
Peak pressure, cm H_2O	31 (9) [31 {25-38}]	31 (9) [32 {25-37}]	32 [32 {2		3 (8) 27-39}]	33 (9) [34 {27-40}]
Plateau pressure, cm H_2O†	22 (6) [20 {17-26}]	22 (6) [21 {17-27}]	23 [23 {18-2		27 (7) 27 {21-30}]	26 (7) [25 {21-30}]
Tidal volume, mL	586 (133) [580 {500-692}]	564 (128) [550 {500-640}]	589 (135) [600 {500-670}]		607 (131) [600 {500-700}]	613 (141) [600 {500-700}]
Tidal volume, mL/kg	8.4 (2.3) [8.3 {6.7-10.0}]	8.0 (2.3) [7.8 {6.4-9.6}]	8.1 (2.6 [7.9 {6.0		8.5 (2.0) 7.3-10.0}]	8.5 (2.0) [8.2 {6.9-10.0}]
Respiratory rate, breaths/min	17 (6) [16 {14-20}]	17 (5) [16 {14-20}]	17 [18 {1		(7) 16-20}]	20 (6) [20 {16-22}]
FIO_2	52 (18) [50 {40-60}]	46 (13) [40 {40-50}]	50 (18 [40 {40-60}		53 (21) [60 {50-80}]	59 (22) [50 {40-74}]
Patients without PEEP, No. (%)	218 (47.6)	128 (45.2)	33 (38.8)	34 (16.0)	14 (8.0)	8 (9.7)
PEEP, cm H_2O	5 (2) [5 {4-5}]	5 (2) [5 {5-6}]	6 (3) [5 {4-7}]	8 (4) [8 {5-10}]	9 (3) [10 {6-12}]	9 (3) [9 {5-12}]

28 (23-33)

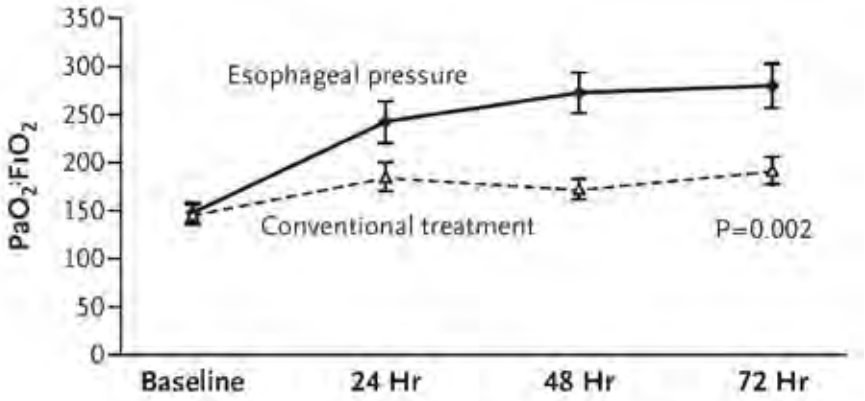
8.6 (7.4-10.0)

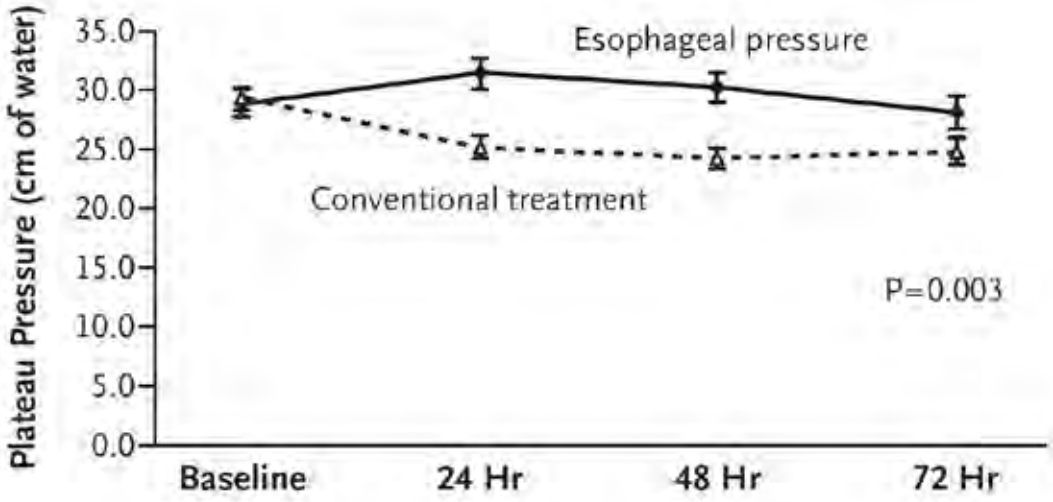
*A/C indicates assist/control ventilation; SIMV, synchronized intermittent mandatory ventilation; PS, pressure support; PCV, pressure-controlled ventilation; IQR, interquartile range; and PEEP, positive end-expiratory pressure.
†Plateau pressure only recorded in patients ventilated with A/C.

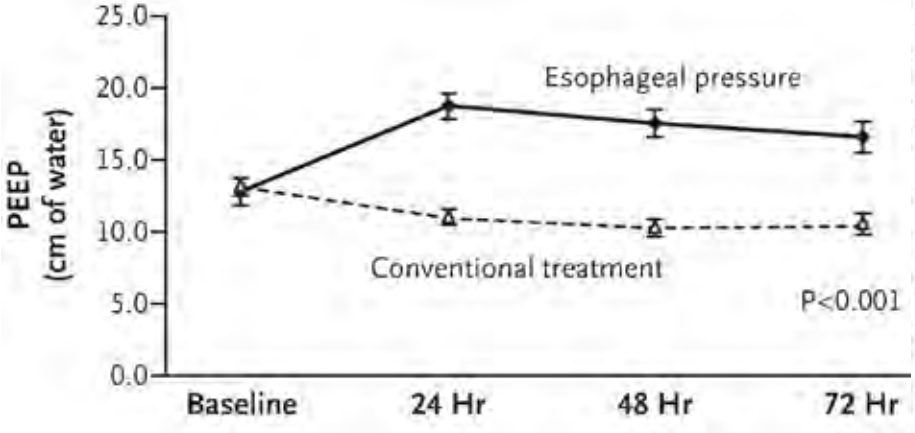
Faut-il, sous prétexte d'ouverture, limiter le débat à…

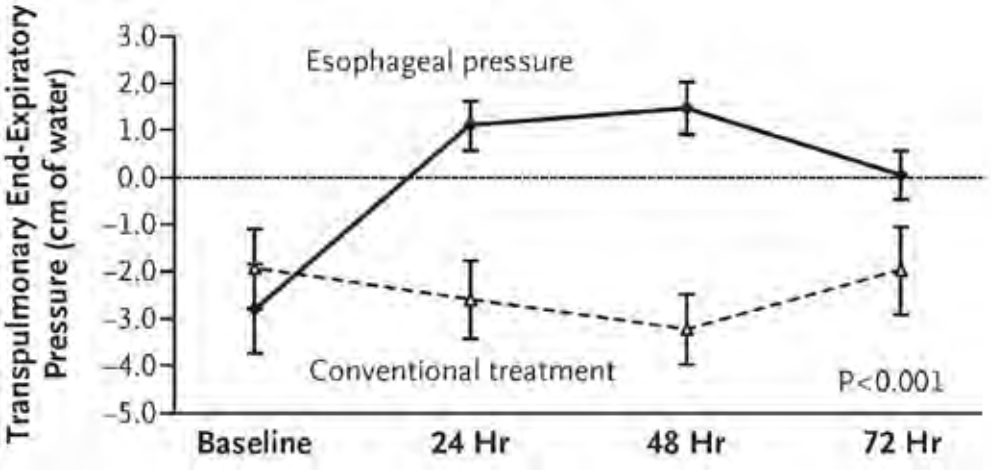
Grand Vt vs. Petit Vt ?

Variables	Day 1			Day 3			Day 7		
	Lung Open Ventilation	Control	*P* Value	Lung Open Ventilation	Control	*P* Value	Lung Open Ventilation	Control	*P* Value
Plateau pressure, mean (SD), cm H_2O	30.2 (6.3)	24.9 (5.1)	<.001	28.6 (6.0)	24.7 (5.7)	<.001	28.8 (6.3)	25.1 (6.8)	<.001
No. of patients	435	424		334	380		174	232	
30.1-35.0	112	33		76	38		37	27	
35.1-40.0	88	4		41	12		27	13	
>40.0	8	1		8	3		4	4	


PaO_2:FIO_2
350
300
250
200
150
100
50
0
Esophageal pressure
Conventional treatment
P=0.002
Baseline
24 Hr
48 Hr
72 Hr


Plateau Pressure (cm of water)
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
Esophageal pressure
Conventional treatment
P=0.003
Baseline
24 Hr
48 Hr
72 Hr

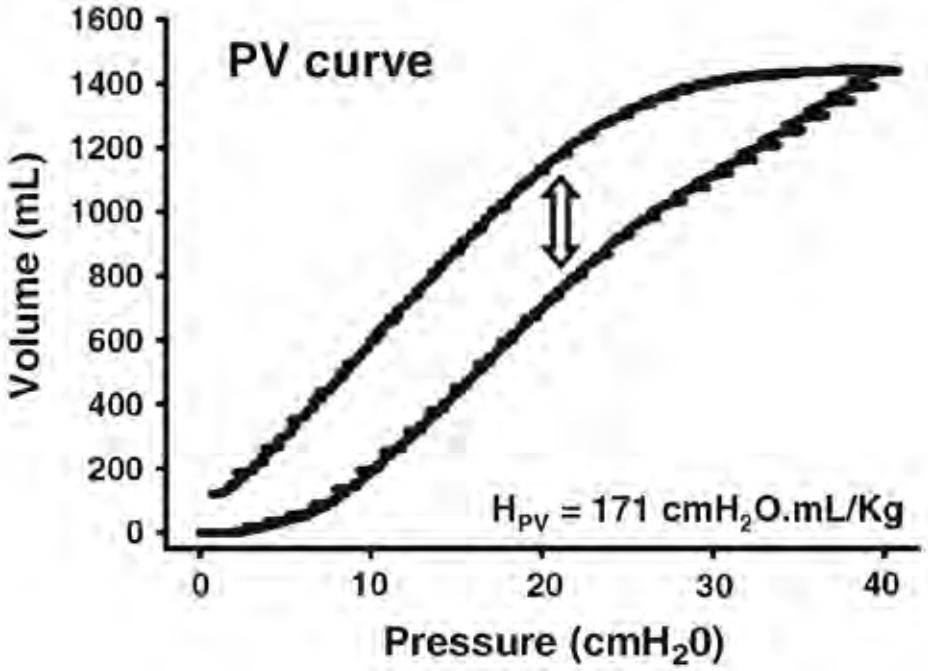

PEEP
(cm of water)
25.0
20.0
15.0
10.0
5.0
0.0
Esophageal pressure
Conventional treatment
P<0.001
Baseline
24 Hr
48 Hr
72 Hr

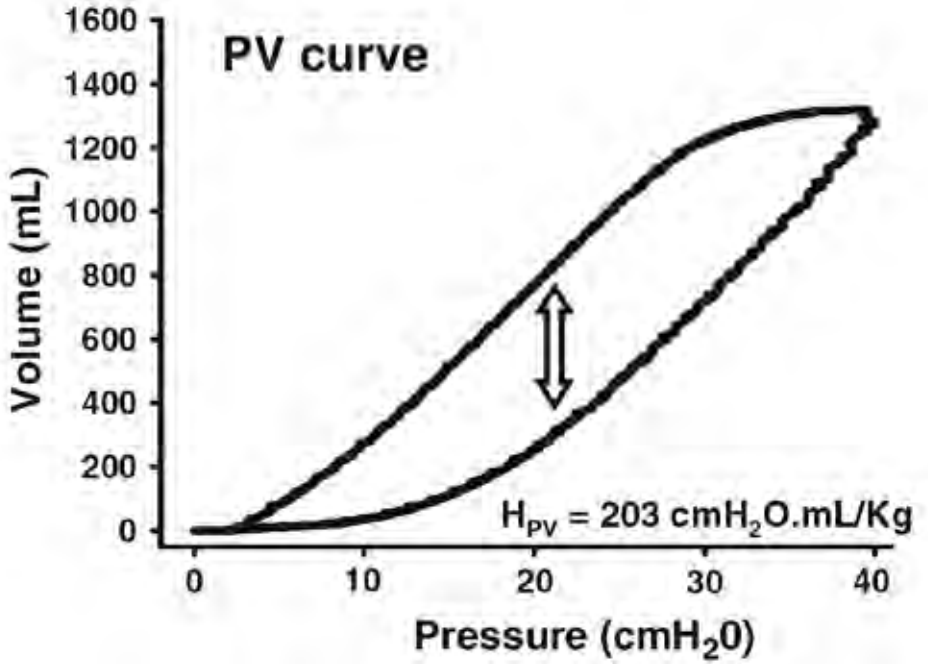

Transpulmonary End-Expiratory Pressure (cm of water)
3.0
2.0
1.0
0.0
−1.0
−2.0
−3.0
−4.0
−5.0
Esophageal pressure
Conventional treatment
P<0.001
Baseline
24 Hr
48 Hr
72 Hr

Outcome	Esophageal-Pressure–Guided (N = 30)	Conventional Treatment (N = 31)	P Value
28-Day mortality — no. (%)	5 (17)	12 (39)	0.055
180-Day mortality — no. (%)	8 (27)	14 (45)	0.13
Length of ICU stay — days			0.16
Median	15.5	13.0	
Interquartile range	10.8–28.5	7.0–22.0	
No. of ICU-free days at 28 days			0.96
Median	5.0	4.0	
Interquartile range	0.0–14.0	0.0–16.0	
No. of ventilator-free days at 28 days			0.50
Median	11.5	7.0	
Interquartile range	0.0–20.3	0.0–17.0	
No. of days of ventilation among survivors			0.71
Median	12.0	16.0	
Interquartile range	7.0–27.5	7.0-20.0	

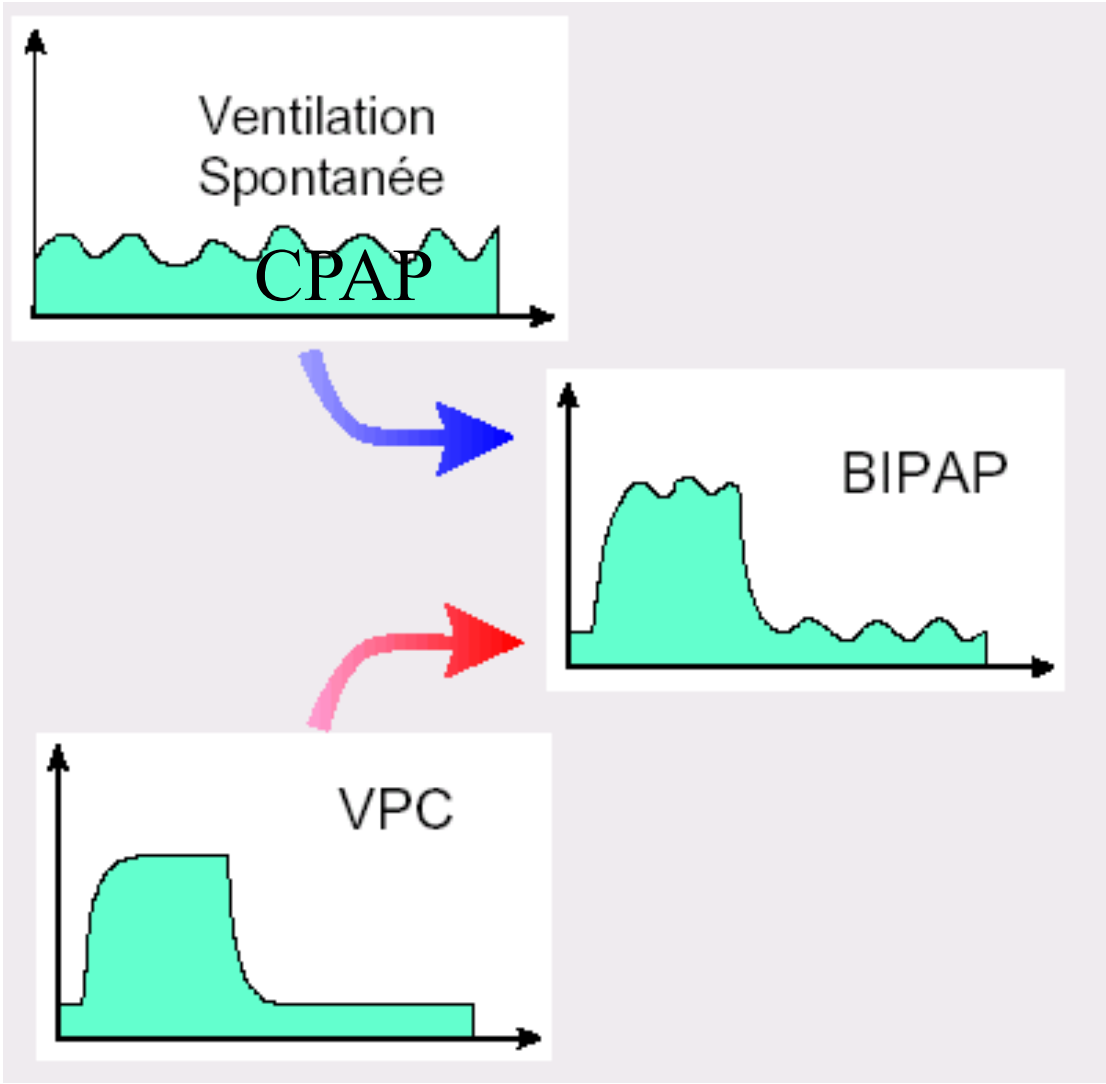
Talmor *et al.* NEJM 2008

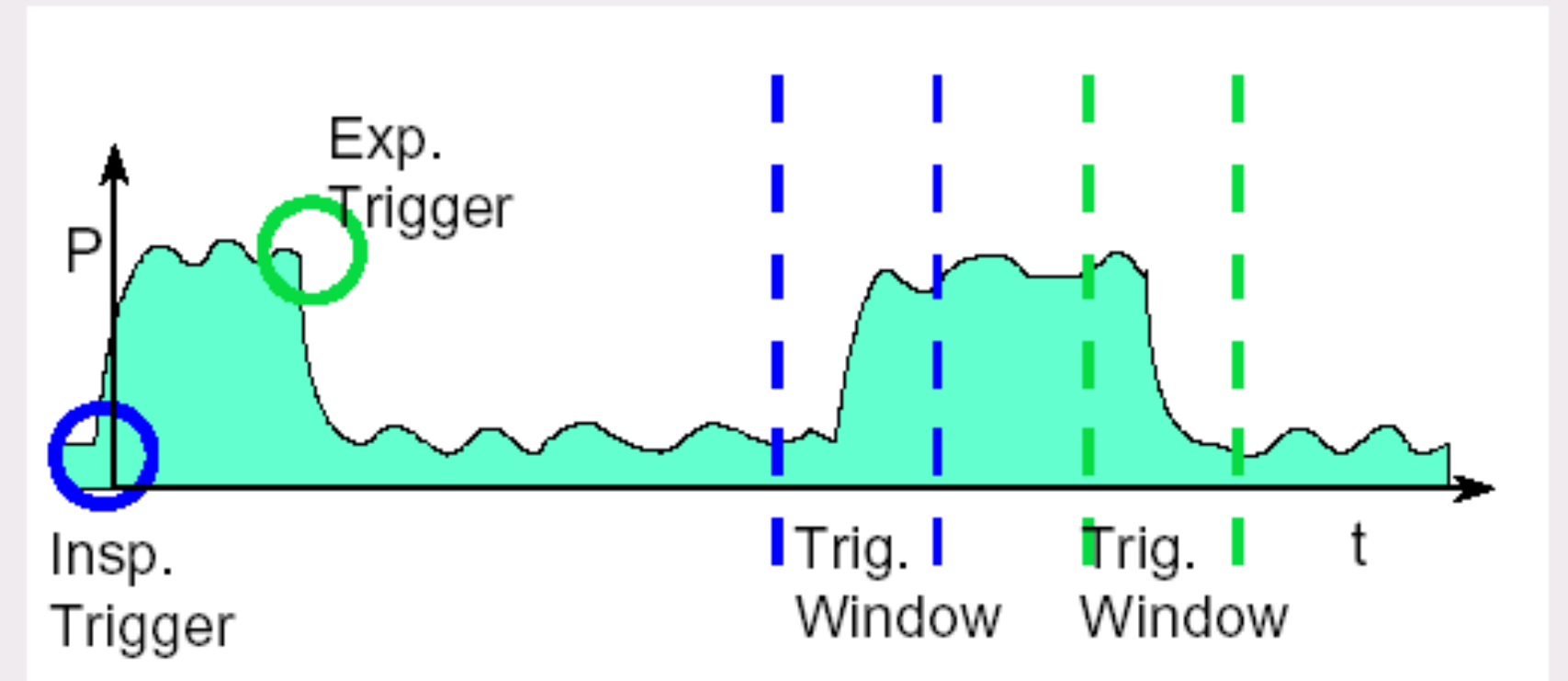
Apprécier l'hystérésis





Demory, Arnal *et al.* Intensive Care Med 2008

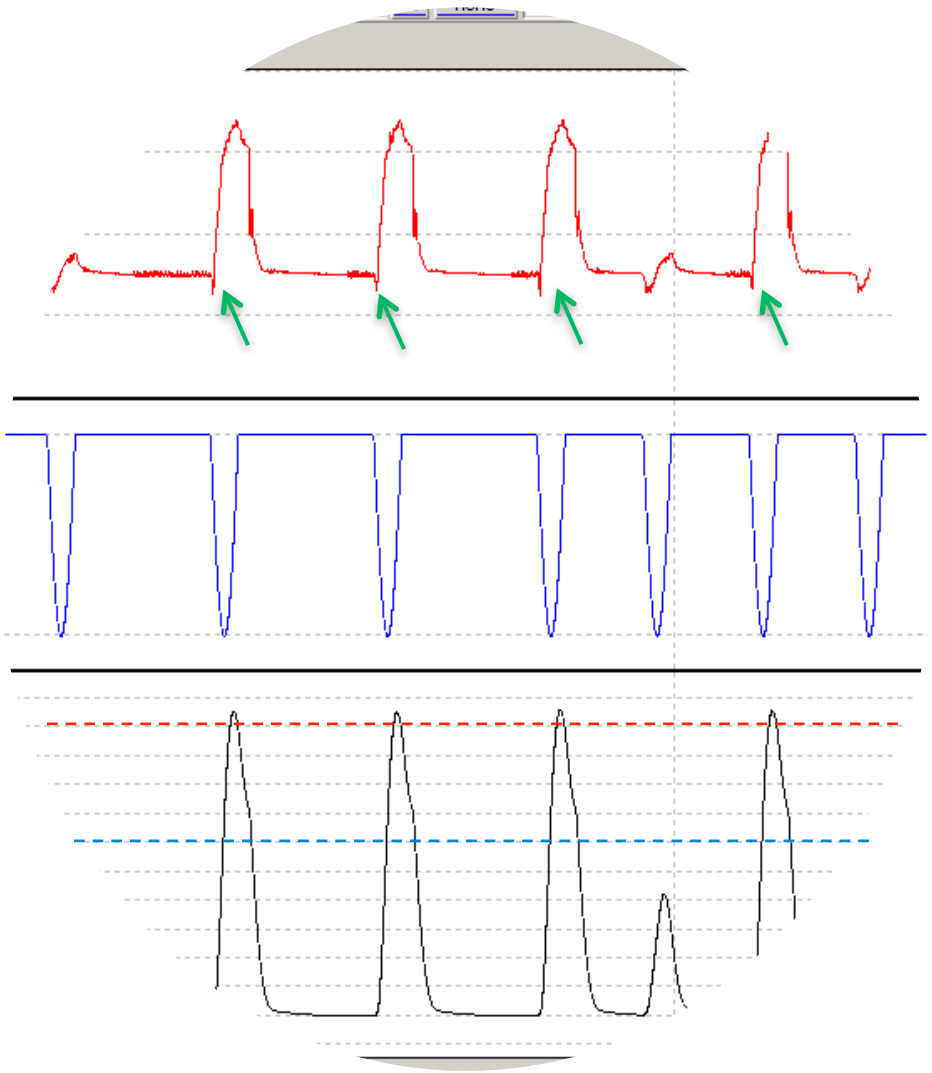

Ventilation
Spontanée
CPAP
BIPAP
VPC

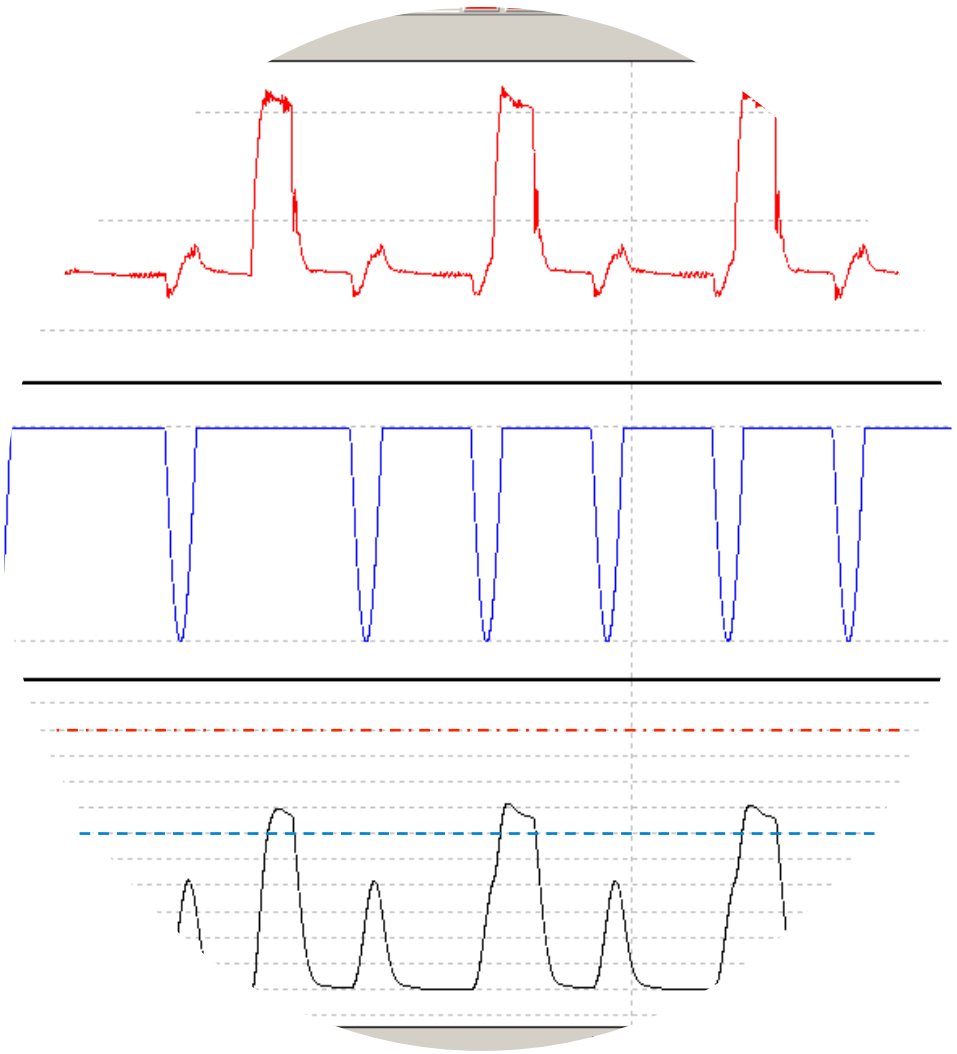


Synchronization may amplify transpulmonary pressure swings

BIPAP

APRV





Synchronized cycles

Non Synchronized cycles

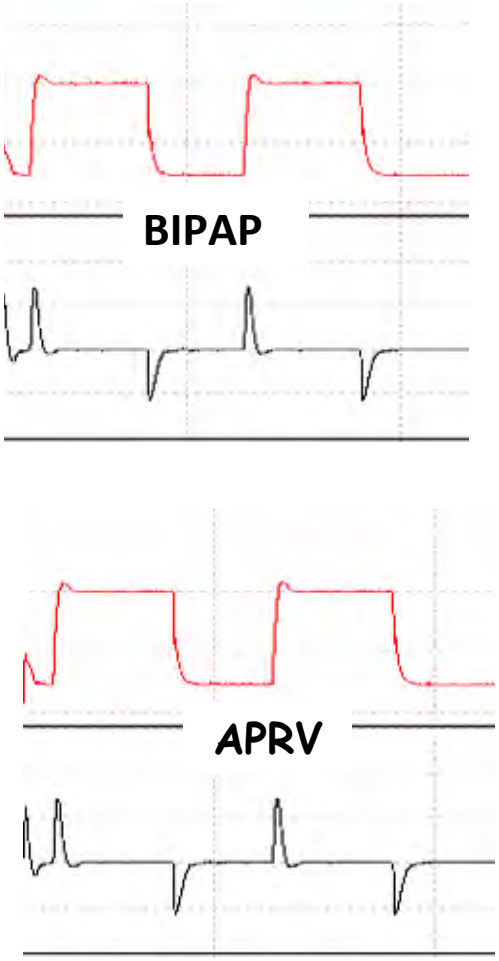
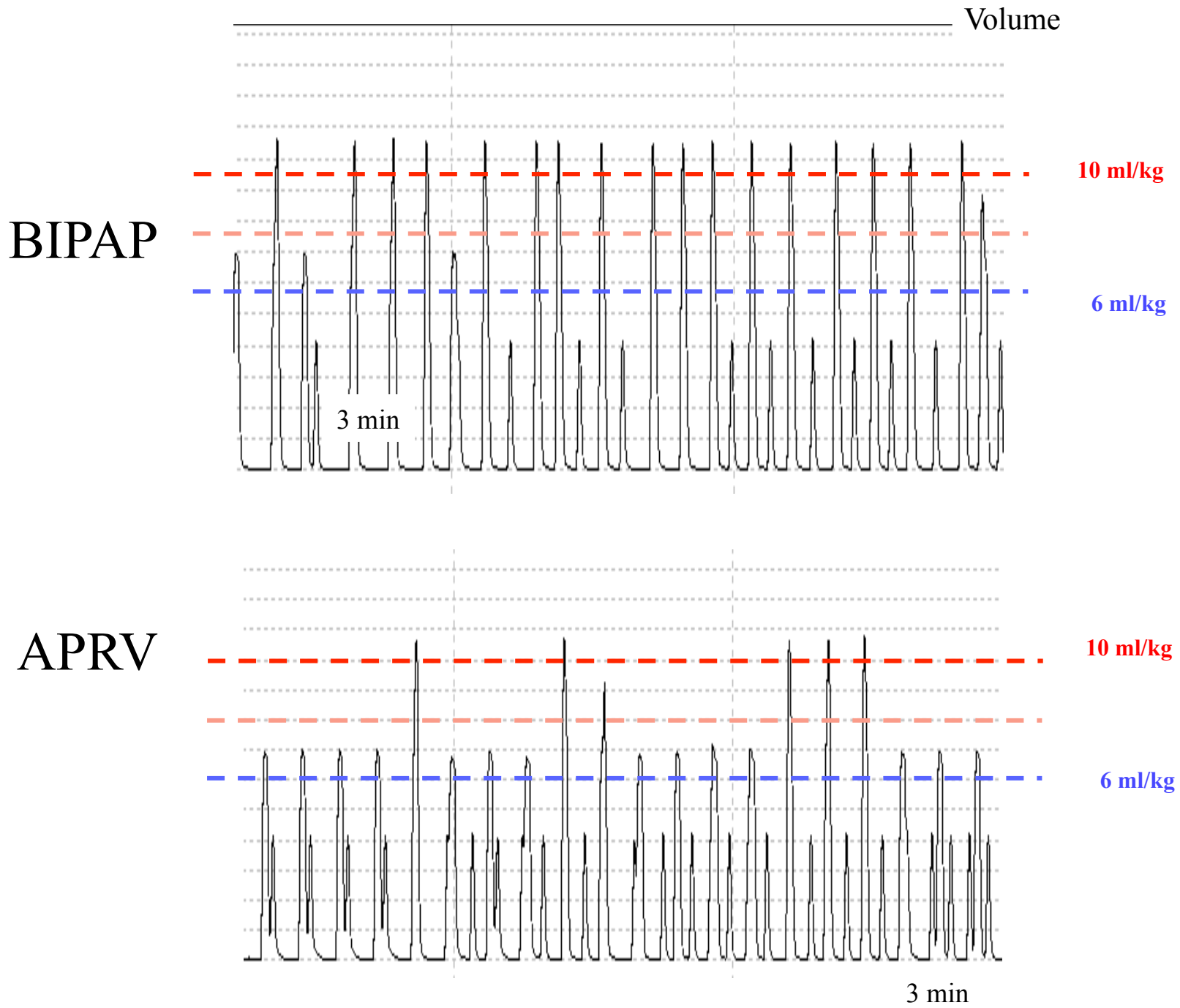


Figure_1 Ventilator waveforms of APRV-BIPAP modes


Volume
BIPAP
10 ml/kg
6 ml/kg
3 min
APRV
10 ml/kg
6 ml/kg
3 min

I:E	Mode	Tidal Volume (ml)	Ptp Maximal (cmH_2O)	Ptp swing (cmH_2O)
1:3	APRV	368 (±195)	32 (±6)	14 (±6)
	BIPAP	466 (±237)	33 (±7)	17 (±8)
	BIPAP + PS	754 (±31)	42 (±0)	27 (±1)

ARDS

	Mild	Moderate	Severe
Timing	Acute onset within 1 week of a known clinical insult or new/ worsening respiratory symptoms		
Hypoxemia	PaO_2/FiO_2 201-300 with PEEP/CPAP ≥ 5	PaO_2/FiO_2 ≤ 200 with PEEP ≥ 5	PaO_2/FiO_2 ≤ 100 with PEEP ≥ 10
Origin of Edema	Respiratory failure not fully explained by cardiac failure or fluid overload**		
Radiological Abnormalities	Bilateral opacities*	Bilateral opacities*	Opacities involving at least 3 quadrants*
Additional Physiological Derangement	N/A	N/A	$V_{E\ Corr}$ > 10 L/min or C_{RS}<40 ml/cmH_2O

*Not fully explained by effusions, nodules, masses, or lobar/lung collapse; use training set of CXRs
**Need objective assessment if no risk factor present (See table)
$V_{E\ Corr} = V_E \times PaCO_2/40$

Caractérisation SDRA

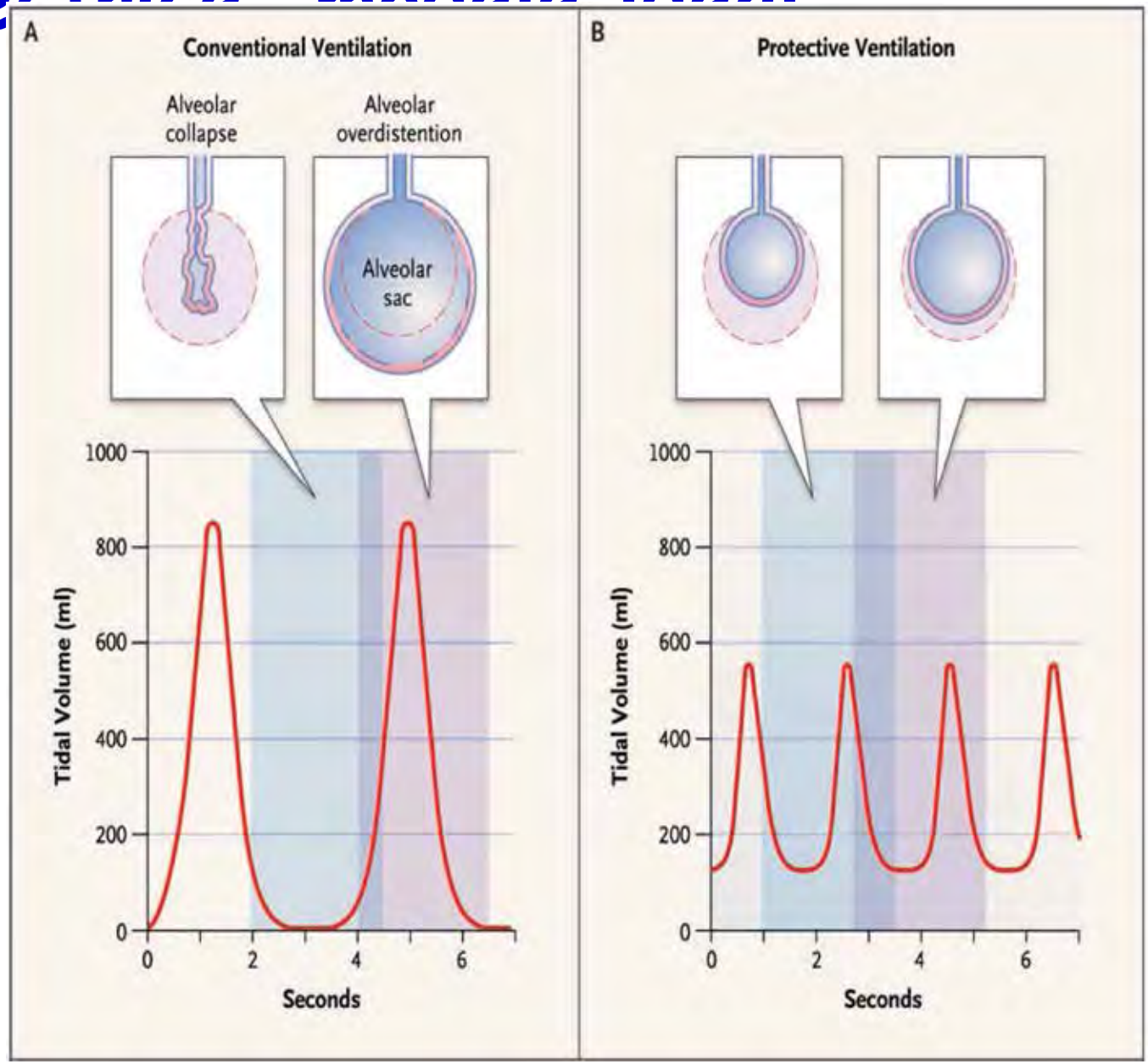
- Gazométrie n°1 à PEEP 5 (et FiO2 = 1)

The "Berlin definition" in:

Ospedale Maggiore, Milano: Luciano Gattinoni: 212 patients

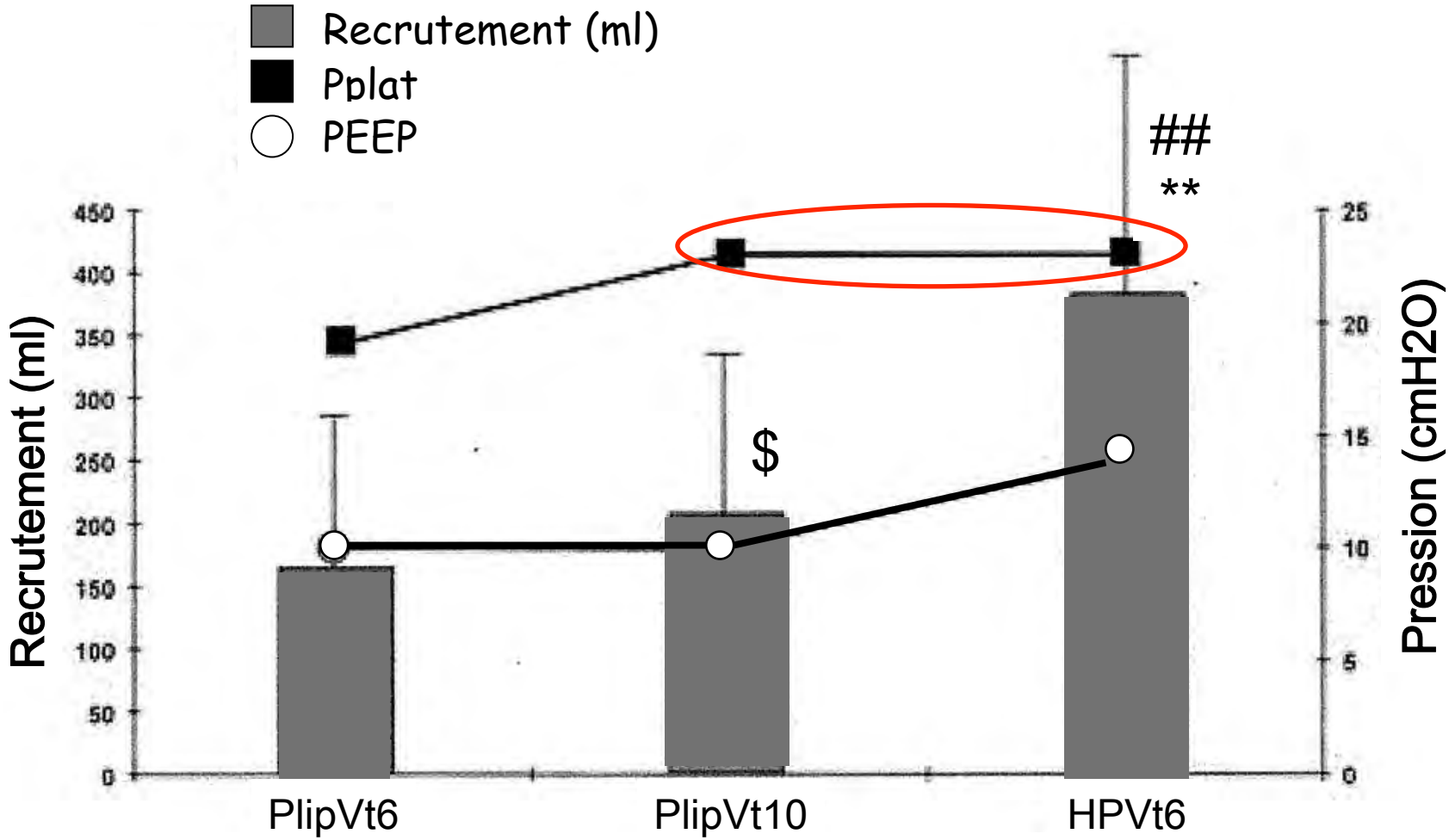
ARDS				
	Mild (23%)	Moderate (63%)	Severe (14%)	
PaO_2/FiO_2	246±41	146±29	75±16	P<0.0001
Lung weight (mg)	1299±274	1458±503	1905±598	P<0.001
Recrutability (%)	7±7	13±10	23±12	P<0.0001
Not inflated tissue (%)	0.30±14	0.39±0.14	0.51±0.17	P<0.0001
Compliance	43±14	39±13	36±16	P=0.23
Corrected VE (L)	9.8±2.3	10.2±3.7	9.8±2.3	P<0.01
Shunt (%)	0.08±0.09	0.19±0.1	9.8±2.3	P<0.0001
MORTALITY (%)	10	32	62	P<0.0001

Ventilation protectrice: modèle idéal



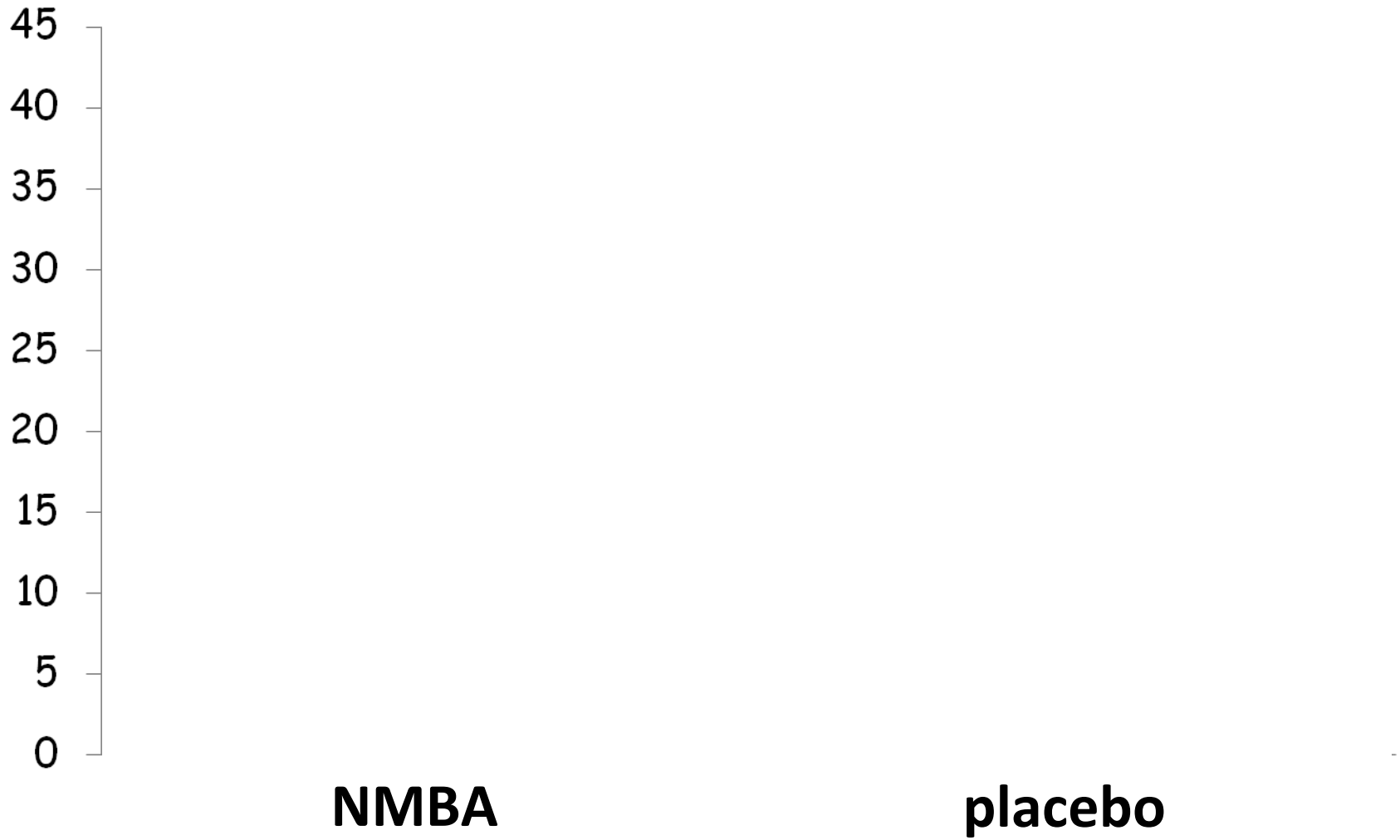
/t, PEEP et recrutement

Richard *et al.* CCM 2003



Unadjusted day 90 mortality

ACURASYS

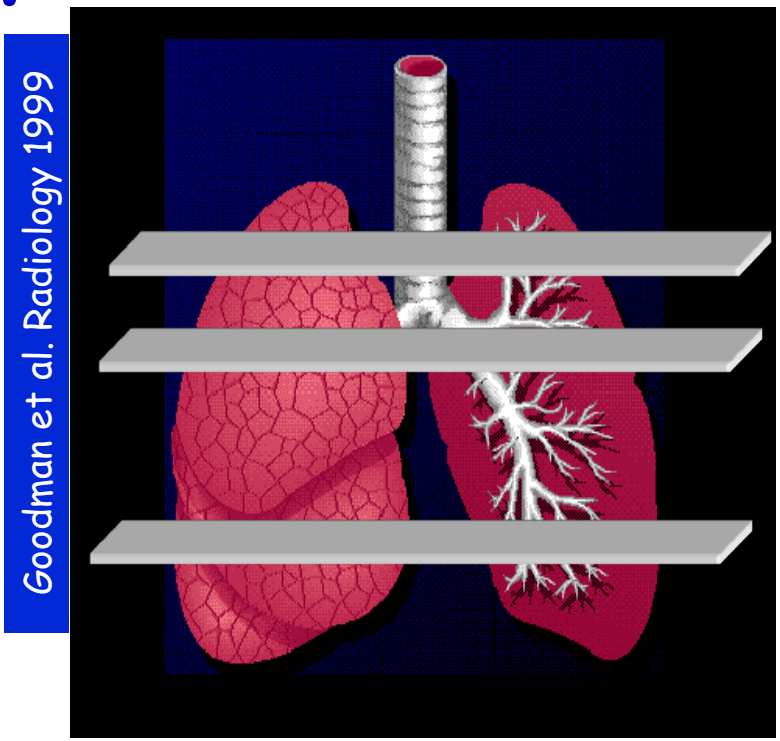


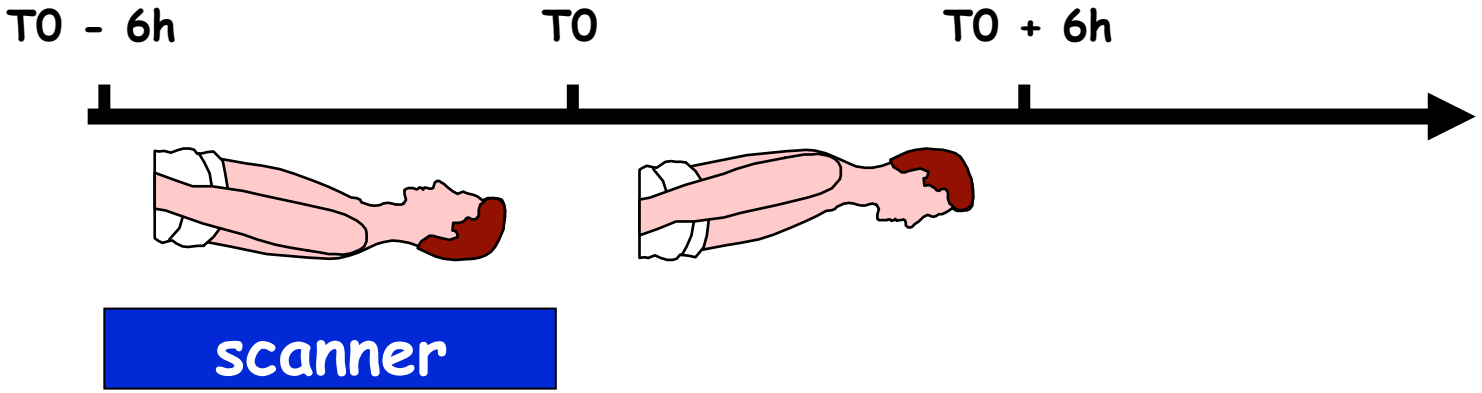
Only patients with dependent opacities?

Evaluation scannographique

Evaluation SQ

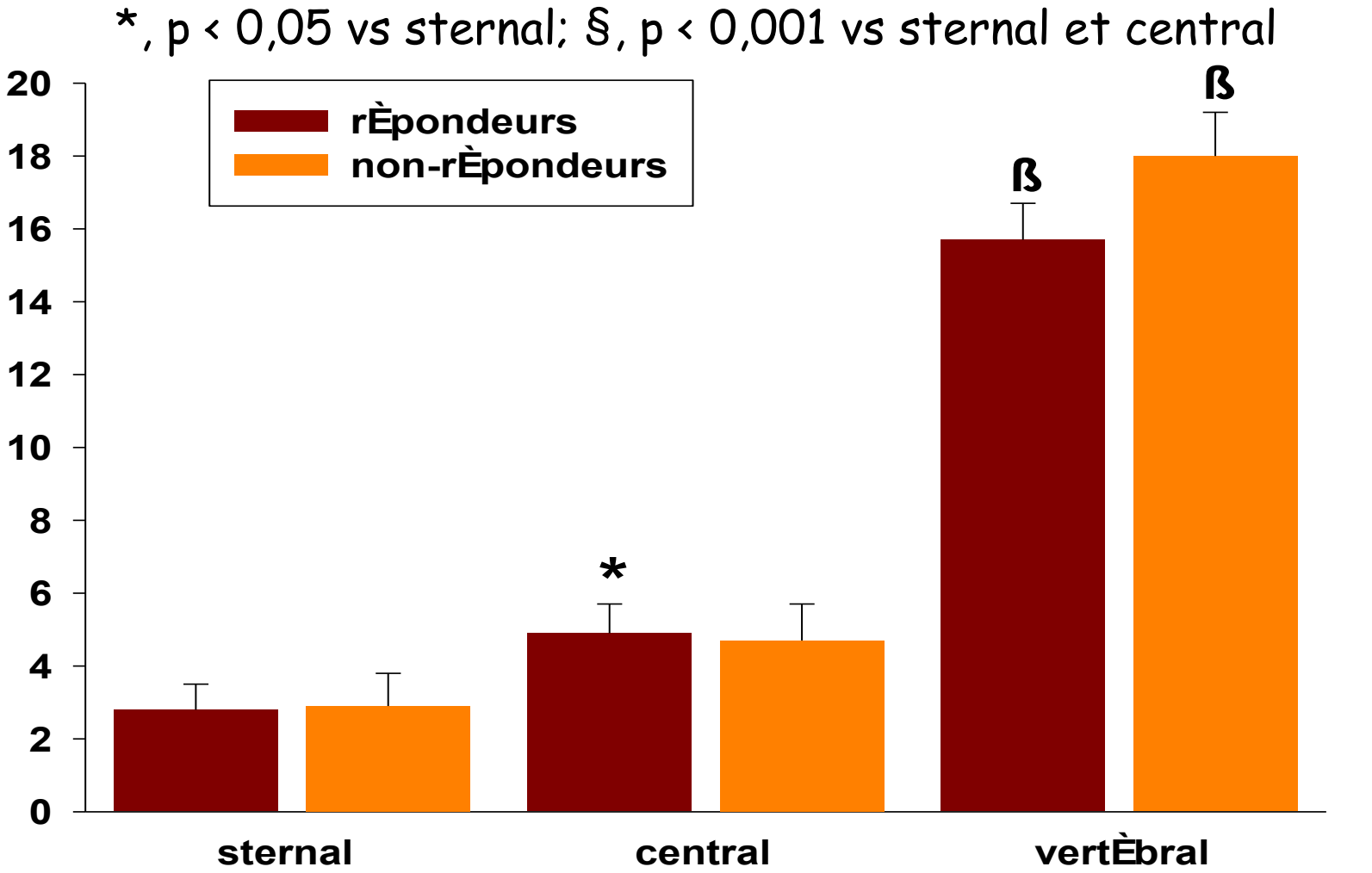
- normal + opacités en verre dépoli (GG) + condensation (CO) = 3
- score = apex + 1,7 hile + 1,8 base (0 - 81)





Réponse = ↗ 33% du rapport PaO2/FiO2

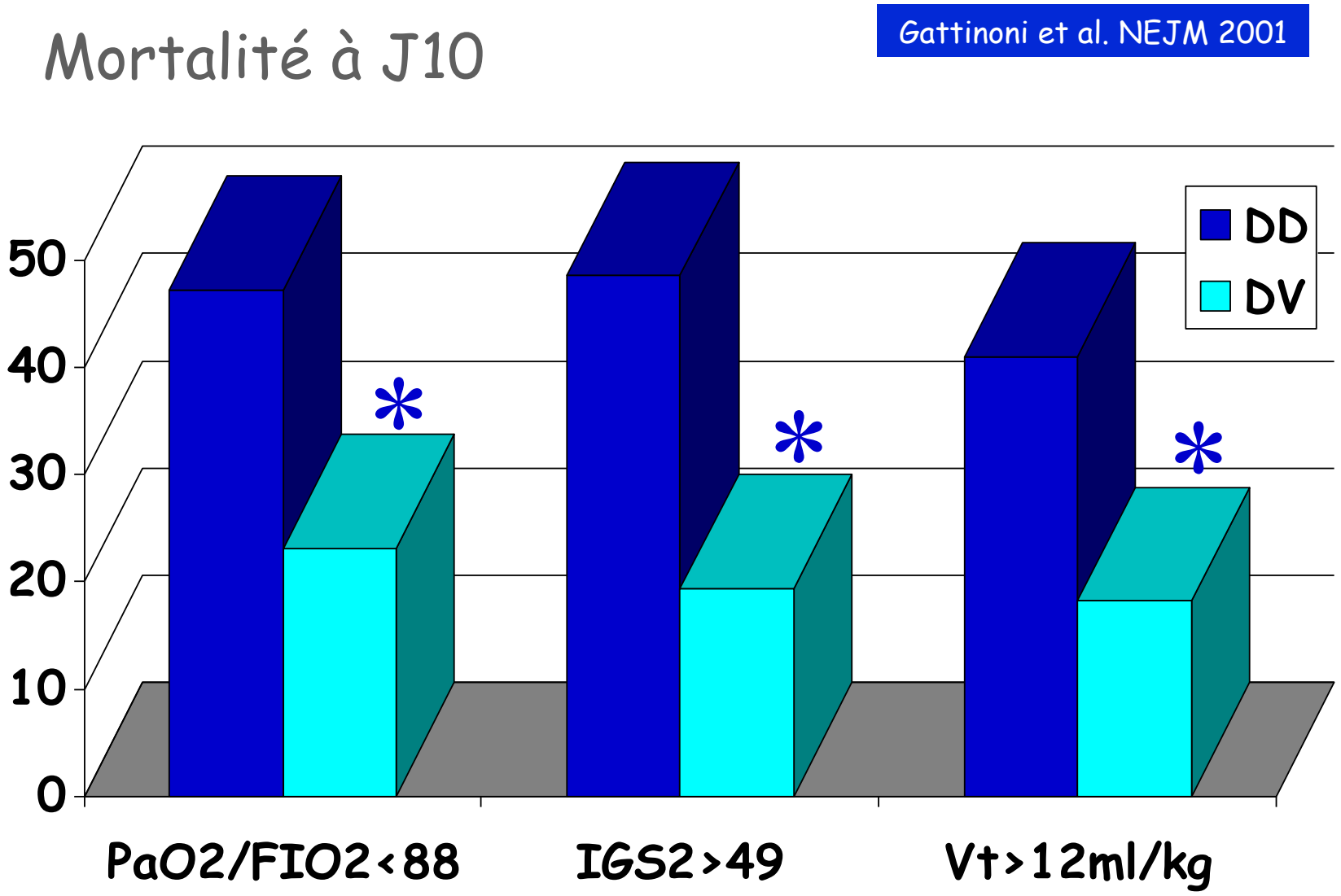
Condensations

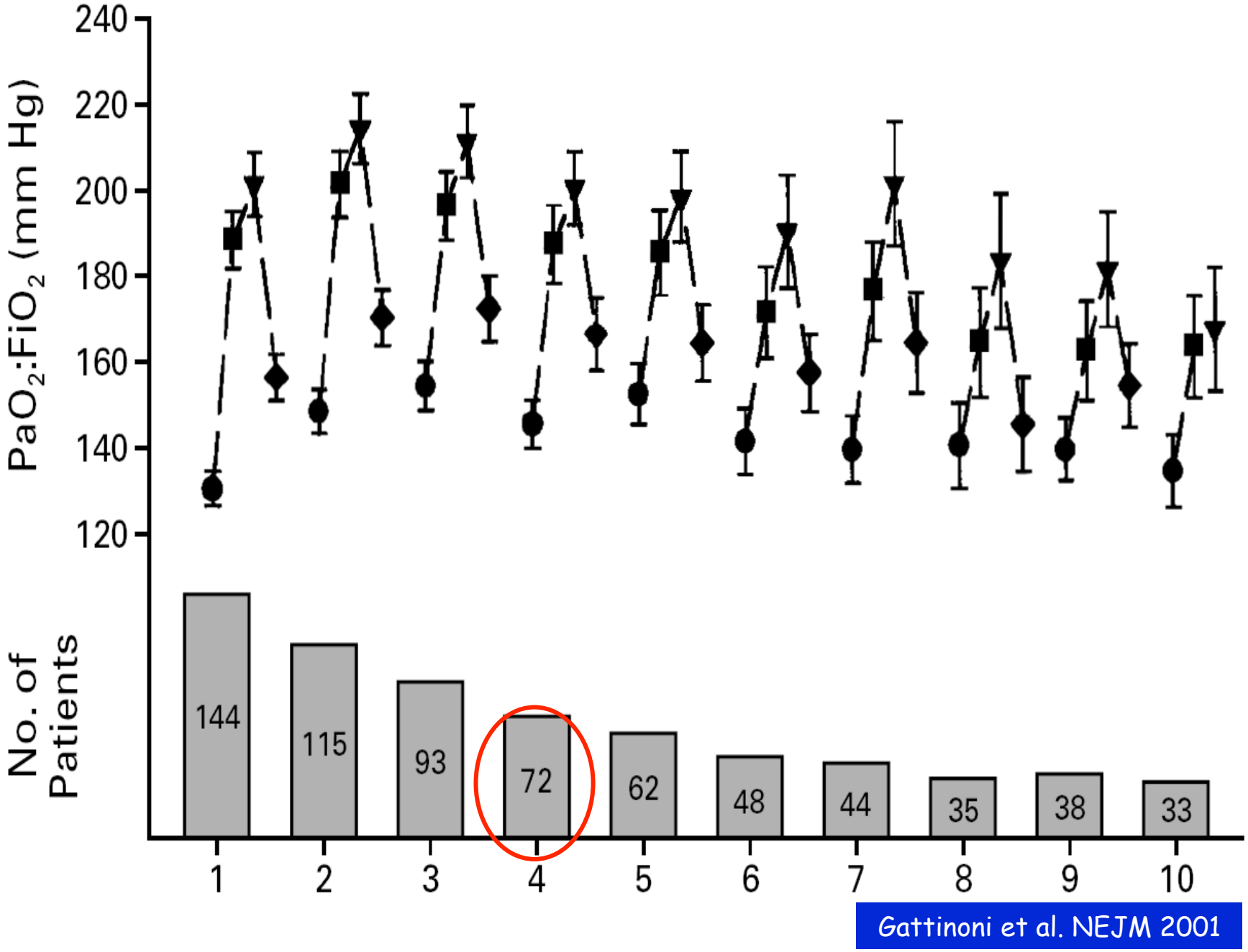


Papazian et al. Anesthesiology 2002

Des raisons d'espérer ?

Gattinoni et al. NEJM 2001





Gattinoni et al. NEJM 2001

	Gattinoni NEJM 2001	Guérin JAMA 2004	Mancebo AJRCCM 2006
N	304	791	136
Type	SDRA ou ALI à PEEP 10	Pneumopathies hypoxémiantes < 300	SDRA
Durée séance DV	Moy 7h	Med 8h	Moy 7h
Durée DV	4,7 j (max 10)	4 (2-6)	10,1±10,3
Mortalité ICU	51/48	42/43 (J90)	58/43
Durée VM	?	14,1/13,7	?
Cross-over	12/0	81/6	4/0
Algorithme O2	Non	Non	Oui
Algorithme Pplat	Non	Non	Oui
Ptc sevrage	Non	Oui	Oui
Vt inclusion	10,3	8,3	8,3
PEEP inclusion	9,6	7,8	12,3
FiO2	73	59	84
Pplat	< 32	?	32

A ce stade

- Optimisation du réglage du respirateur
- Curariser
- DV
  - Hypoxémie profonde (< 100-120???)
  - Surtout si présentation lobaire
  - Au moins 12h en DV

A ce stade

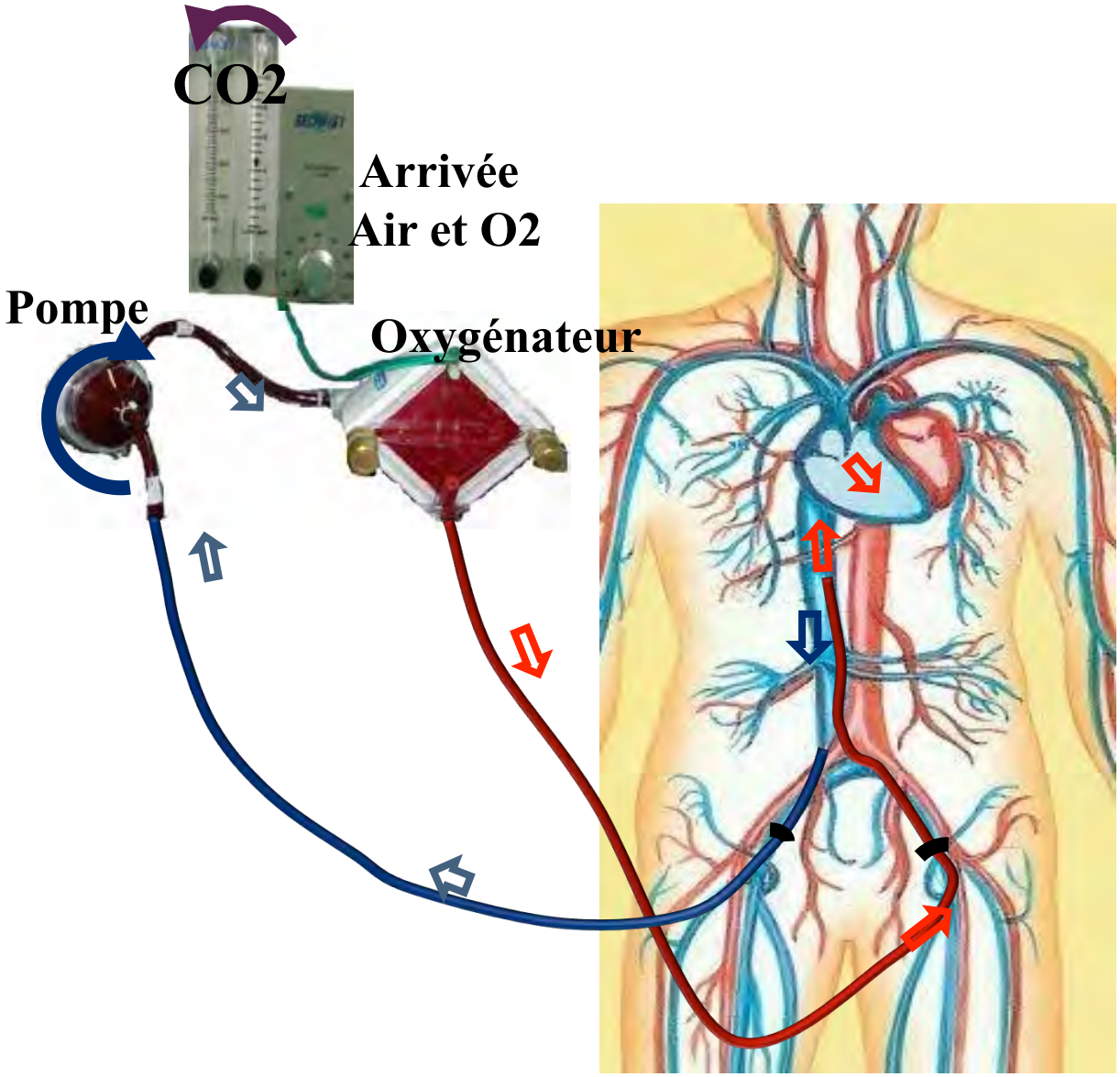
- Optimisation du réglage du respirateur
- Curariser
- DV
- NO
  - Défaillance VD
  - Echec DV
  - Réévaluer dose
- Eau et sel
  - Raisonnable

Prise en charge et pronostic

% des admissions réa	ANZIC NEJM 2009	Canada JAMA 2009	Mexico JAMA 2009	REVA
VM	64,6	76	75,9	74,5
ECMO	11,6	4,2	0	11,4
Décès	16,9	17,3	41	19

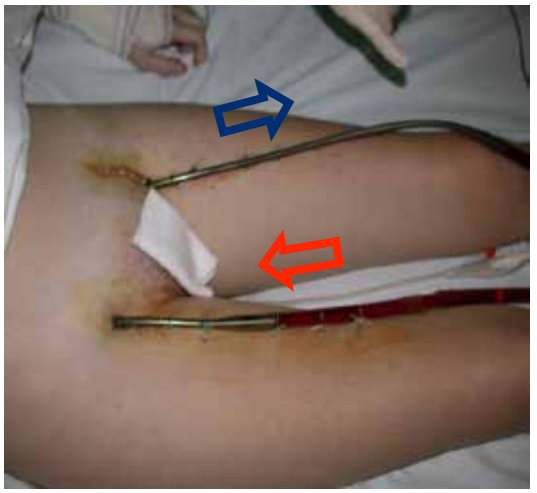
ECMO

ECMO V V = Suppléance respiratoire



Voies fémorales ou jugulaires

Canules veineuses



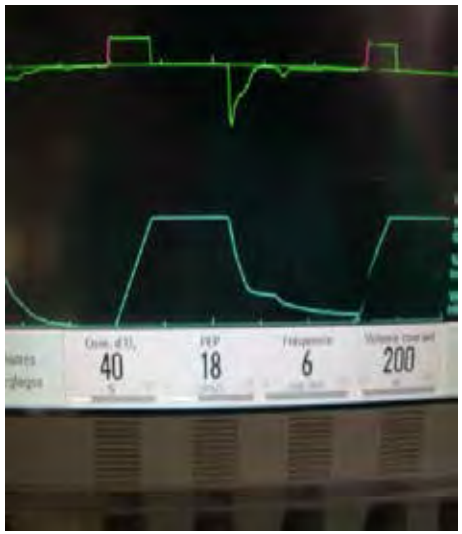
ECMO

Adapter ECMO et Ventilateur

- Débit: vitesse de pompe
- FIO2 (Oxygénation)
- Balayage (élimination CO2)

- Vt < 4 ml/kg
- FR 4 - 8 cycles /min
- PEP 15 - 25 cmH2O

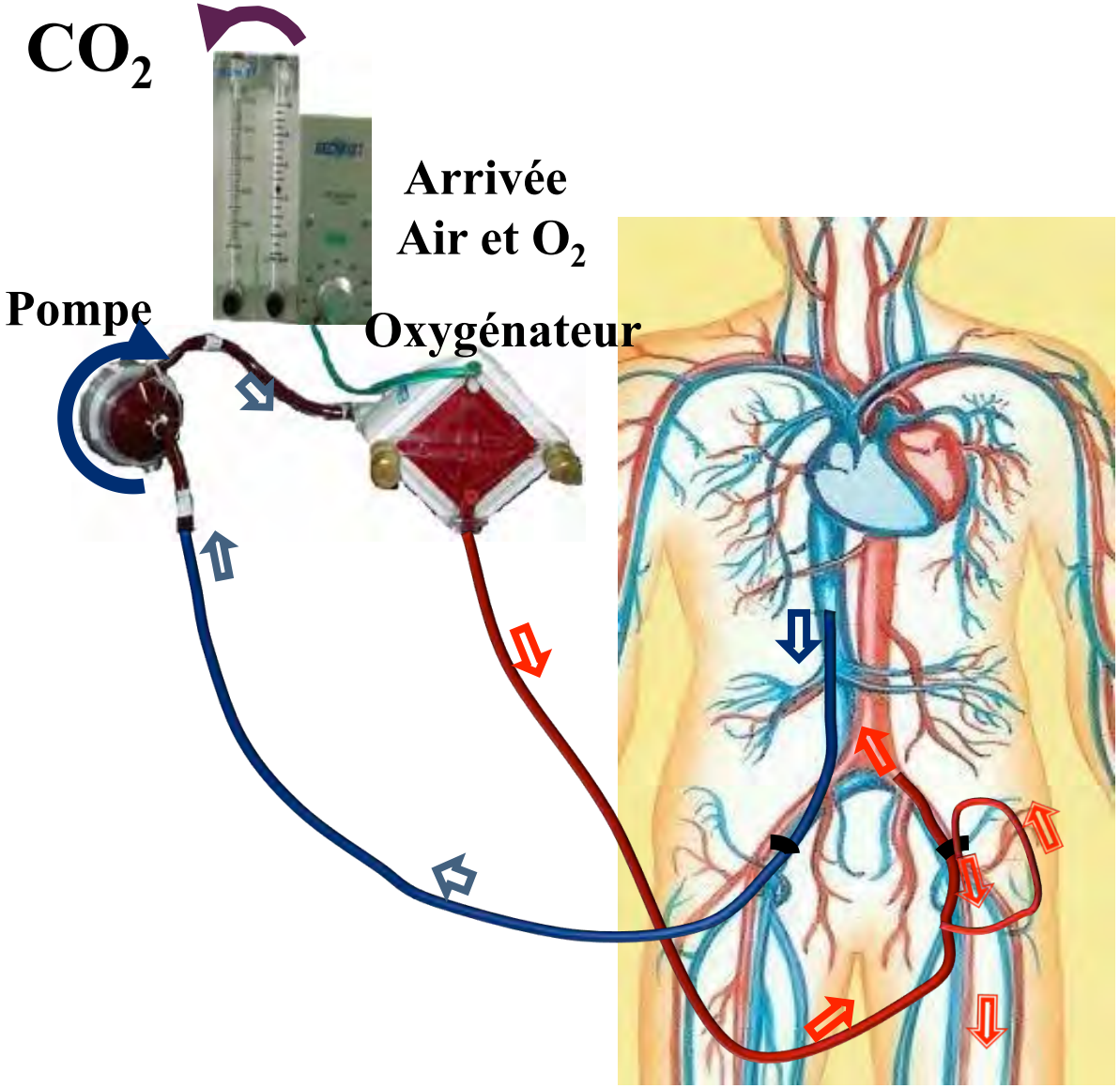
CO2



- **Gazométries artérielle et veineuse (SvO2)**
- **Lactates**
- **Coloration circuit CEC**

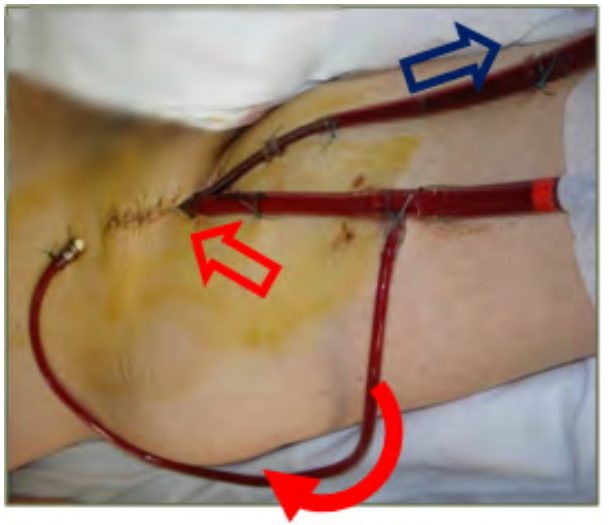
ECMO

ECMO V A = Suppléance cardio respiratoire



Voies fémorales ou jugulaires

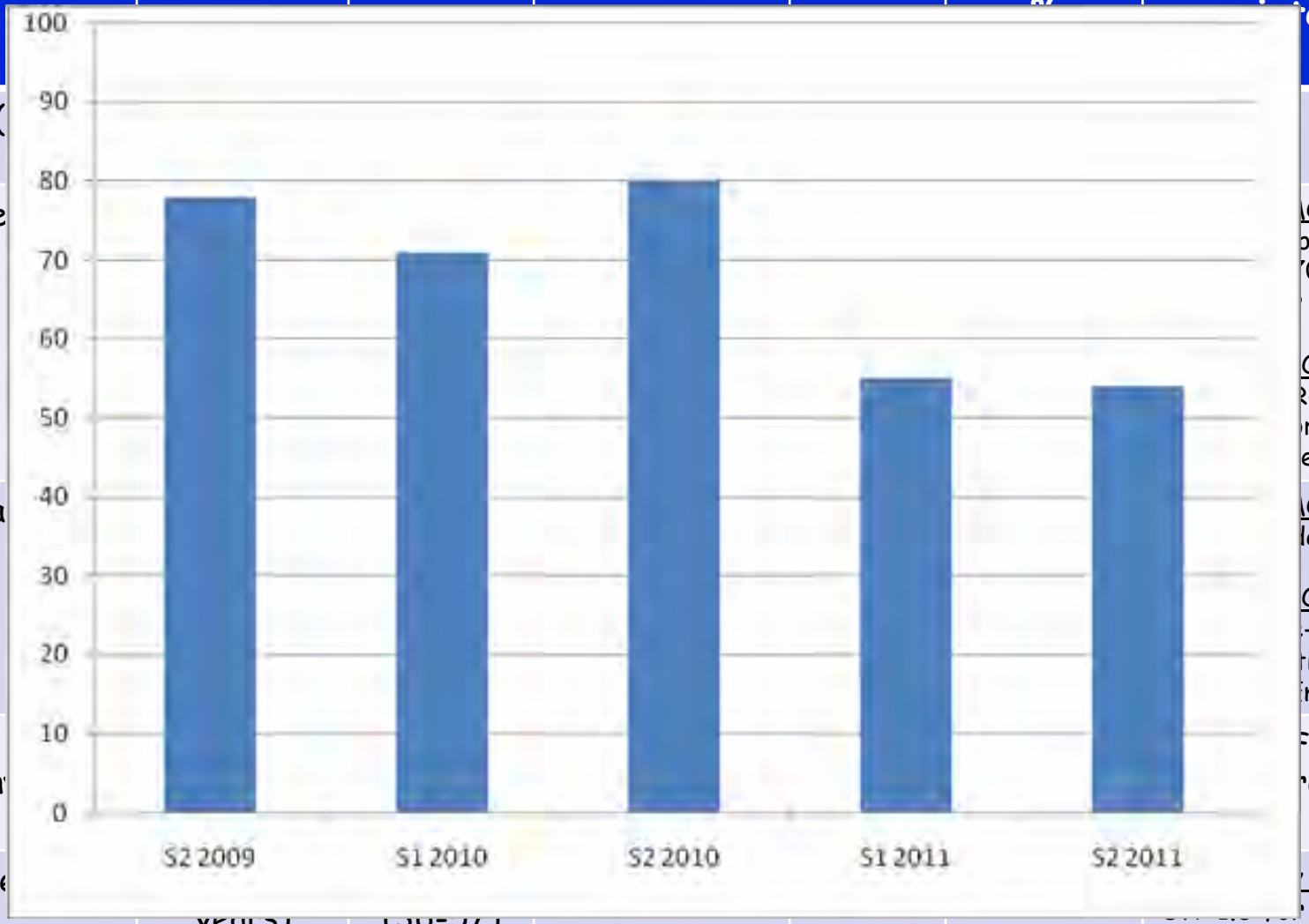
Canules : veineuse et artérielle



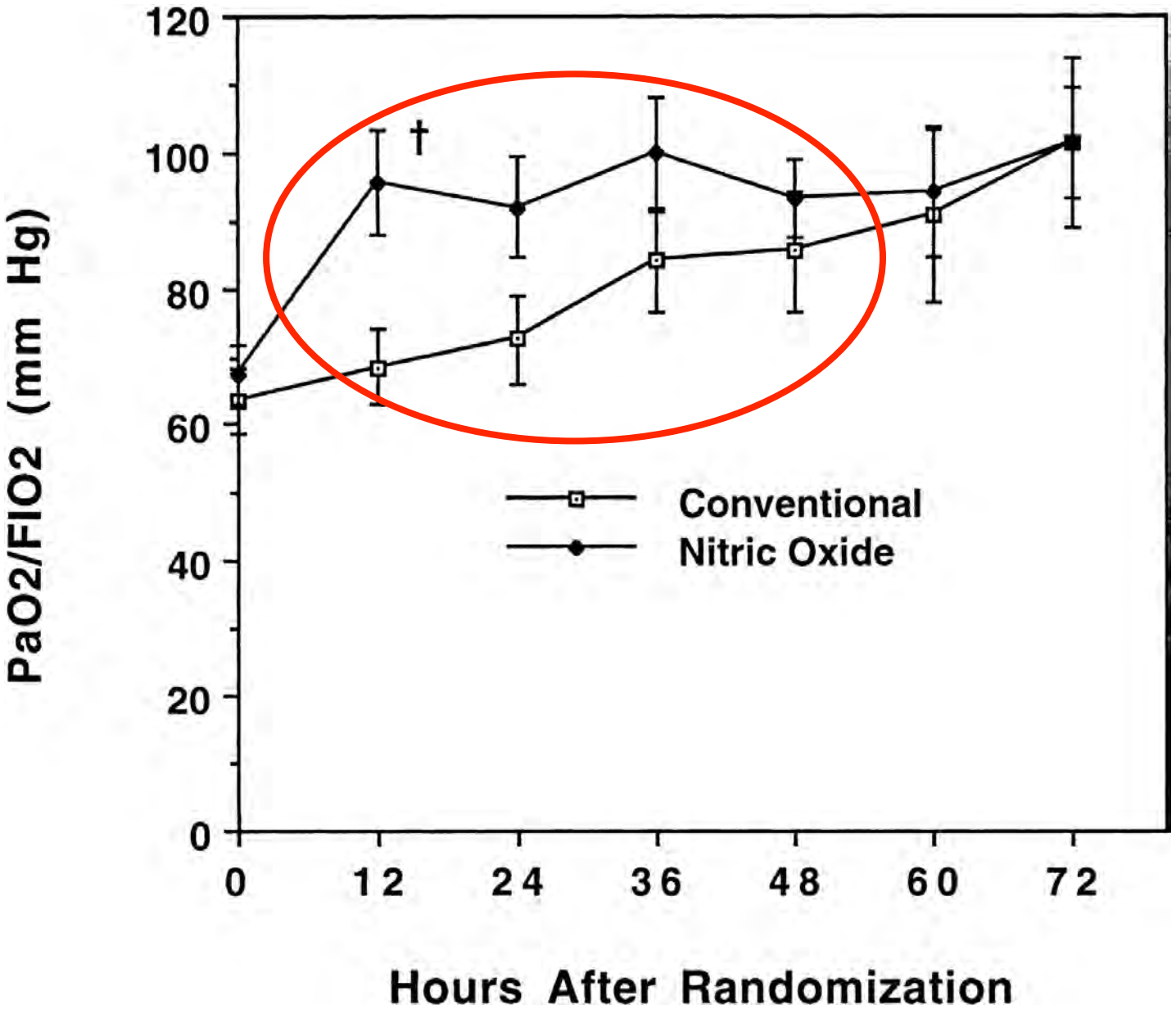
revascularisation du membre canulé

Studies and Registries about ECMO in adults with severe ARDS

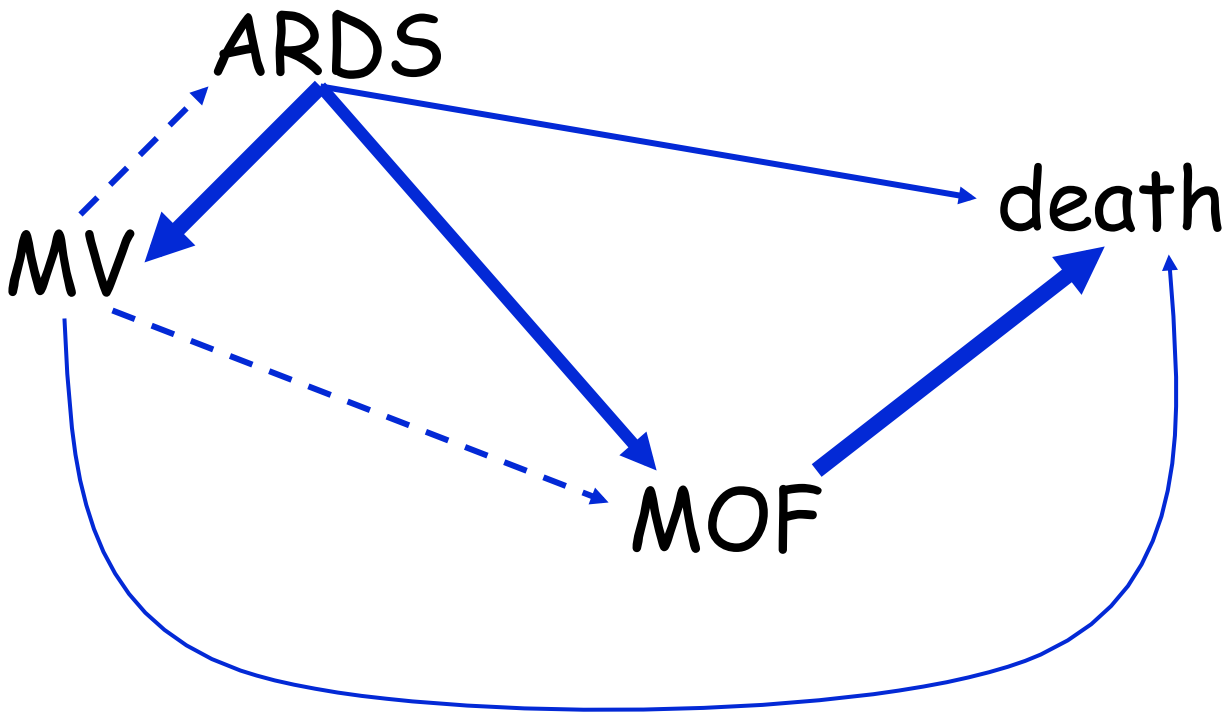
Study (year)	Number	Age	PaO2/FiO2	LIS	Survival	Factors ...ed with
CESAR (						
ELSO re (2009)						...O: Age- ...pH<7.18 ...70 ... switch VV to ...O: Circuit ...R-ARF with ...r Pulmonary ...emorrhage
Hemmila (2004)						...O: Age- ...ler-pH<7.10- ...O: Surgical ...- CPR- RRT- ...rion- ...mbolism
Schmid (Germany (2009)						...FA-ARF ...re ECMO
Marseille (2011)		...years)	(36-57)			... 1 on ECMO) ... 1 point increase SOFA > 10, 100% †



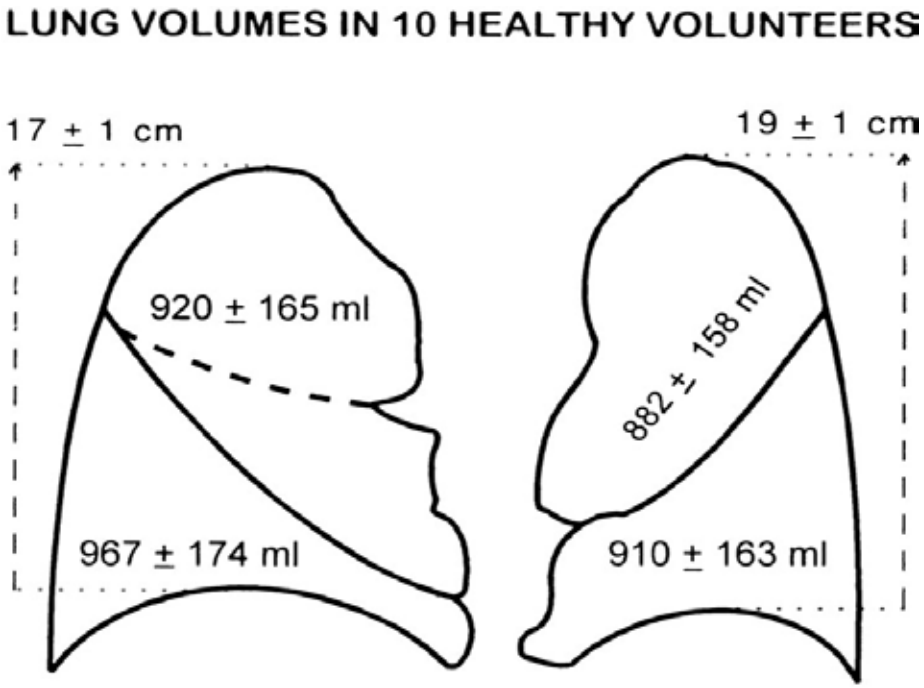
Michael et al. AJRCCM 98

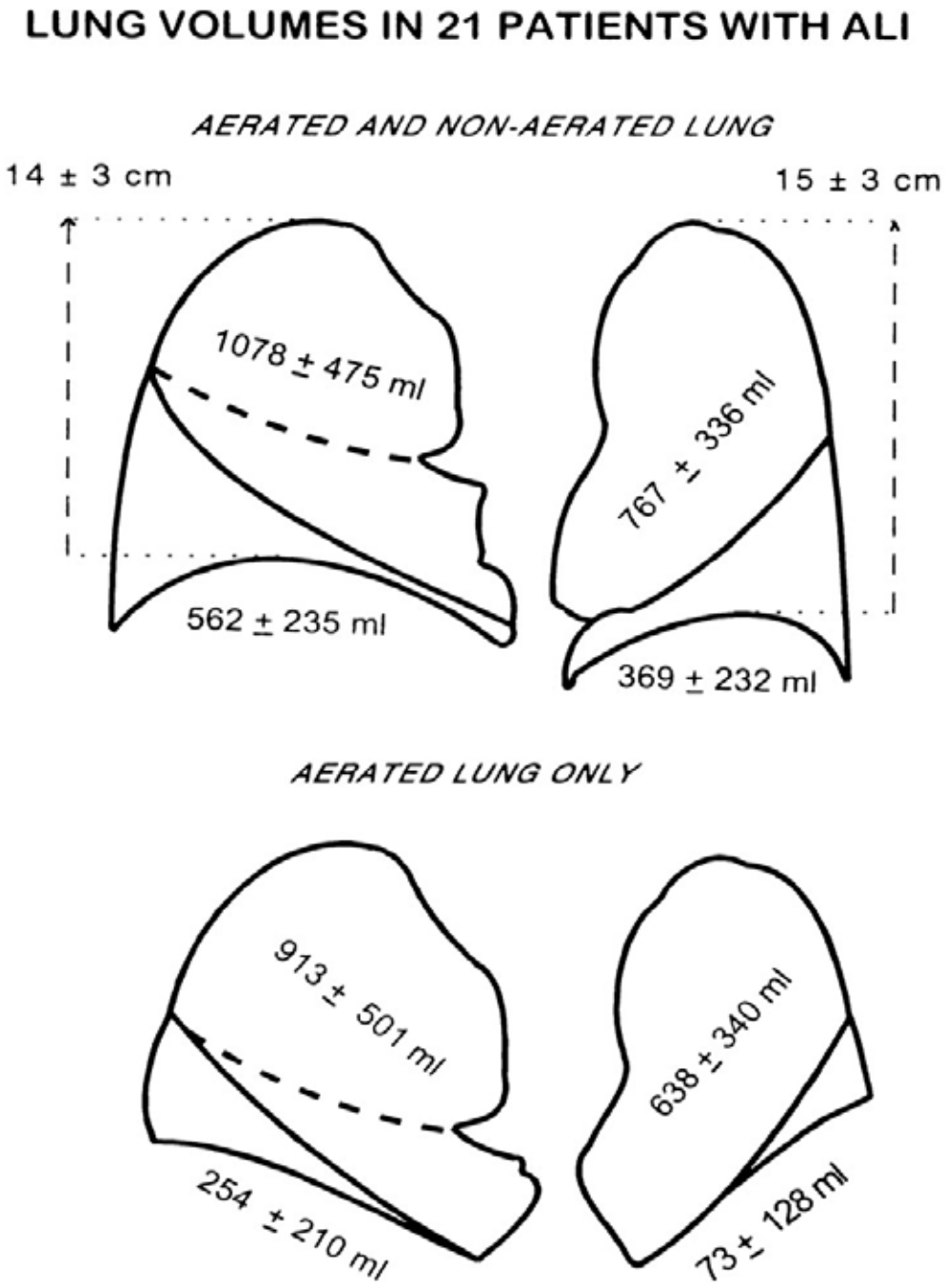


ARDS, MV and outcome



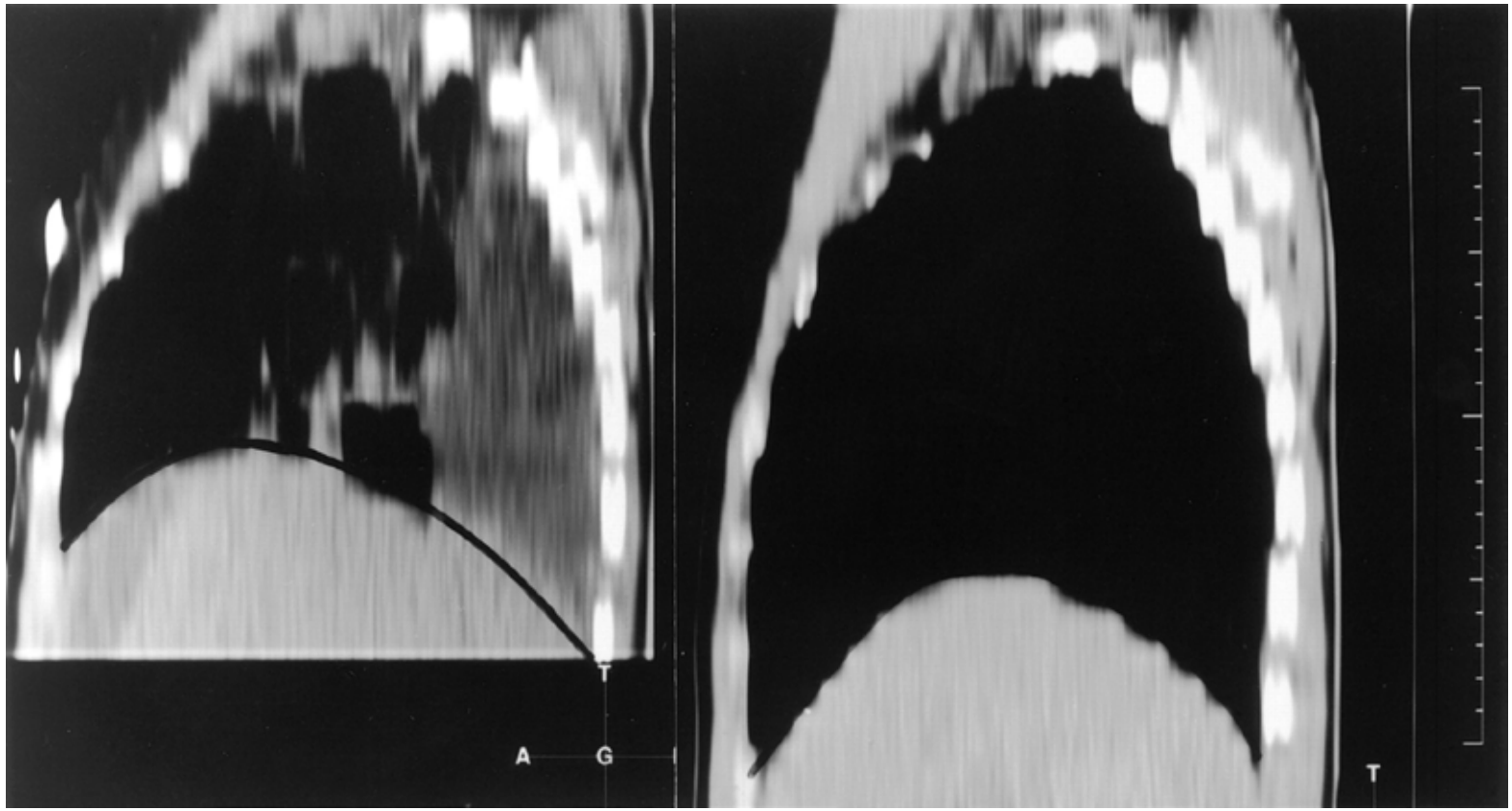
Lung volume reduction





Puybasset et al. AJRCCM 98

Lung volume reduction



Puybasset et al. AJRCCM 98

ExPress

VT 6 ml / kg (PBW)

RR ≤ 35 / mn ; 7.30 < pH < 7.45

55 mmHg < PaO2 < 80 mmHg

88% < SpO2 < 95%

Minimal alveolar distension

PEEP set for

5 ≤ PEEPtot ≤ 9

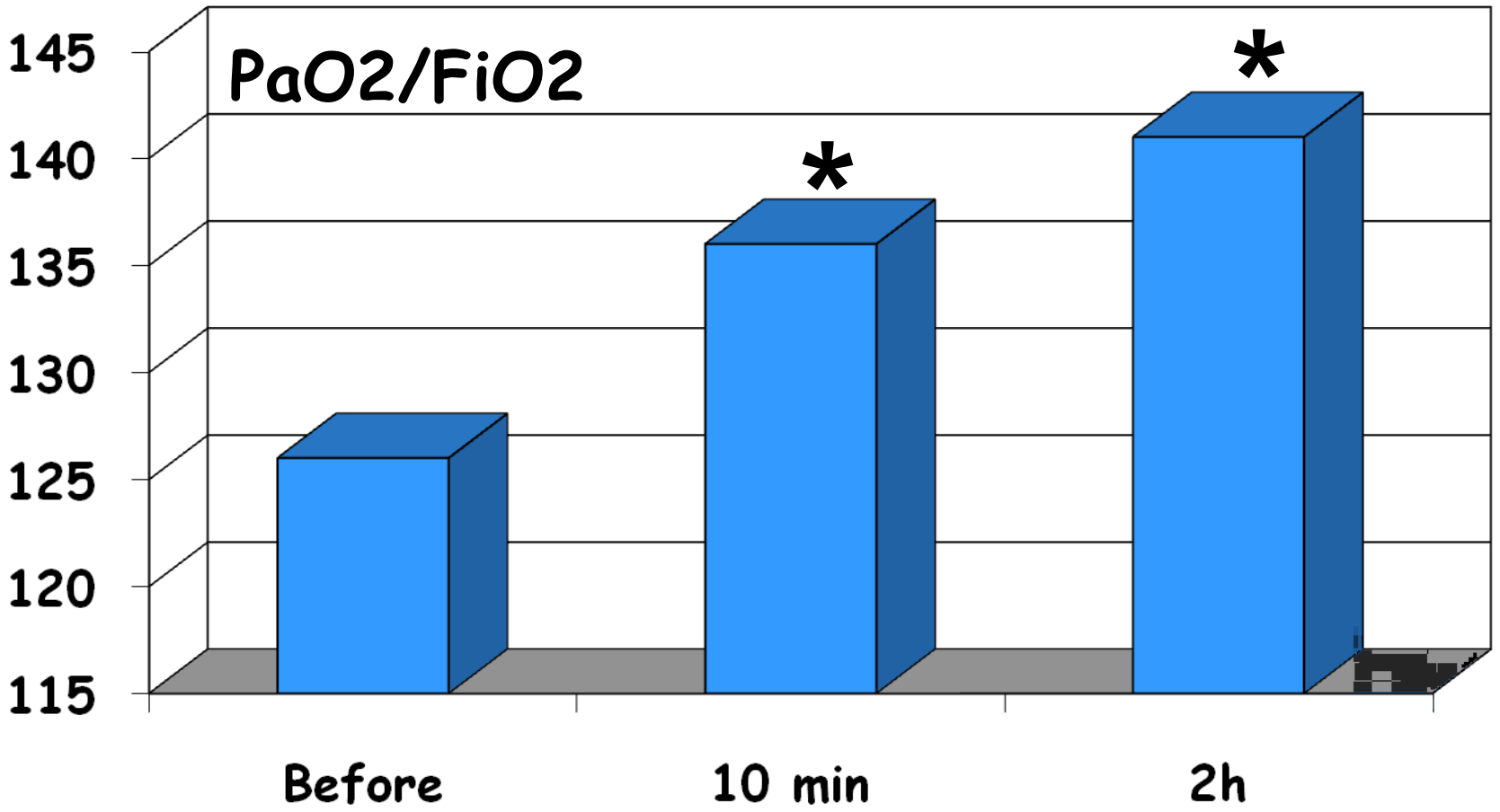
Maximal alveolar recruitment

PEEP set for

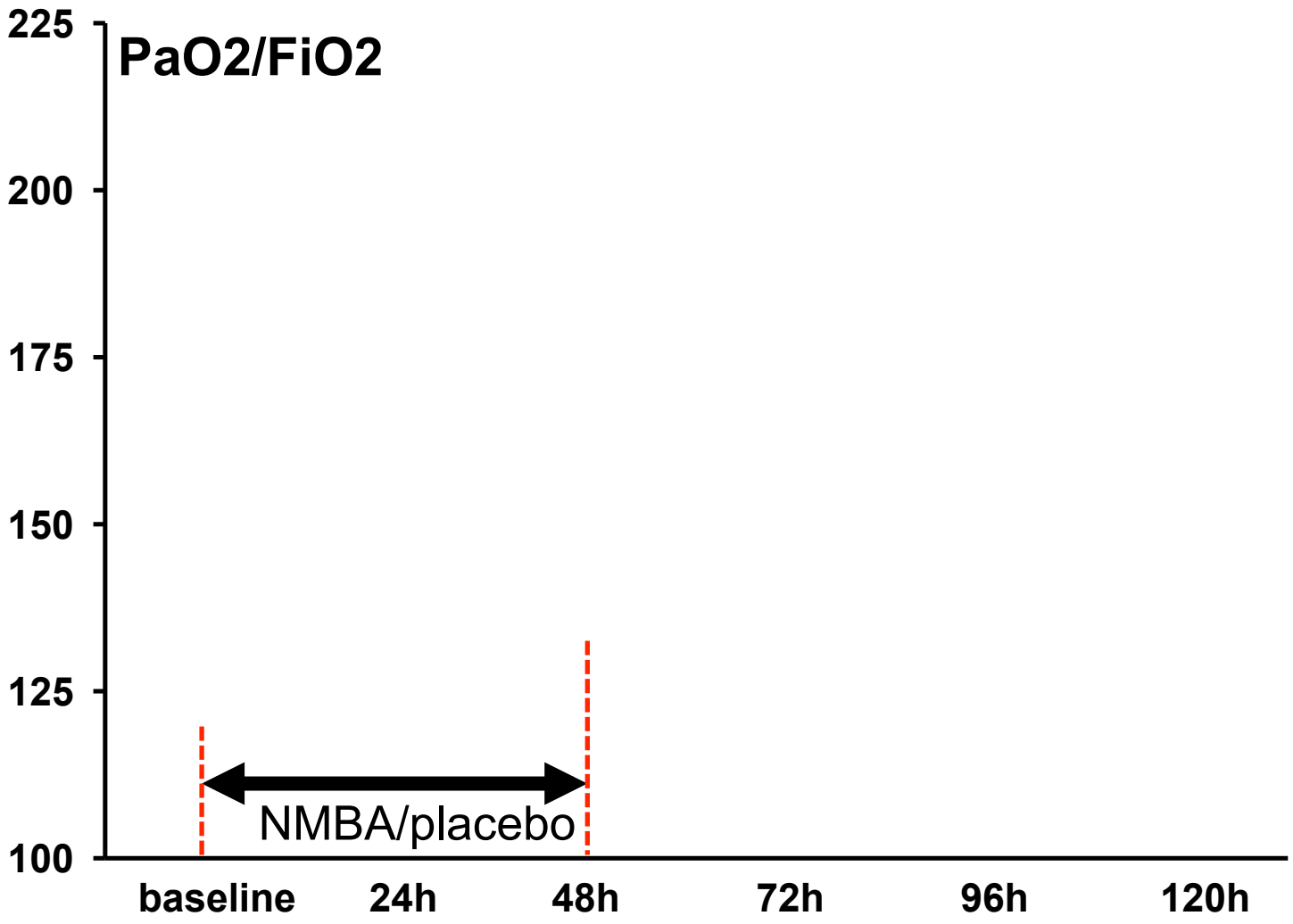
28 ≤ Pplat ≤ 30

Physiological effects
n hypoxemic patients

Lagneau *et al.* ICM 2002



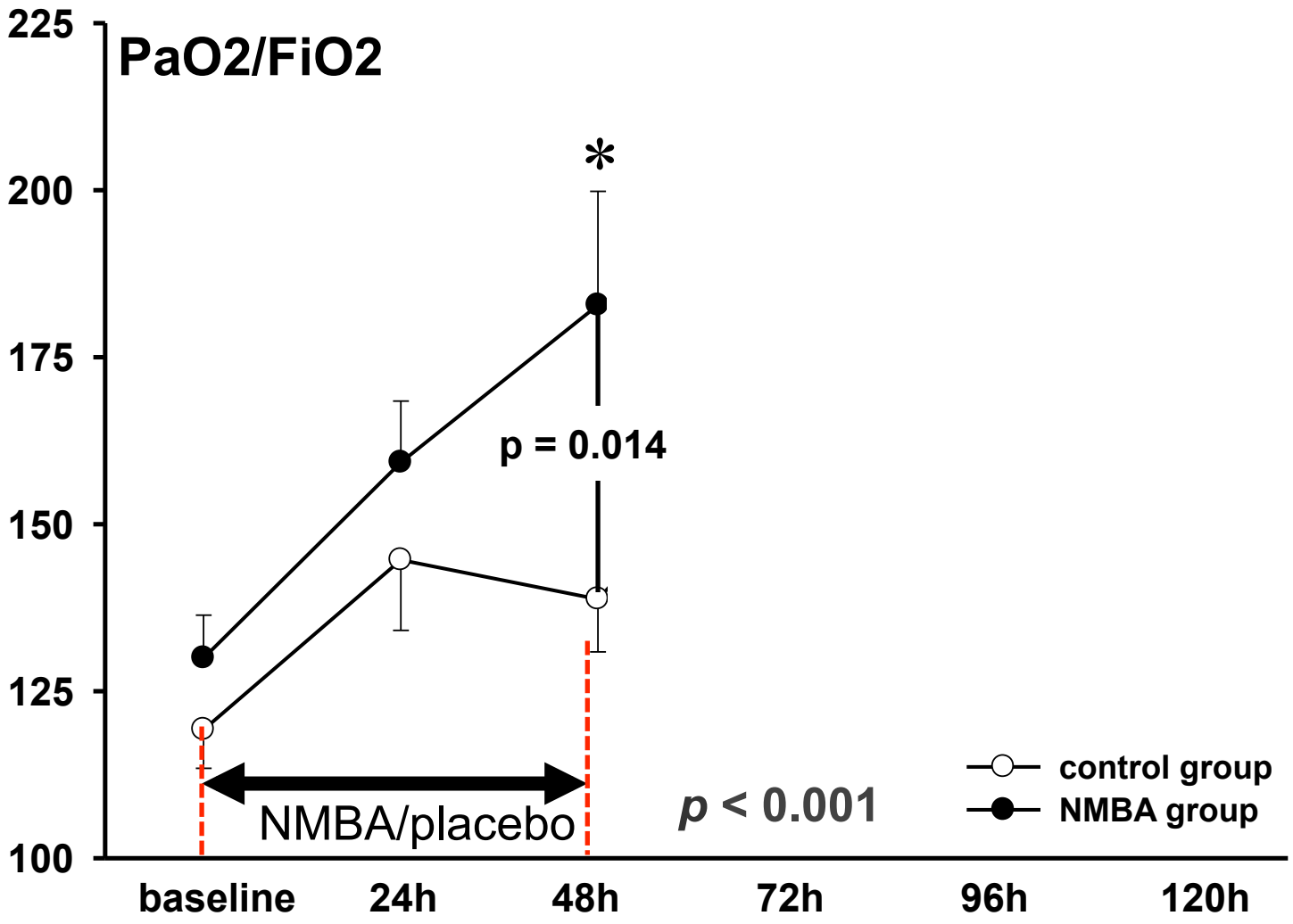
Effect of cisatracurium on oxygenation



4 ICUs – 56 patients

Gainnier *et al.* Crit Care Med 2004

Effect of cisatracurium on oxygenation



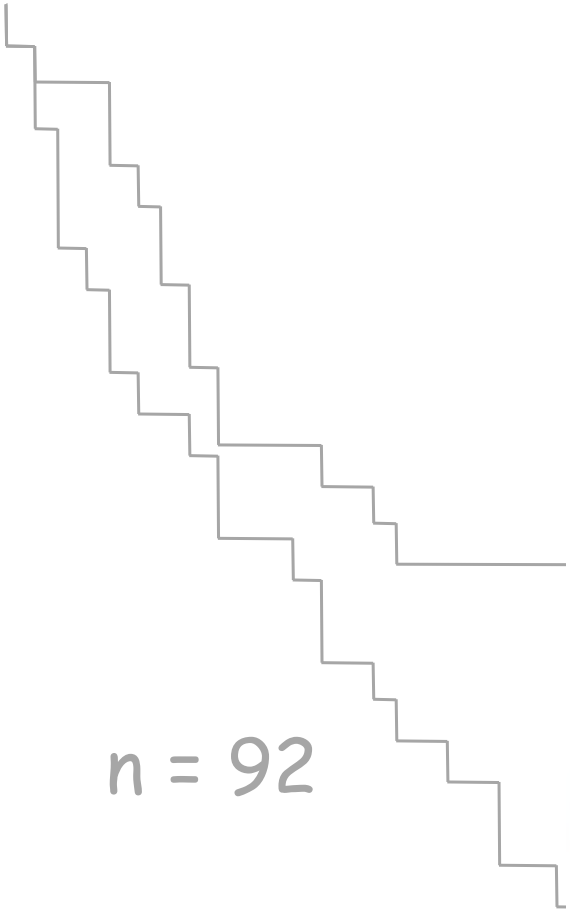
4 ICUs – 56 patients

Gainnier *et al.* Crit Care Med 2004

	NMBA Group (n = 28)	Control Group (n = 28)	*p* Value
VFD at day 28, days	3.7 ± 7.2	1.7 ± 5.3	.24
Median (25th–75th percentiles)	0 (0–5)	0 (0–0)	.24
VFD at day 60, days	19.0 ± 20.3	9.8 ± 16.9	.071
Median (25th–75th percentiles)	14 (0–37)	0 (0–18)	.11
Mortality at day 28 after inclusion, n (%)	10 (35.7)	17 (60.7)	.061
Mortality at day 60 after inclusion, n (%)	13 (46.4)	18 (64.3)	.18
ICU mortality, n (%)	13 (46.4)	20 (71.4)	.057

Gainnier *et al.* Crit Care Med 2004

Mortality



n = 92

Gainnier *et al.* CCM 2004

Forel *et al.* CCM 2006

ACURASYS

The NEW ENGLAND JOURNAL of MEDICINE

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

Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome

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

Important methodological aspects (2)

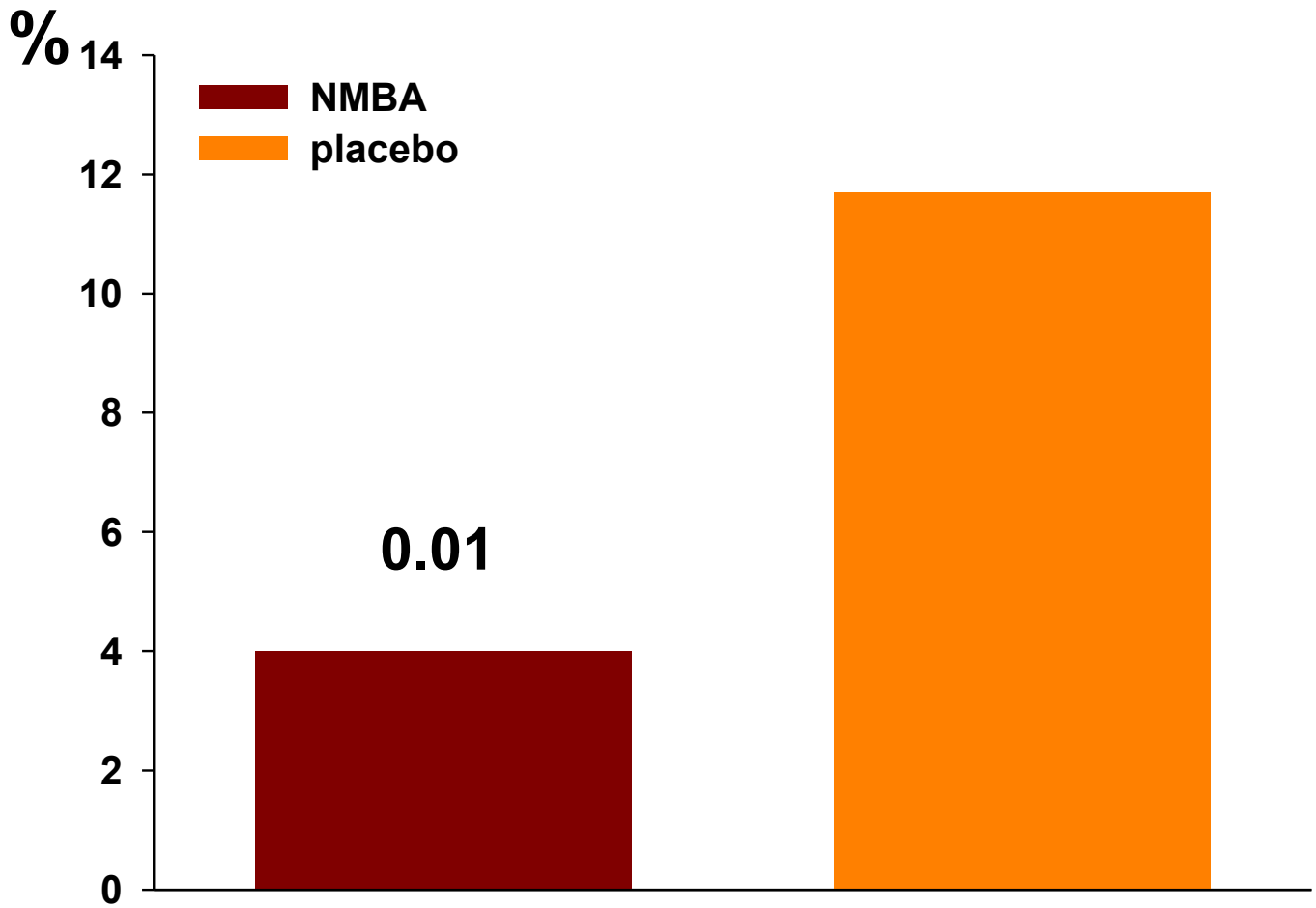
- Prior to infusion : Ramsay 6
- Cisatracurium: 6 x 150 mg / day for 2 days

- Volume-assist control mode
- PEEP and FiO2 according to the ARMA study
- Weaning started on day 3 if FiO2 ≤ 0.6

ACURASYS

Pneumothorax

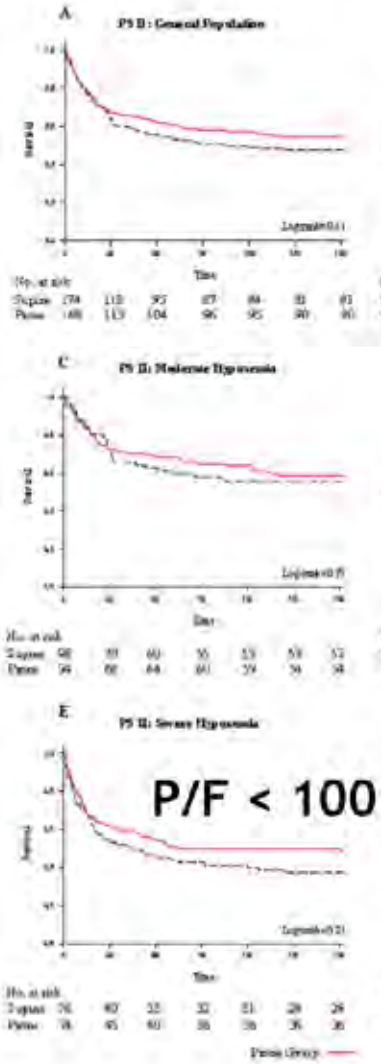
ACURASYS



To summarize

- MV optimization
- NMBA
  - Cisatracurium
  - ESS
    - Early (< 48h)
    - Short duration
    - Severe ARDS

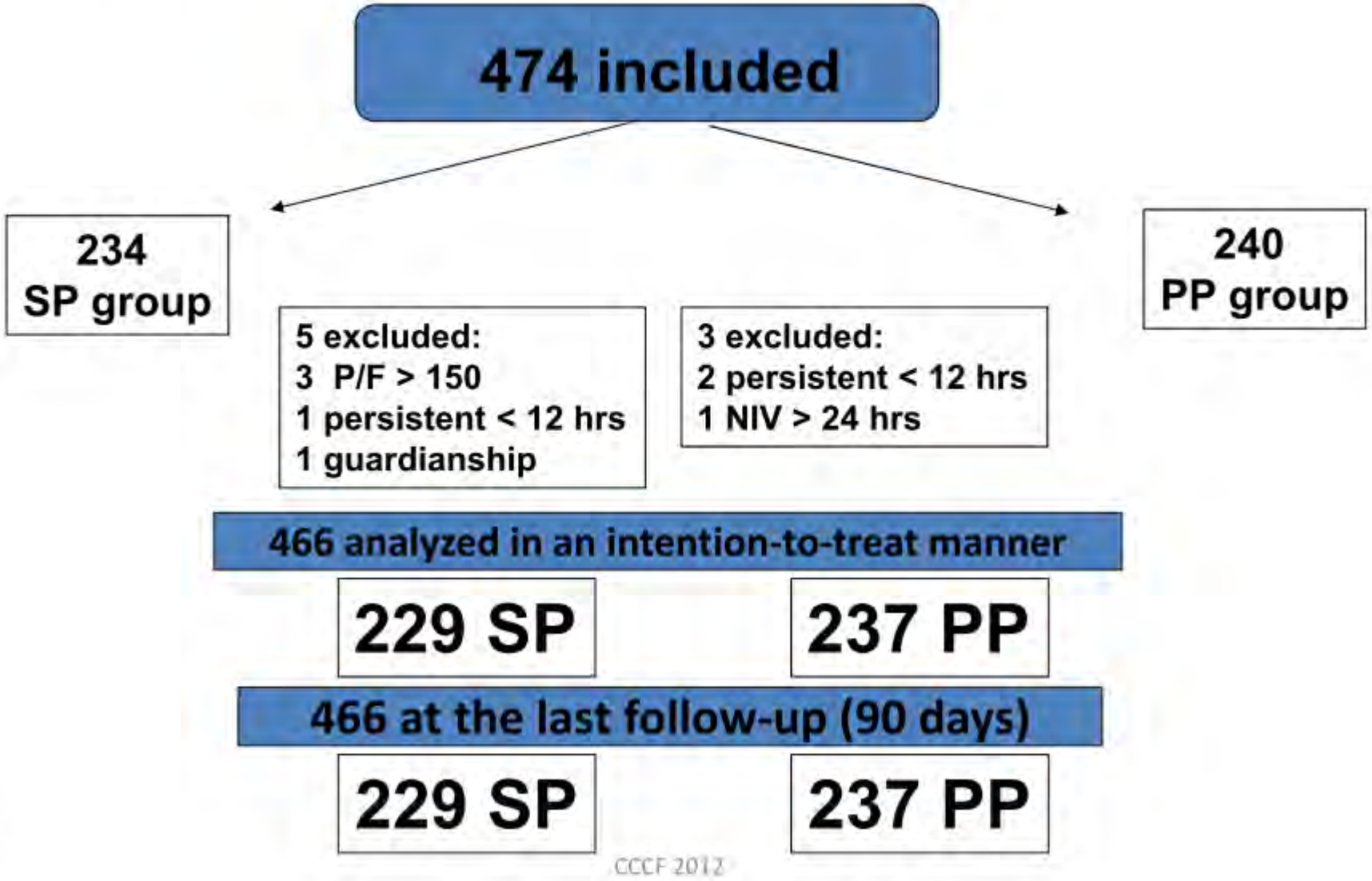
PS II


A
PS II : General Population
C
PS II: Moderate Hypoxemia
E
PS II: Severe Hypoxemia
P/F < 100

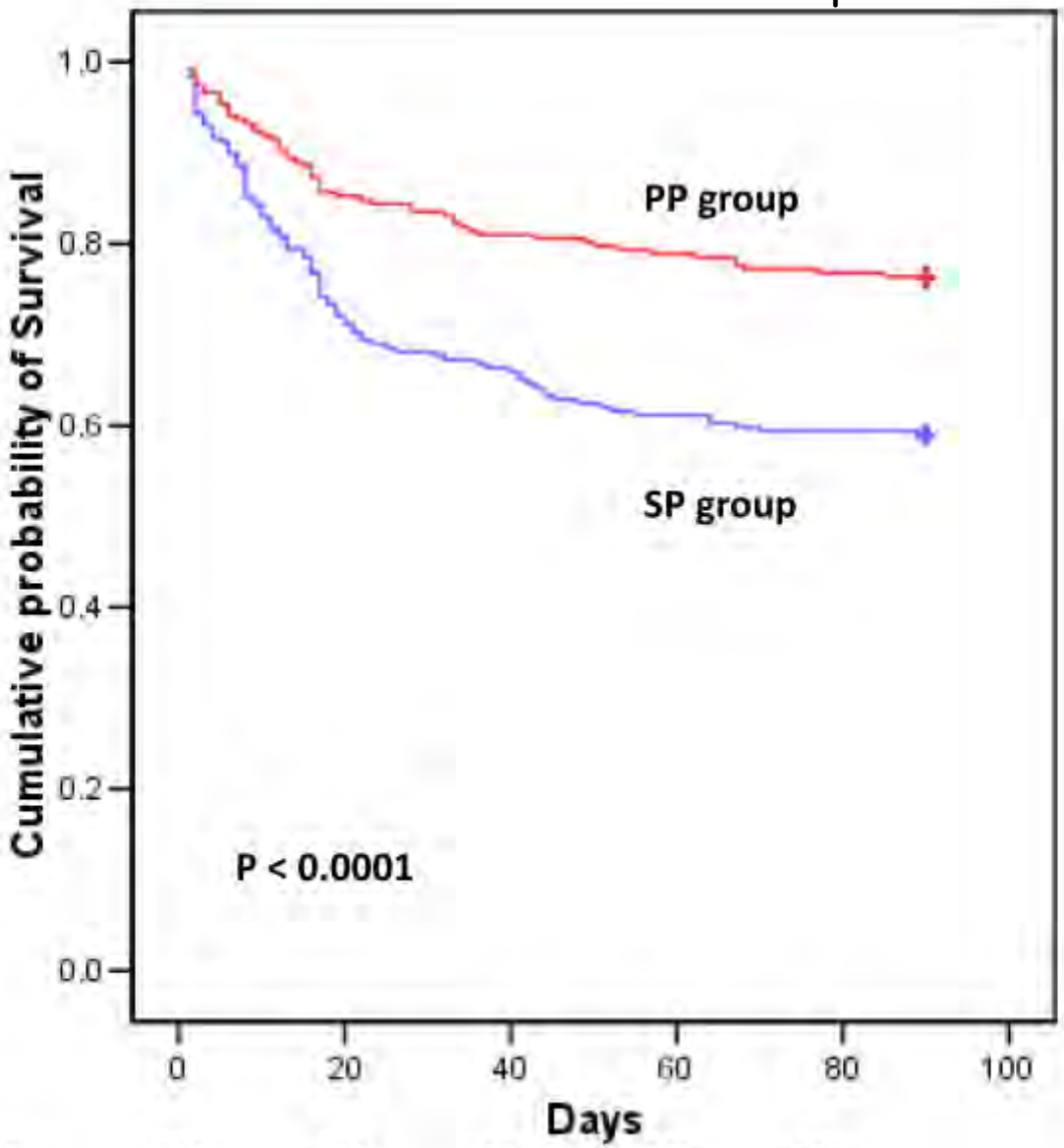
Characteristic	Supine Group (N = 229)	Prone Group (N = 237)
Age — yr	60±16	58±16
Male sex — no. (%)	152 (66.4)	166 (70.0)
Setting from which patient was admitted to ICU — no. (%)		
Emergency room	98 (42.8)	101 (42.6)
Acute care facility	87 (38.0)	86 (36.3)
Home	26 (11.4)	31 (13.1)
ICU	9 (3.9)	11 (4.6)
Other	9 (3.9)	8 (3.4)
SAPS II‡	47±17	45±15
Sepsis — no./total no. (%)§	195/229 (85.2)	194/236 (82.2)
SOFA score¶	10.4±3.4	9.6±3.2
ARDS due to pneumonia	133 (58.1)	148 (62.4)
Body-mass index‖	29±7	28±6

PROSEVA

Slide provided by C. Guérin



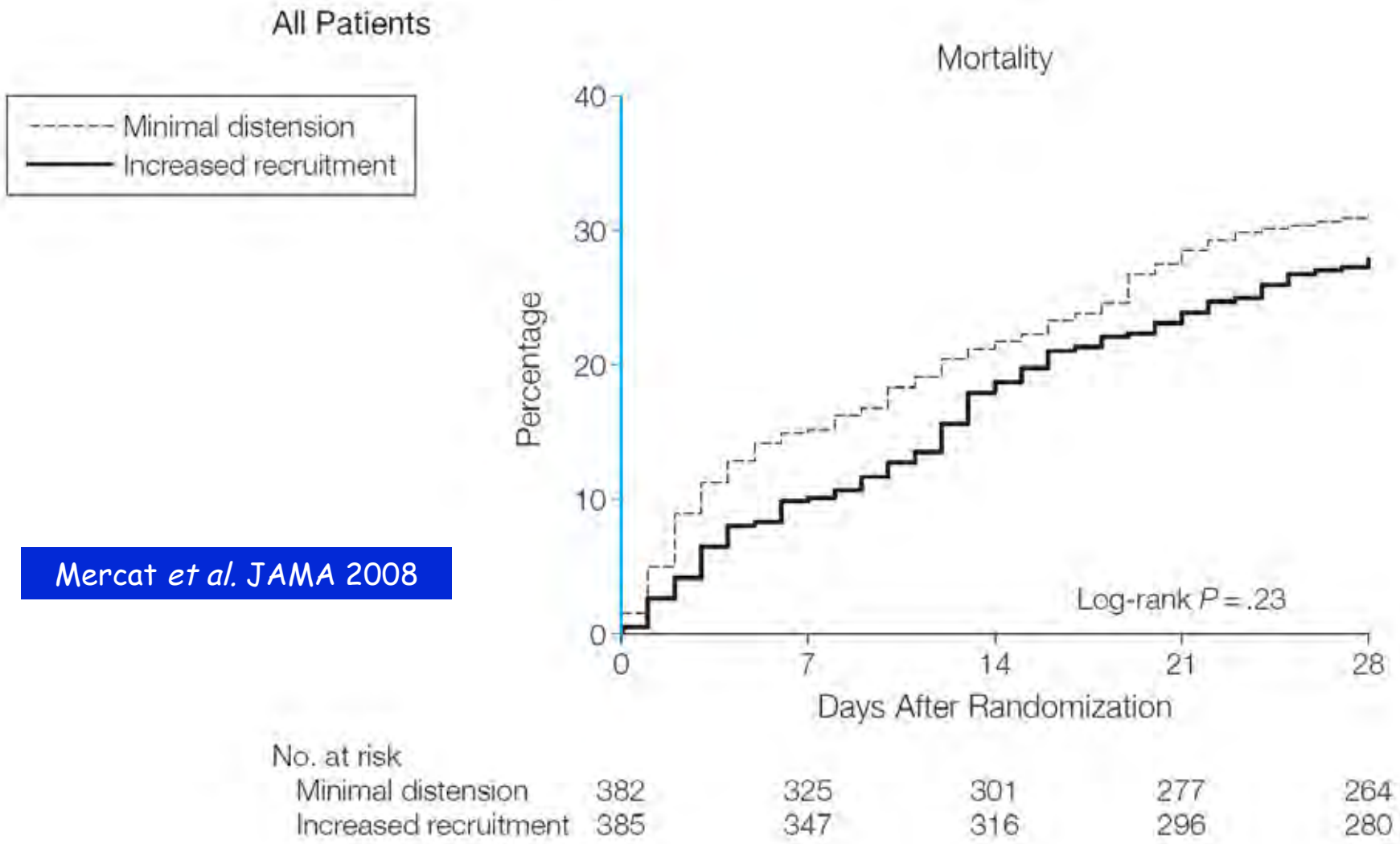
Slide provided by C. Guérin



Subjects at risk						
	PP	237	202	191	186	182
	SP	229	163	150	139	136

PEEP

Minimal distension group	Total PEEP between 5 and 9 cm H_2O
Increased recruitment group	Plateau pressure between 28 and 30 cm H_2O

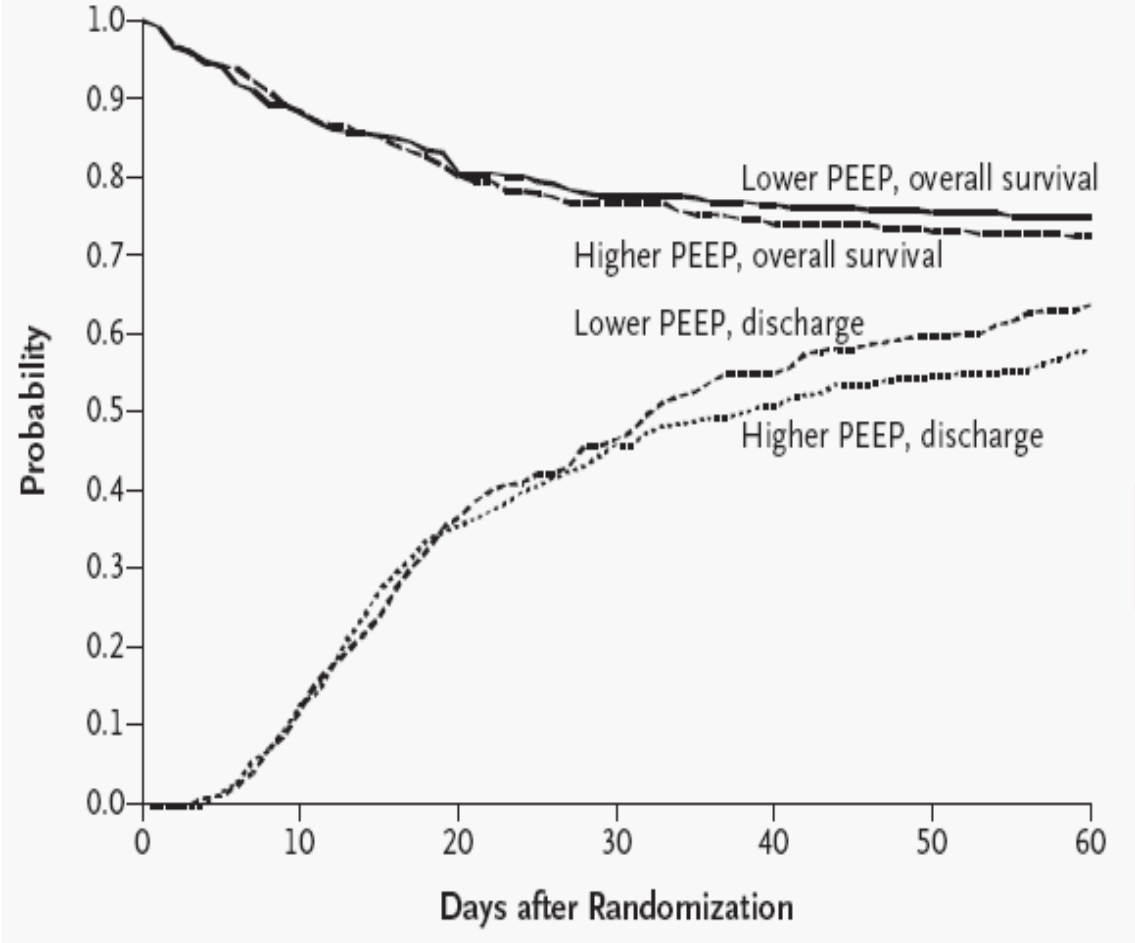


Mercat *et al.* JAMA 2008

ALVEOLI

ARDSnet NEJM 2004

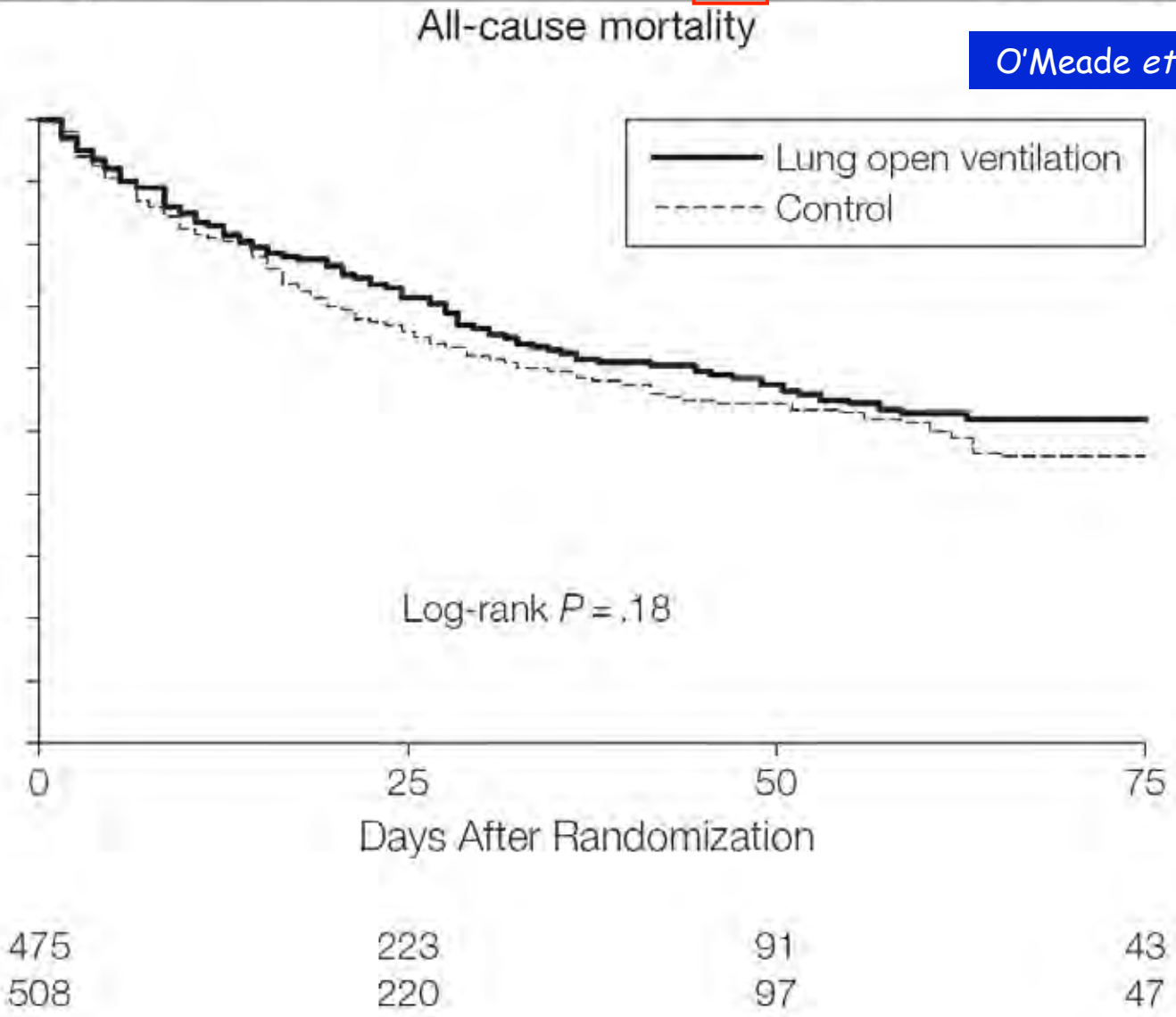
Lower-PEEP group														
FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	18–24
Higher-PEEP group (before protocol changed to use higher levels of PEEP)														
FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.5–0.8	0.8	0.9	1.0	
PEEP	5	8	10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



Variable	Day 1	
	Lower-PEEP Group	Higher-PEEP Group
Tidal volume (ml/kg of predicted body weight)	6.1±0.8	6.0±0.9†
No. of patients	236	258
Plateau pressure (cm of water)	24±7	27±6†
No. of patients	230	252
Mean airway pressure (cm of water)	15±5	20±5†
No. of patients	233	261
Respiratory rate (breaths/min)	29±7	29±7
No. of patients	248	263
Minute ventilation (liters/min)	12±4	12±3
No. of patients	247	264
FiO_2	0.54±0.18	0.44±0.17†
No. of patients	249	264
PEEP (cm of water)		
All patients	8.9±3.5	14.7±3.5‡
No. of patients	249	264
First 171 patients	9.1±3.3	14.2±3.2
No. of patients	76	82
Subsequent 378 patients	8.9±3.6	14.9±3.6
No. of patients	173	182
PaO_2/FiO_2	168±66	220±89‡

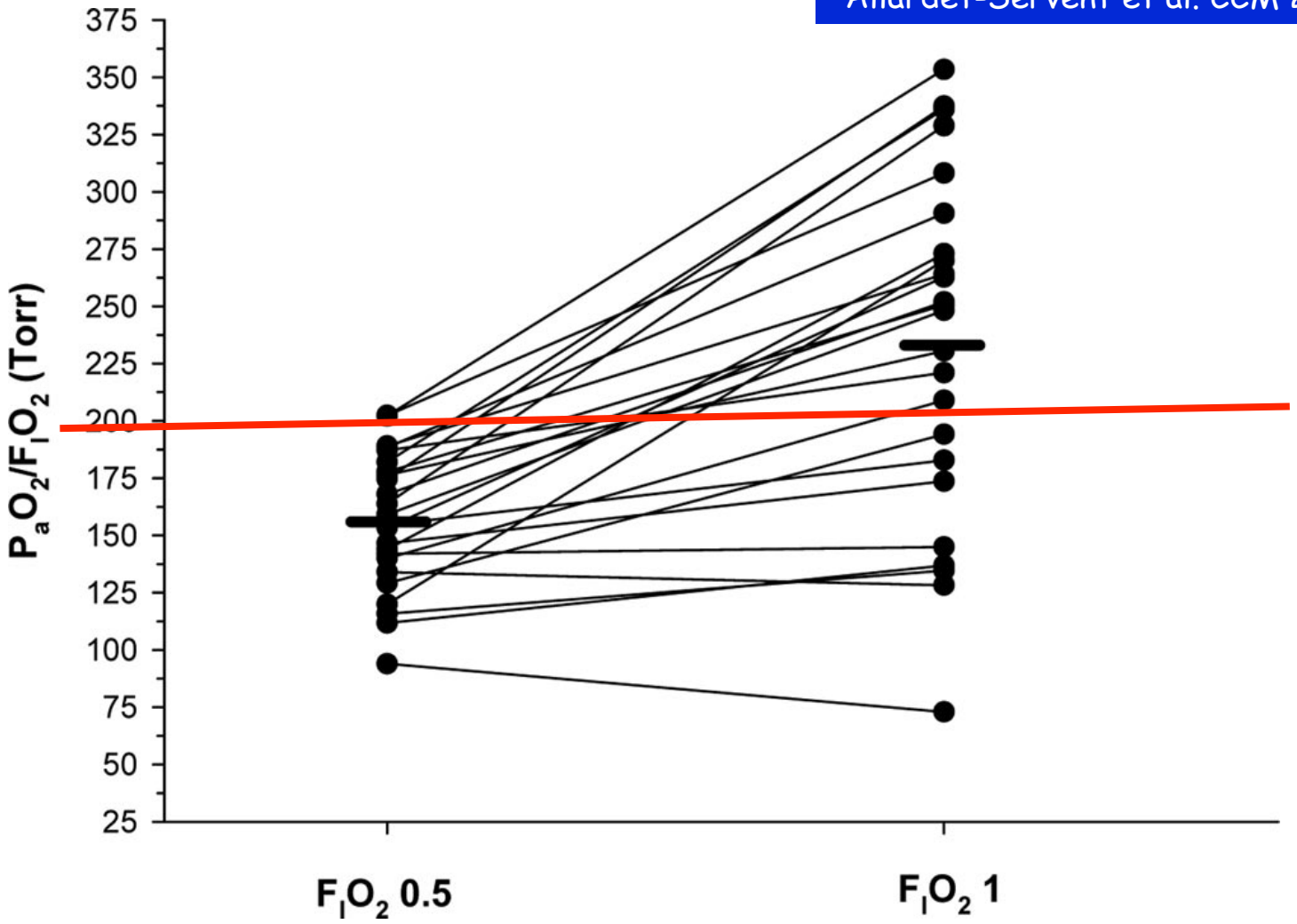
	Fraction of Inspired Oxygen (FIO_2)							
	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0
Control PEEP ranges, cm H_2O	5	5-8	8-10	10	10-14	14	14-18	18-24
Lung open ventilation PEEP ranges, cm H_2O								
Before protocol change	5-10	10-14	14-20	20	20	20	20	20-24
After protocol change	5-10	10-18	18-20	20	20	20-22	22	22-24

O'Meade *et al.* JAMA 2008

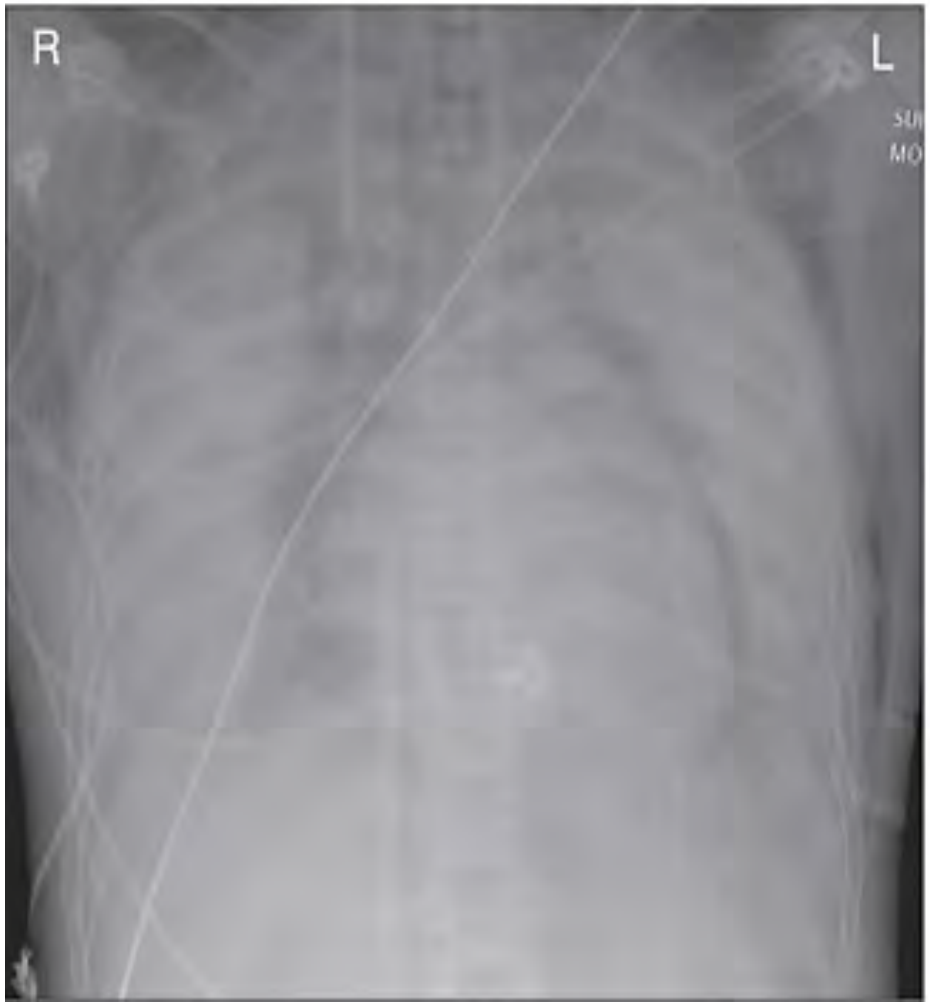


Is it really a moderate to severe ARDS?

Allardet-Servent et al. CCM 2009



Chest radiograph



Computed tomogram

Acute lung injury score[a]	3.8 (3.3-4.0)

Berlin definition

	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

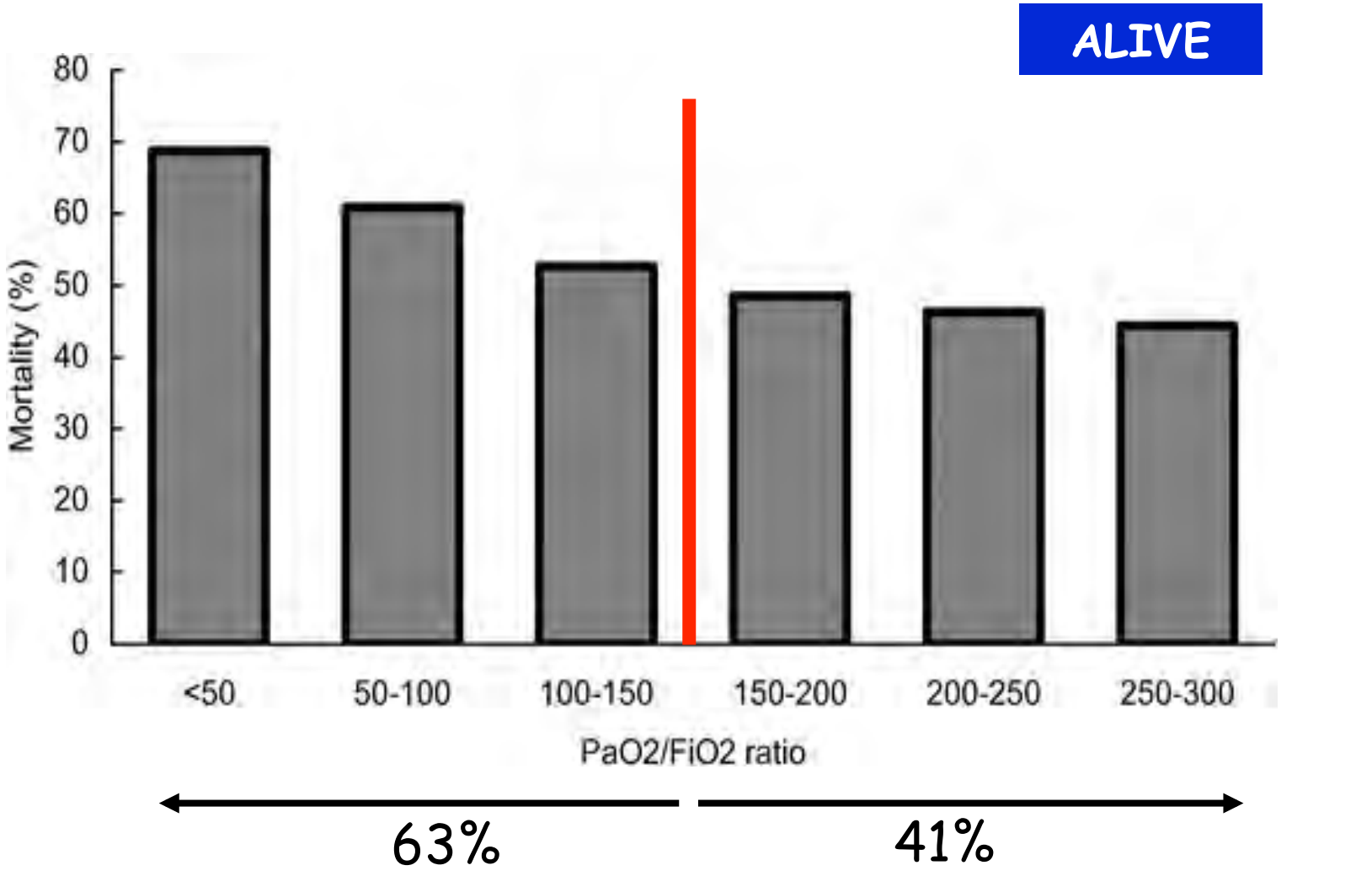
Abbreviations: CPAP, continuous positive airway pressure; FIO_2, fraction of inspired oxygen; PaO_2, partial pressure of arterial oxygen; PEEP, positive end-expiratory pressure.

[a] Chest radiograph or computed tomography scan.

[b] If altitude is higher than 1000 m, the correction factor should be calculated as follows: [PaO_2/FIO_2 × (barometric pressure/760)].

[c] This may be delivered noninvasively in the mild acute respiratory distress syndrome group.

PaO2/FIO2 and mortality

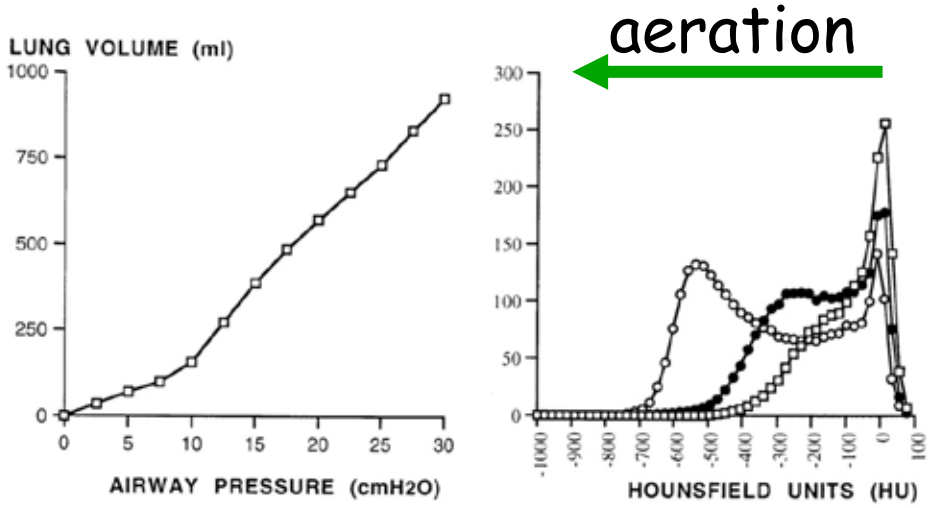


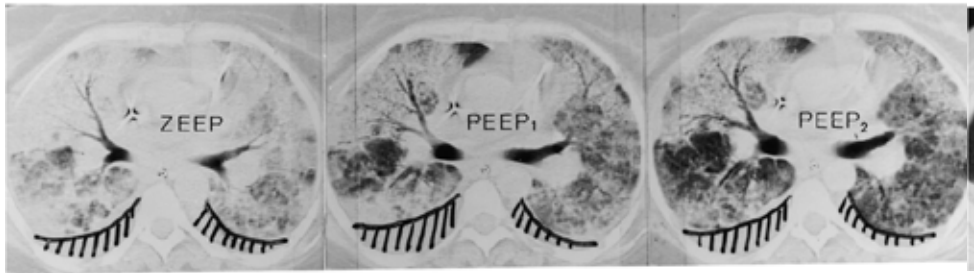
Brun-Buisson et al. ICM 2004

Recruitment, overdistension, and PEEP

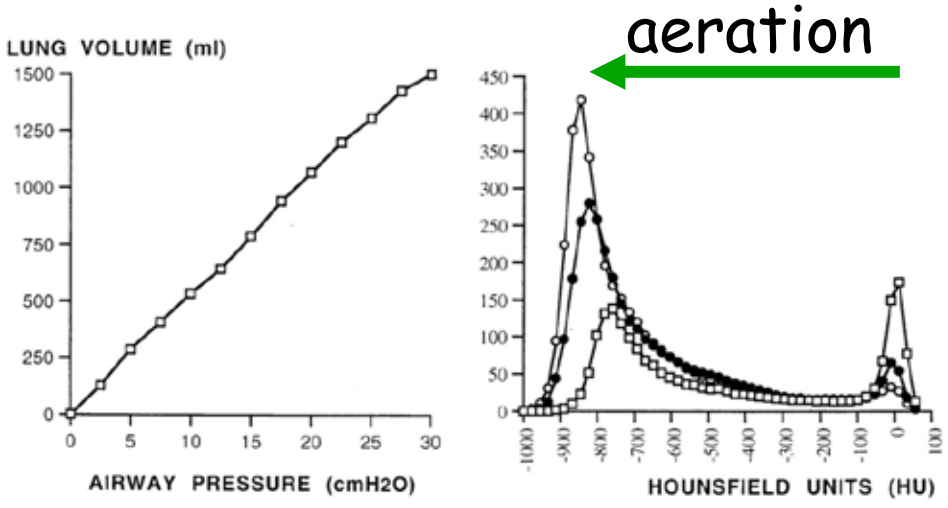
Viera et al. AJRCCM 99

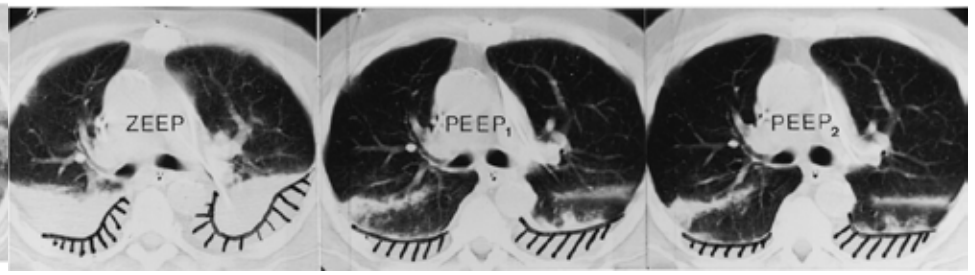
With LIP





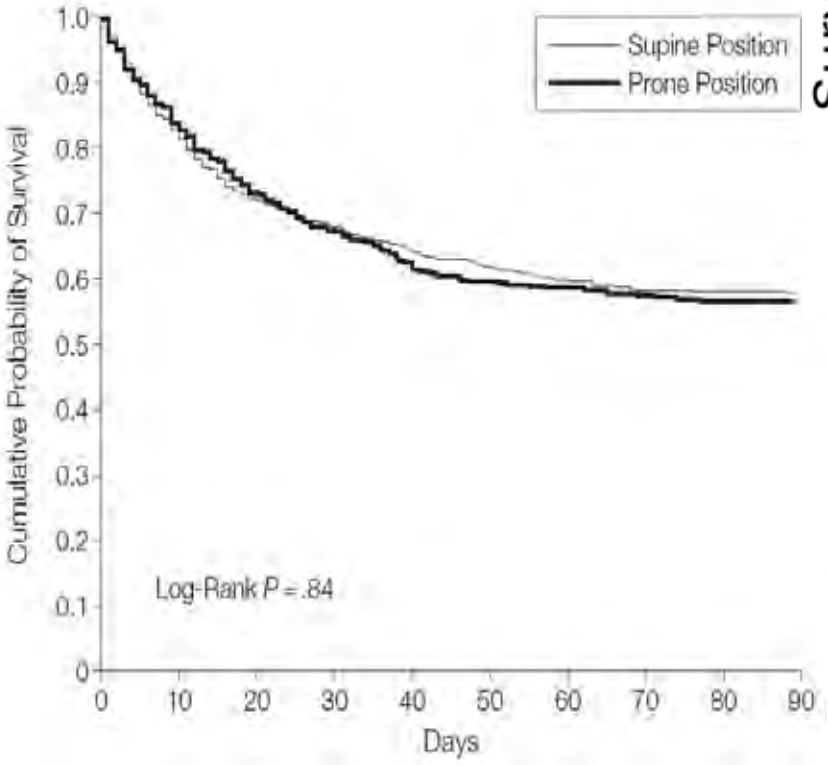
Without a LIP

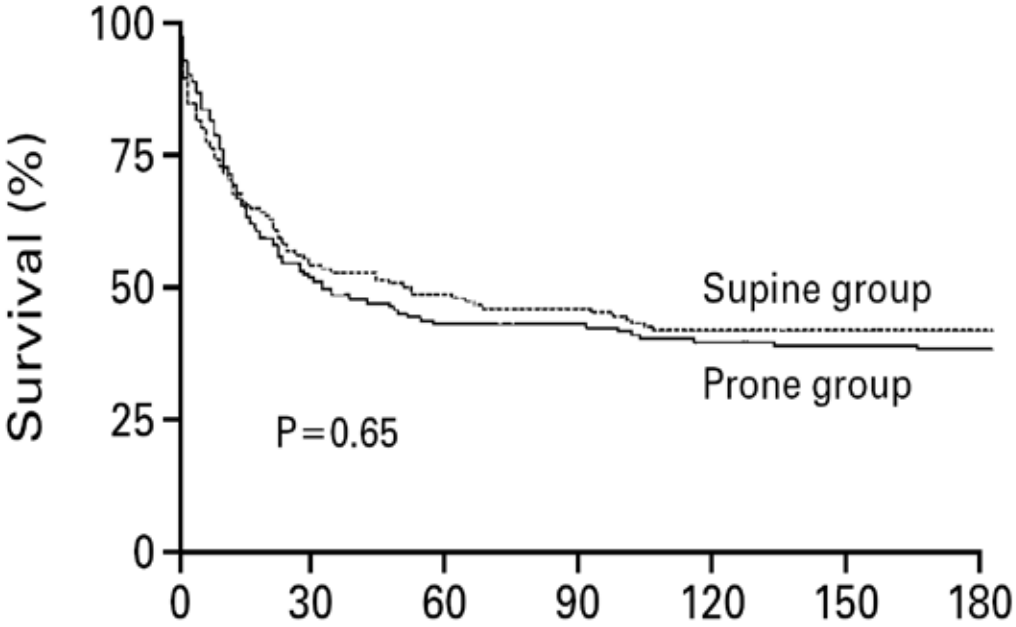


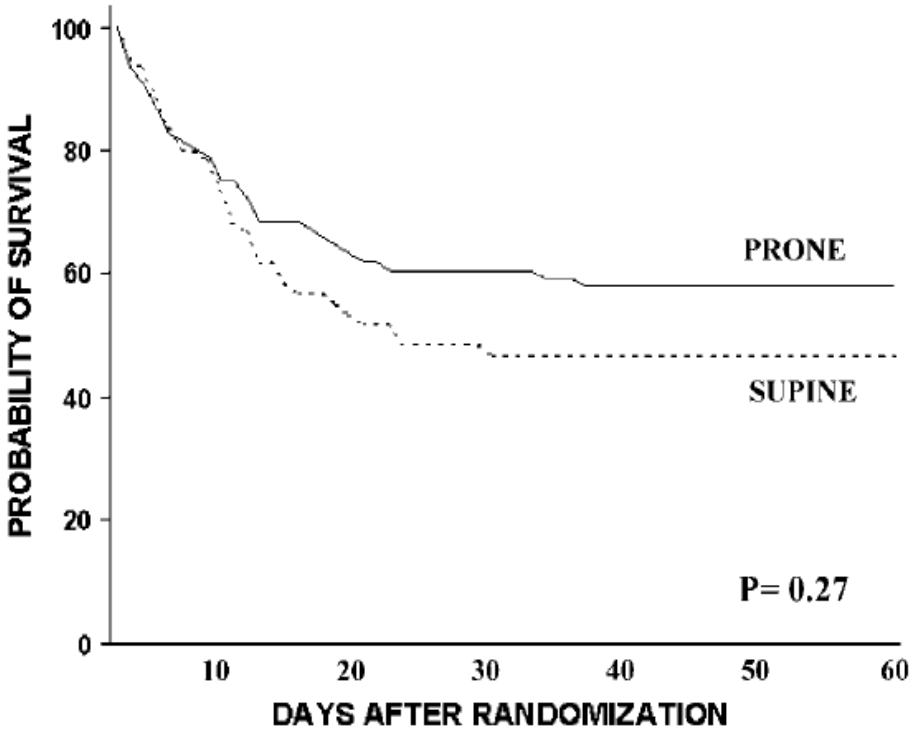


To summarize

- Goal: PaO2 55-70 mmHg
- MV optimization
  - Reduced tidal volume (6-8 ml/kg…)
  - Pplat limitation (Pplat < 28-30 cmH2O)
  - High PEEP level
  - To set PEEP
    - Pragmatic approach
    - Diffuse:lobar
    - P/V curves
    - Transpulmonary pressure


Supine Position
Prone Position
Cumulative Probability of Survival
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Log-Rank P = .84
0
10
20
30
40
50
60
70
80
90
Days


Survival (%)
100
75
50
25
0
Supine group
Prone group
P=0.65
0
30
60
90
120
150
180

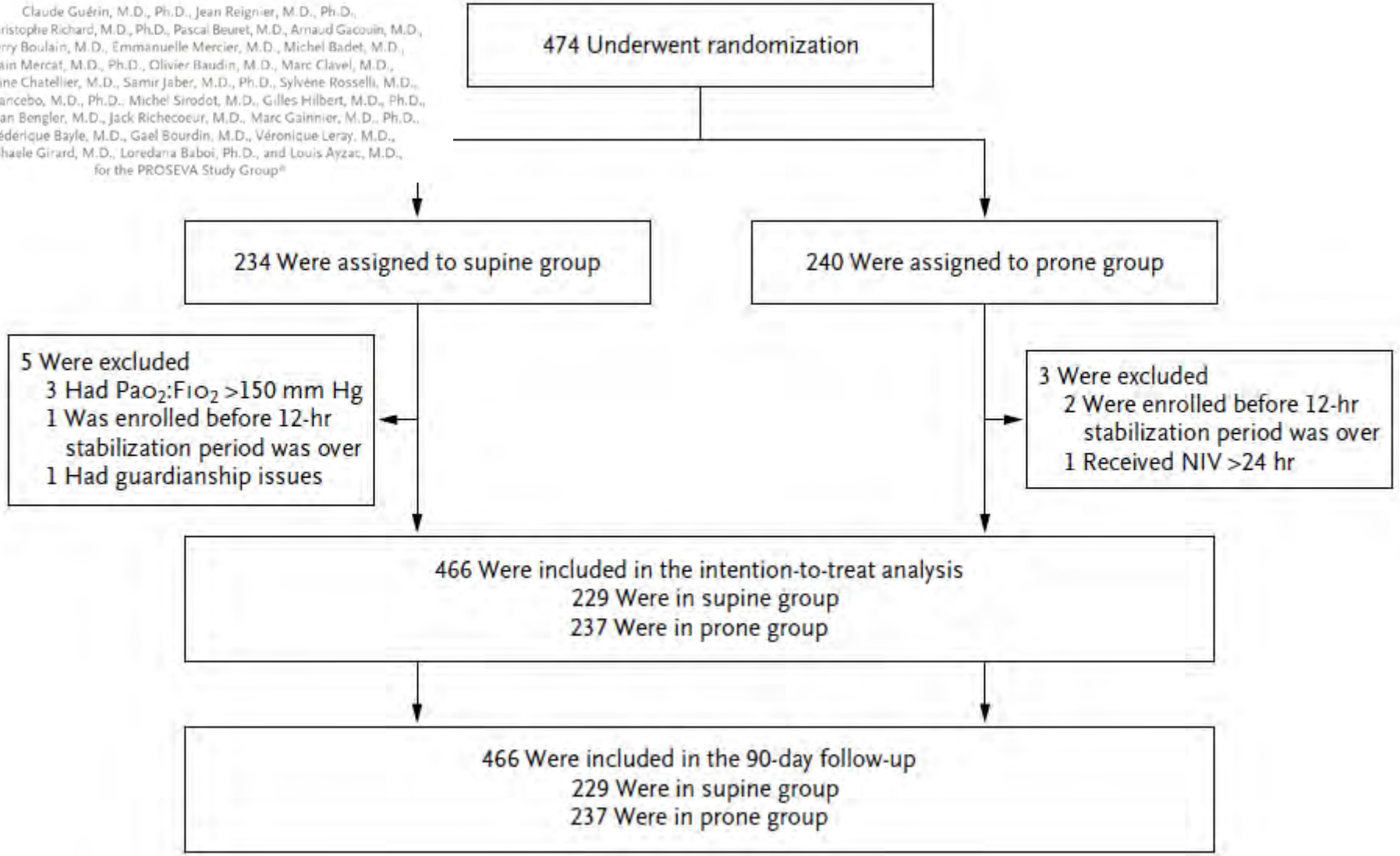

PROBABILITY OF SURVIVAL
100
80
60
40
20
0
PRONE
SUPINE
P= 0.27
10
20
30
40
50
60
DAYS AFTER RANDOMIZATION

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Prone Positioning in Severe Acute Respiratory Distress Syndrome

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



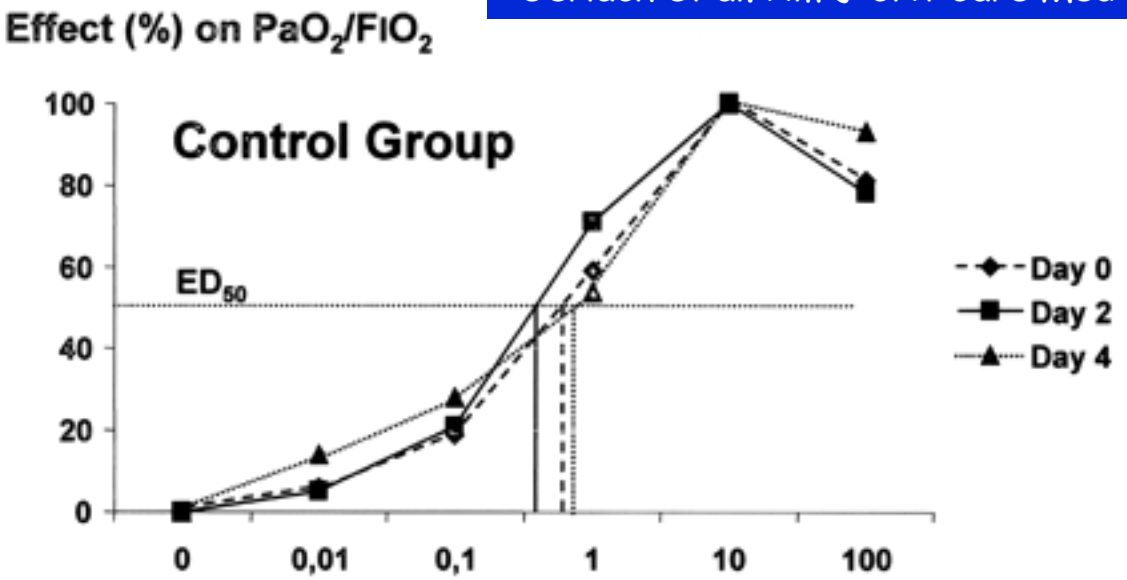
Outcome is related to the delay

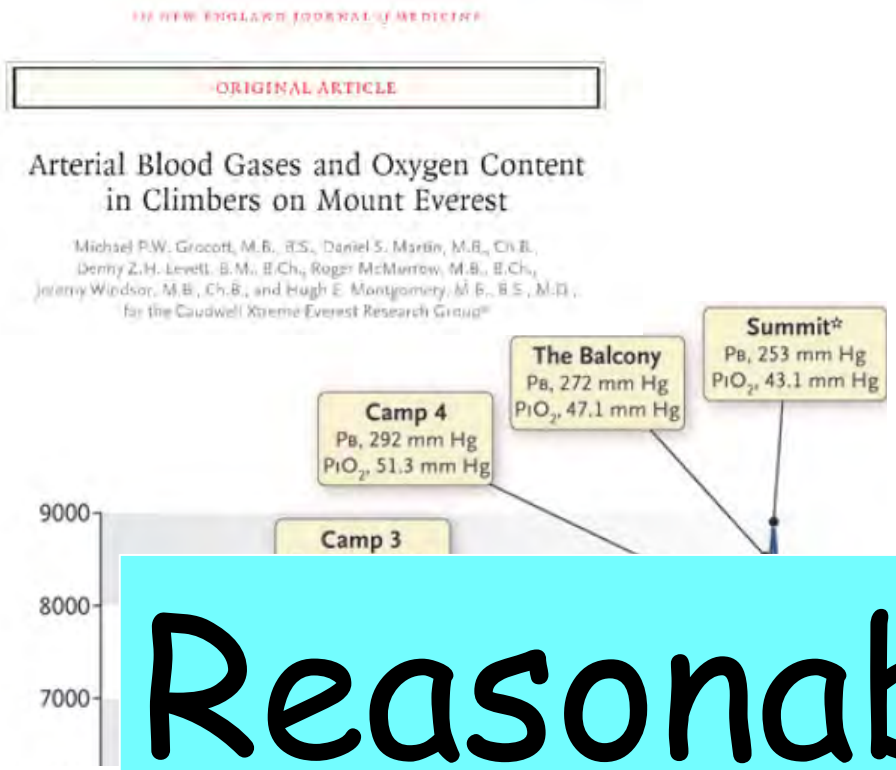
	Survivors (n = 132)		Nonsurvivors (n = 123)		
	Mean ± SD	Range	Mean ± SD	Range	*P* Value
Age, y	37.2 ± 13.1	17–68	39.7 ± 13.2	17–69	NS
Male/female, %	56.1/43.9		40.7/59.3		0.02
Weight, kg	82.2 ± 21.9	39–156	82.7 ± 23.9	36–150	NS
Duration of ECLS, h	180.2 ± 136.1	23–735	261.6 ± 238.6	3–1358	0.0009
PaO_2/FiO_2 ratio	56.6 ± 15.5	26–129	53.1 ± 16.1	28–123	NS
Shunt (Qs/Qt)	0.54 ± 0.17	—	0.56 ± 0.21	—	NS
A-aDO_2 gradient, mm Hg	612 ± 19	538–651	611 ± 22	523–658	NS
Pre-ECLS ventilator days	3.2 ± 2.6	0–16	4.5 ± 3.7	0–22	0.002

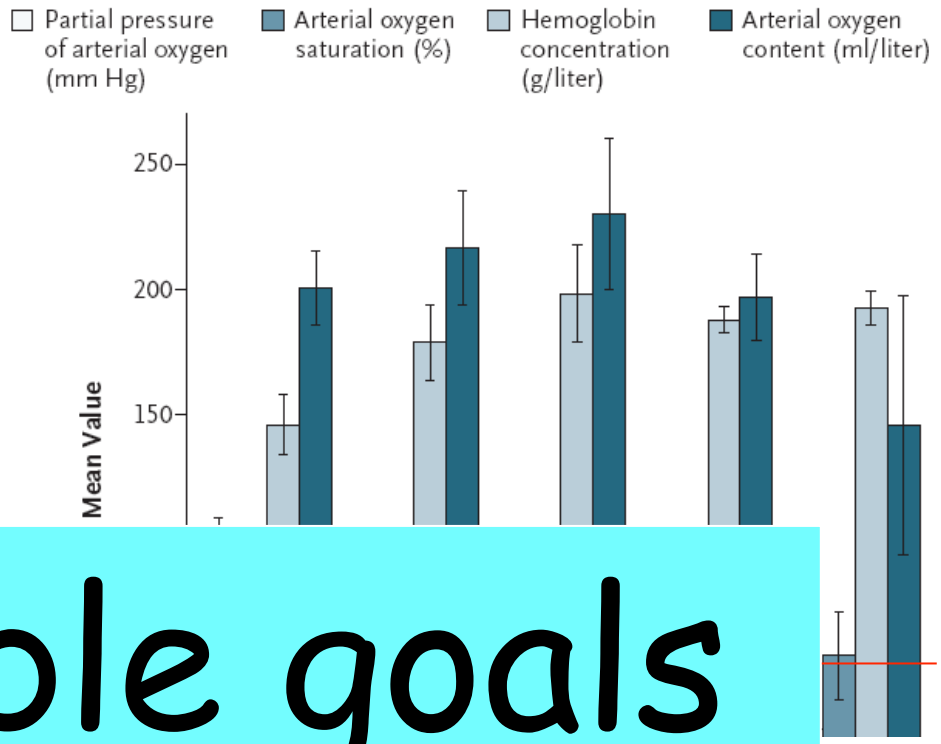
Hemmila *et al.* Ann Surg 2004

Daily re-evaluation of the dose

Gerlach et al. Am J Crit Care Med 2003







Reasonable goals

Variab … up Mean

	1	2	3	4	
pH	7.55	7.45	7.52	7.60	7.53
PaO_2 (mm Hg)†	29.5	19.1	21.0	28.7	24.6
$PaCO_2$ (mm Hg)†	12.3	15.7	15.0	10.3	13.3
Bicarbonate (mmol/liter)‡	10.5	10.67	11.97	9.87	10.8
Base excess of blood‡	−6.3	−9.16	−6.39	−5.71	−6.9
Lactate concentration (mmol/liter)	2.0	2.0	2.9	1.8	2.2
SaO_2 (%)‡	68.1	34.4	43.7	69.7	54.0
Hemoglobin (g/dl)§	20.2	18.7	18.8	19.4	19.3