22° Annual Meeting

Tuscany

Critical Care Group

Firenze, 25/26 Settembre 2019

ARDS: Sempre grave come 20 anni fa?

Davide Chiumello, MD
Dipartimento di Scienze della Salute – Università degli Studi di Milano
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UNIVERSITÀ DEGLI STUDI DI MILANO

2019

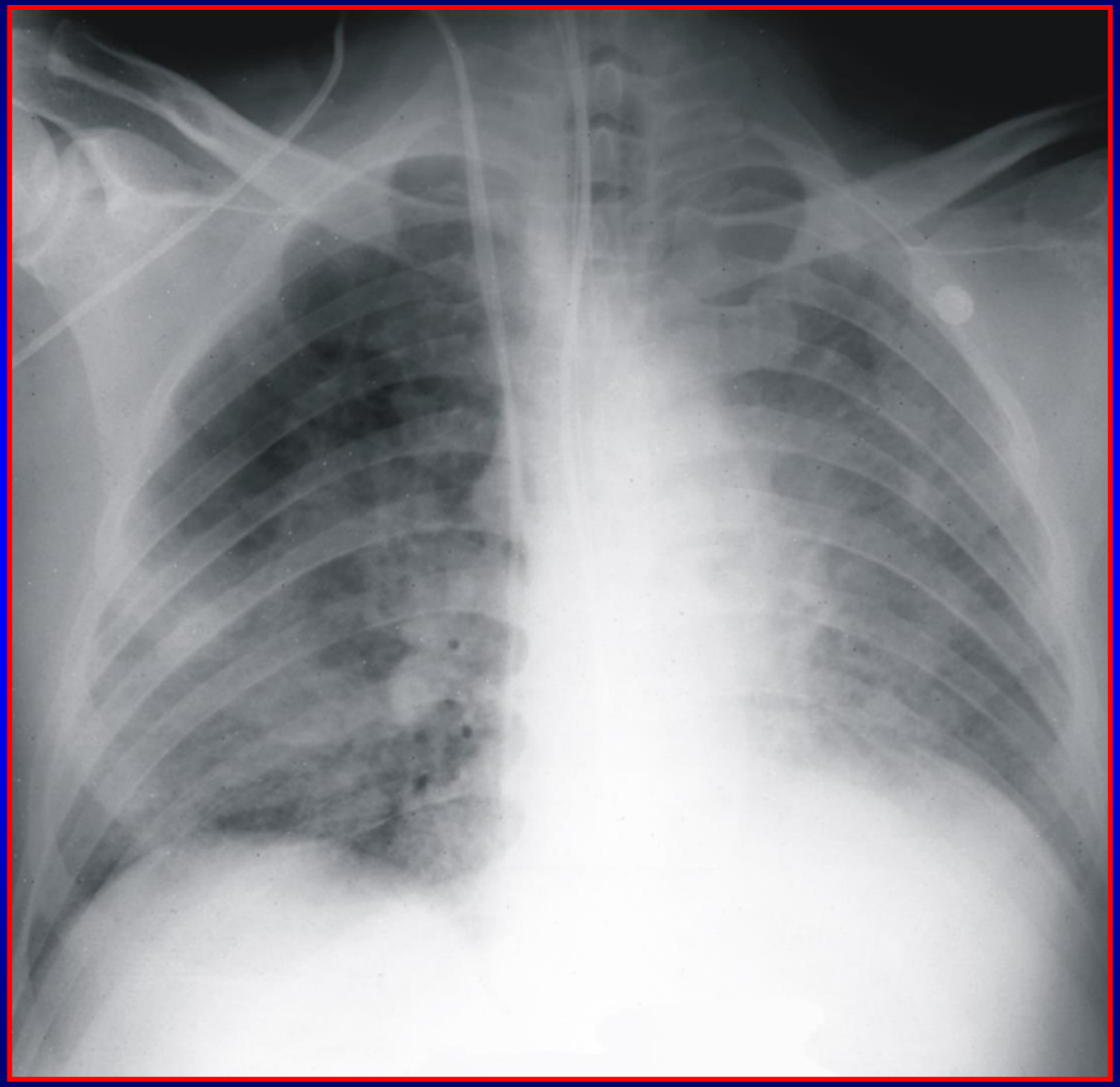
Ospedale San Paolo
Polo Universitario

Sistema Socio Sanitario
Regione Lombardia
ASST Santi Paolo e Carlo

History

…in 1967, Ashbaugh and colleagues described 12 patients with acute respiratory distress, cyanosis refractory to oxygen therapy, decreased lung compliance and diffuse infiltrates evident on the chest radiograph.

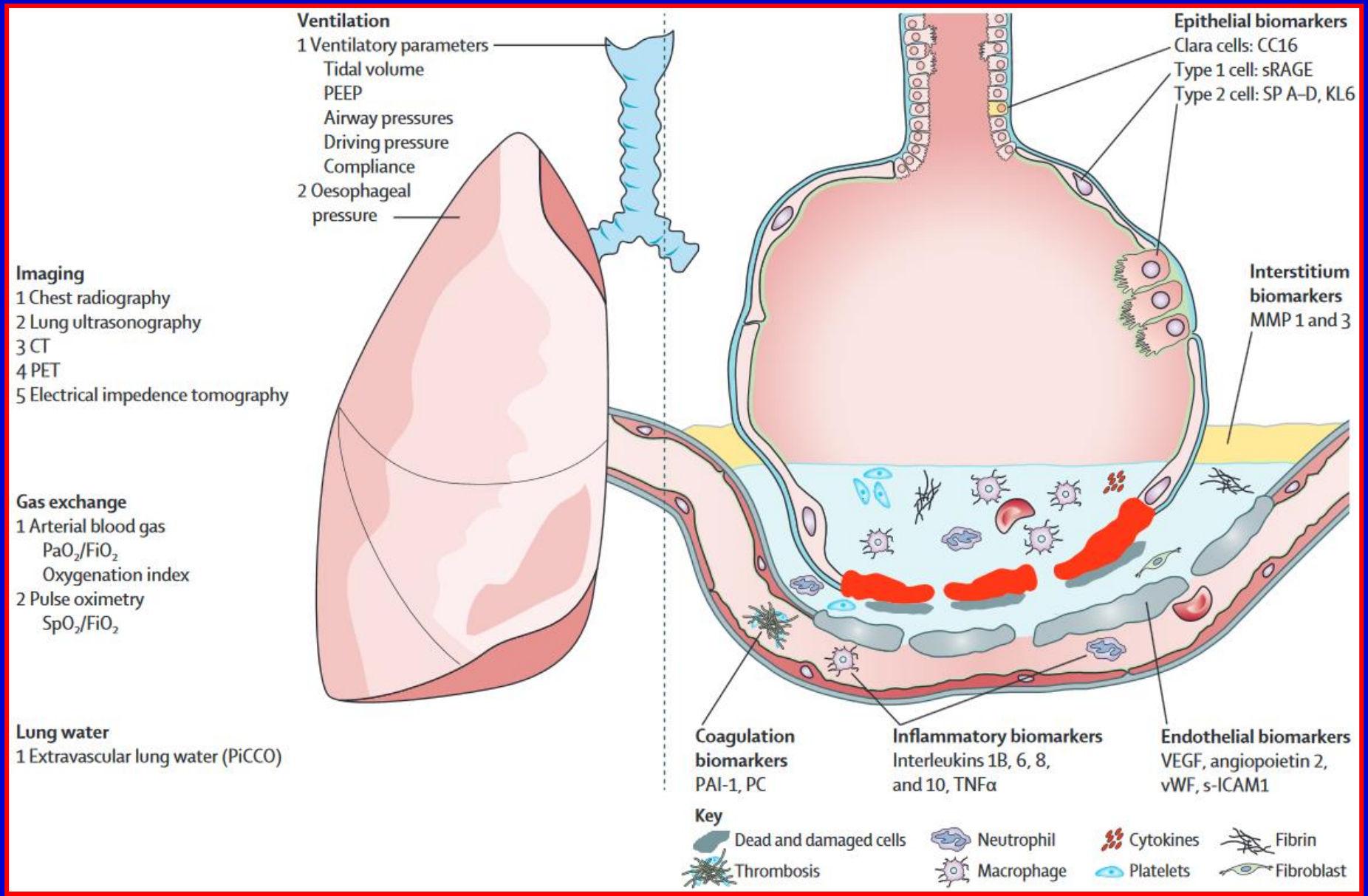
Lancet 1967;2:319-323

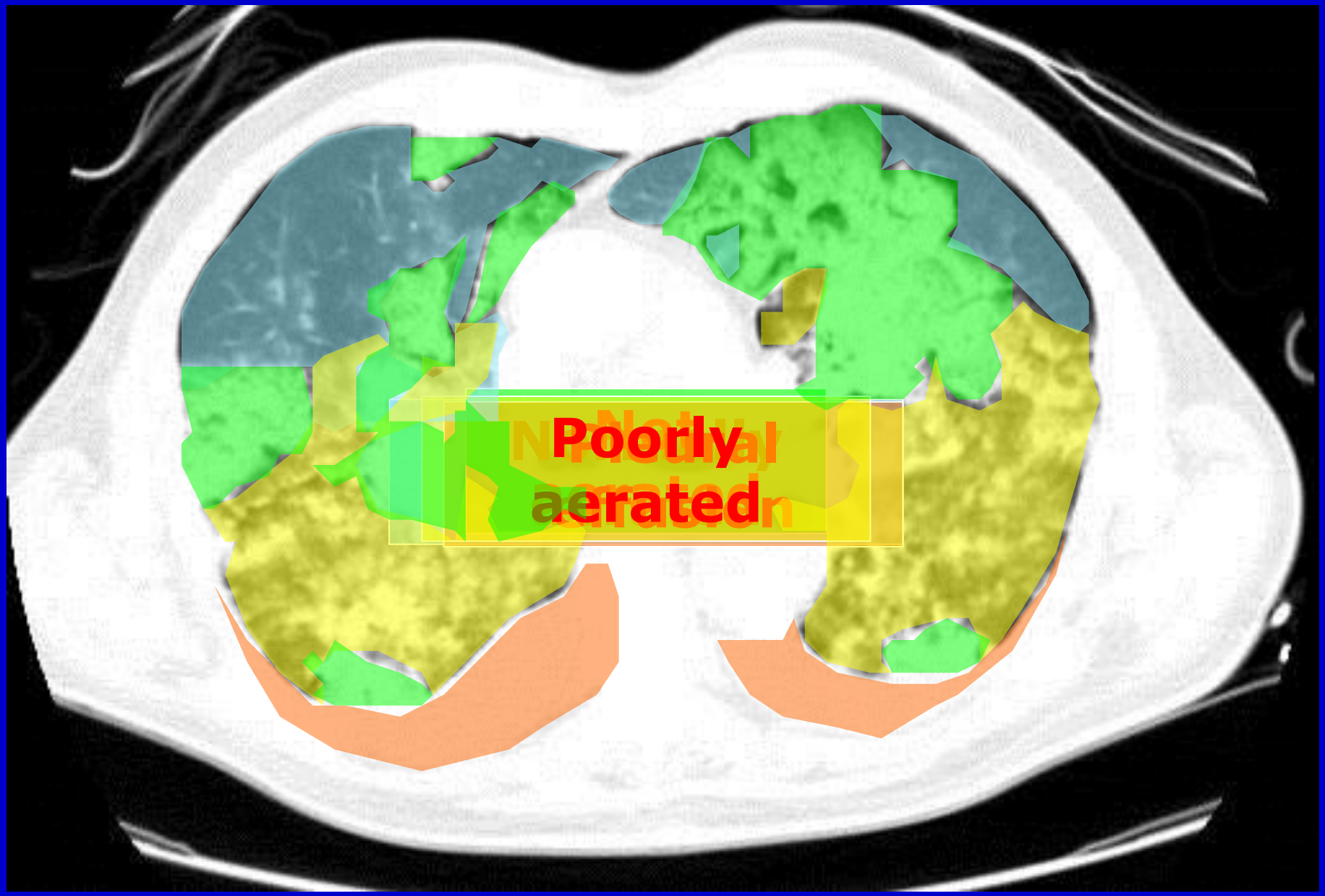


Acute respiratory distress syndrome

Rob Mac Sweeney, Daniel F McAuley

Lancet 2016; 388: 2416–30




Poorly aerated

Acute respiratory distress syndrome

Rob Mac Sweeney, Daniel F McAuley

Lancet 2016; 388: 2416–30

	Murray, 1988[2]	AECC, 1994[3]	Ferguson, 2005[4]	Berlin, 2012[5]
Onset	Acute or chronic, not specified	Acute, not specified	Within 72 h	New or worsening within 1 week
Risk factor	Required	Not required	Required	Not required
Oxygenation (mm Hg)	PaO_2/FiO_2 >300 (0) PaO_2/FiO_2 225–299 (1) PaO_2/FiO_2 175–224 (2) PaO_2/FiO_2 100–174 (3) PaO_2/FiO_2 <100 (4)	Acute lung injury: PaO_2/FiO_2 <300 Acute respiratory distress syndrome: PaO_2/FiO_2 ≤200	PaO_2/FiO_2 <200	Mild: PaO_2/FiO_2 200–300 Moderate: PaO_2/FiO_2 100–199 Severe: PaO_2/FiO_2 <100
PEEP (cm H_2O)	≤5 (0) 6–8 (1) 9–11 (2) 12–14 (3) ≥15 (4)	Not specified	≥10	Minimum PEEP of 5 required
Infiltrates on chest radiograph	No quadrants (0) One quadrant (1) Two quadrants (2) Three quadrants (3) Four quadrants (4)	Bilateral infiltrates on a frontal chest radiograph	Bilateral airspace disease involving two or more quadrants on a frontal chest radiograph	Bilateral infiltrates involving two or more quadrants on a frontal chest radiograph or CT
Heart failure	..	Pulmonary artery wedge pressure ≤17 mm Hg Absence of left atrial hypertension	No clinical evidence of congestive heart failure (based on pulmonary artery catheter with or without echocardiogram)	Left ventricular failure insufficient to solely account for clinical state
Static compliance (mL/cm H_2O)	≥80 (0) 60–79 (1) 40–59 (2) 20–39 (3) ≤19 (4)	..	Static compliance <50 (with patient sedated, tidal volume 8 mL/kg ideal bodyweight, PEEP ≥10)	Removed
Severity	Mild Moderate Severe	Based on oxygenation criteria	..	Based on oxygenation criteria
Specificity for diffuse alveolar damage	Autopsy: 74%[6] (lung injury score ≥2·5)	Autopsy: 30%,[6] 50%,[7] 66%,[8] 70%[9] Biopsy: 29%,[10] 47%,[11] 40%[12]	Autopsy: 69%[6]	Autopsy: 45%[13] Biopsy: 58%[14]

Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries

Extent of ARDS Recognition	All (n=2377)	Mild (n=714; 30.0%)	Moderate (n=1106; 46.5%)	Severe (n=557; 23.4%)	P value [1]
ARDS Recognition at any time No. (%) (95% CI)	1525 (64.2%) (62.2-66.1)	366 (51.3%) (47.5-55.0)	722 (65.3%) (62.4-68.1)	437 (78.5%) (74.8-81.8)	<0.001
Effect of ARDS Recognition on Day 1 variables					
Tidal volume (ml/kg PBW)	P=0.014	P=0.34	P=0.247	P=0.22	
- ARDS Recognized, mean (95% CI)	7.5 (7.4-7.6)	7.7 (7.5-7.9)	7.5 (7.4-7.7)	7.4 (7.2-7.6)	0.12
- ARDS Unrecognized, mean (95% CI)	7.7 (7.6-7.9)	7.8 (7.6-8.0)	7.7 (7.5-7.9)	7.7 (7.3-8.0)	0.53
PEEP (cmH_2O)	P<0.001	P<0.001	P<0.001	P=0.001	
- ARDS Recognized , mean (95% CI)	8.9 (8.8-9.1)	7.8 (7.5-8.1)	8.7 (8.5-9.0)	10.3 (9.9-10.7)	<0.001
- ARDS Unrecognized, mean (95% CI)	7.5 (7.3-7.7)	7.0 (6.7-7.2)	7.5 (7.2-7.7)	9.3 (8.8-9.8)	<0.001

Bellani, JAMA 2016

The acute respiratory distress syndrome: incidence and mortality, has it changed?

Jesús Villar[a,b,c], *Demet Sulemanji*[d,e], *and Robert M. Kacmarek*[d,e]

Curr Opin Crit Care 2014, 20:3–9

	Linko *et al.* [9]	**Li *et al.* [10]**	**Villar *et al.* [11]**	**Sigurdsson *et al.* [12▪]**
Country	Finland	USA	Spain	Iceland
Study period	8 weeks April–June 2007	8 years 2001–2008	1 year Nov 2008–Oct 2009	23 years 1988–2010
Study design	Prospective	Retrospective	Prospective	Retrospective
Single/multicentre	Multicentre	Two centres	Multicentre	Single centre
Catchment's population (adult)	4 164 980	124 277	3 546 629	262 136
ARDS cases/100 000 population	5.0	33.8 (as 2008 only)	7.2	7.2
ARDS cases/hospital/year	11.6 (estimated by us)	21 (in 2008)	15	18.9

FIFTY YEARS OF RESEARCH IN ARDS

The Epidemiology of Acute Respiratory Distress Syndrome

A 50th Birthday Review

Tài Pham[1,2] and Gordon D. Rubenfeld[1,3]

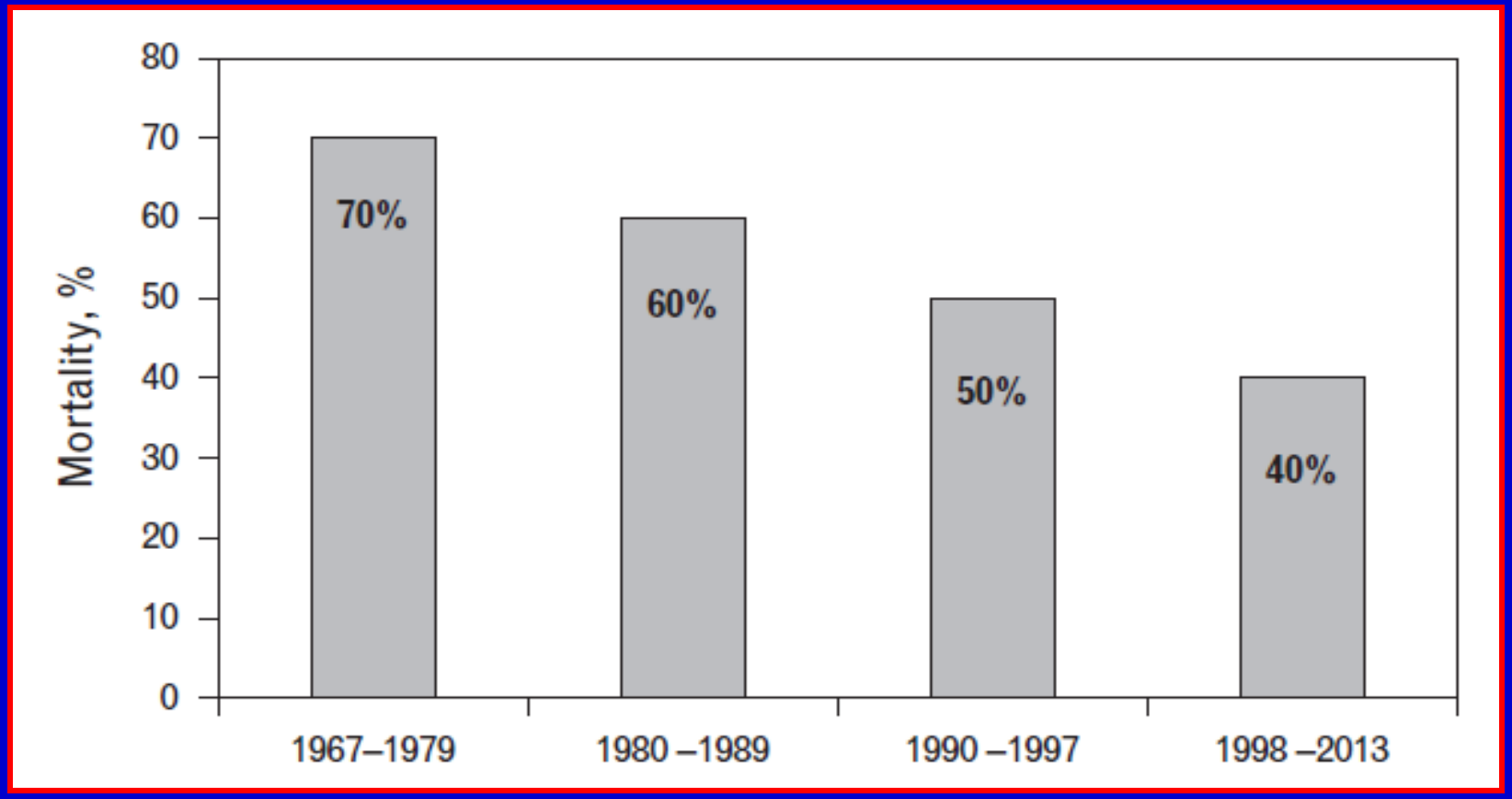
Am J Respir Crit Care Med Vol 195, Iss 7, pp 860–870, Apr 1, 2017

Study	Year(s) of Data Collection	Length of Inclusion	Country and No. of Centers	Population	Incidence (*per 100,000 Person-Years*) or Proportion (%)*	Mortality
Population-based studies						
Sigurdsson (56)	1988–2010	13 yr	Iceland: 1 hospital, 2 ICUs	Entire Icelandic population	3.65–9.63 (moderate and severe ARDS)	27% (30-d mortality); 38% (90-d mortality)
Nolan (38)	1990–1994	4 yr	Australia: 1 ICU	109,601	7.3–9.3 (moderate and severe ARDS)	47% (ICU mortality); 59% (hospital mortality)
Luhr (39)	1997	8 wk	Scandinavia (Sweden, Denmark, Iceland, Norway): 132 ICUs	11,738,992	17.9 (all ARDS); 13.5 (moderate and severe ARDS)	42.2% (90-d mortality, mild ARDS); 41.2% (90-d mortality, moderate and severe ARDS)
Bersten (40)	1999	2 mo	Australia (South, Western and Tasmania): 21 ICUs	2,941,137	34 (all ARDS); 28 (moderate and severe ARDS)	15% (28-d mortality, mild ARDS); 34% (28-d mortality, (moderate and severe ARDS)
Rubenfeld (41)	1999–2000	12 mo	King County, WA: 21 hospitals	1,740,000	78.9 (all ARDS); 58.7 (moderate and severe ARDS)	28.6% (hospital mortality, mild ARDS); 38.5% (hospital mortality, all ARDS); 41.1% (hospital mortality, moderate and severe ARDS)
Manzano (42)	2001	5 mo	Granada, Spain: 9 ICUs	633,187	25.5 (all ARDS); 23 (moderate and severe ARDS)	52% (moderate and severe ARDS, 28-d mortality); 66% (moderate and severe ARDS, hospital mortality)
Li (43)	2001–2008	8 yr	Olmsted County, MN: 2 hospitals	Entire population of Olmsted County	81.0 (moderate and severe ARDS in 2001); 38.3 (moderate and severe ARDS in 2008)	28% (hospital mortality in 2001); 45% (hospital mortality in 2008)
Caser (44)	2006–2007	15 mo	Vitoria region, Brazil: 14 hospitals, 14 ICUs	1,454,000	10.1 (all ARDS); 6.3 (moderate and severe ARDS)	30.6% (mild ARDS, Day 28 mortality); 43.2% (moderate and severe ARDS, Day 28 mortality)
Linko (45)	2007	8 wk	Finland: 18 hospitals, 25 ICUs	4,164,980	10.6 (all ARDS); 5.0 (moderate and severe ARDS)	47% (all ARDS, Day 90 mortality)
Villar (46)	2008–2009	12 mo	Spain: 17 centers	Total population >18 yr in the recruiting area	7.2 (moderate and severe ARDS)	42.7% (moderate and severe ARDS, ICU mortality); 47.8% (moderate and severe ARDS, hospital mortality)

The acute respiratory distress syndrome: incidence and mortality, has it changed?

Curr Opin Crit Care 2014, 20:3–9

Jesús Villar[a,b,c], *Demet Sulemanji*[d,e], *and Robert M. Kacmarek*[d,e]



ARDS is a syndrome

Medical treatment should treat
the etiology,
the phatophysiology
and the symptoms

The New England Journal of Medicine

The Acute Respiratory Distress Syndrome

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

Clinical Disorders Associated with the Development of the Acute Respiratory Distress Syndrome.

Direct Lung Injury	Indirect Lung Injury
Common causes	**Common causes**
Pneumonia	Sepsis
Aspiration of gastric contents	Severe trauma with shock and multiple transfusions
Less common causes	**Less common causes**
Pulmonary contusion	Cardiopulmonary bypass
Fat emboli	Drug overdose
Near-drowning	Acute pancreatitis
Inhalational injury	Transfusions of blood products
Reperfusion pulmonary edema after lung transplantation or pulmonary embolectomy	

Mechanical ventilation

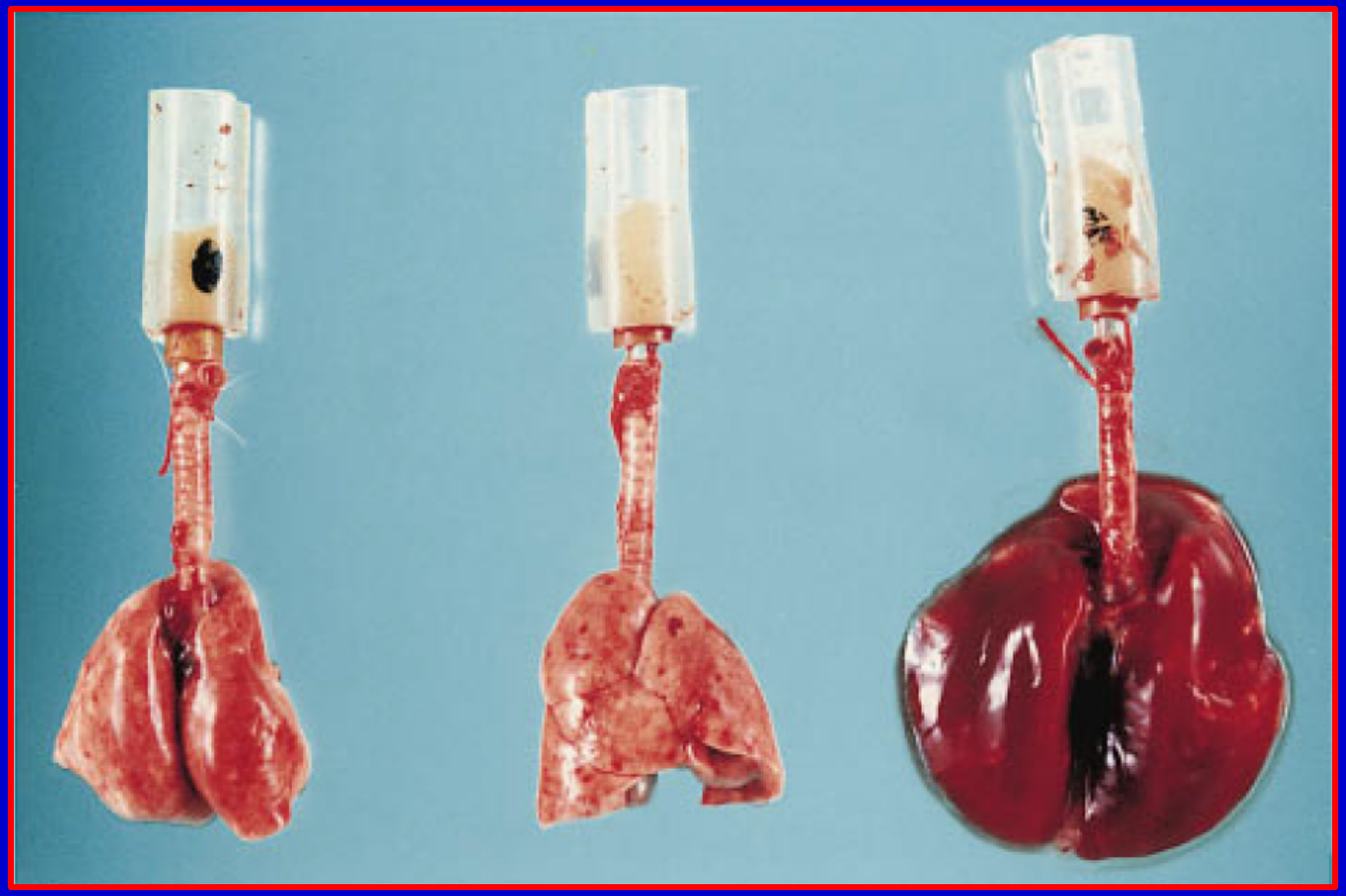
Mechanical ventilation could:
«cure» the impaired gas exchange,
act on the pathophysiology of edema
formation and clearance

Ventilator-induced Lung Injury

Lessons from Experimental Studies

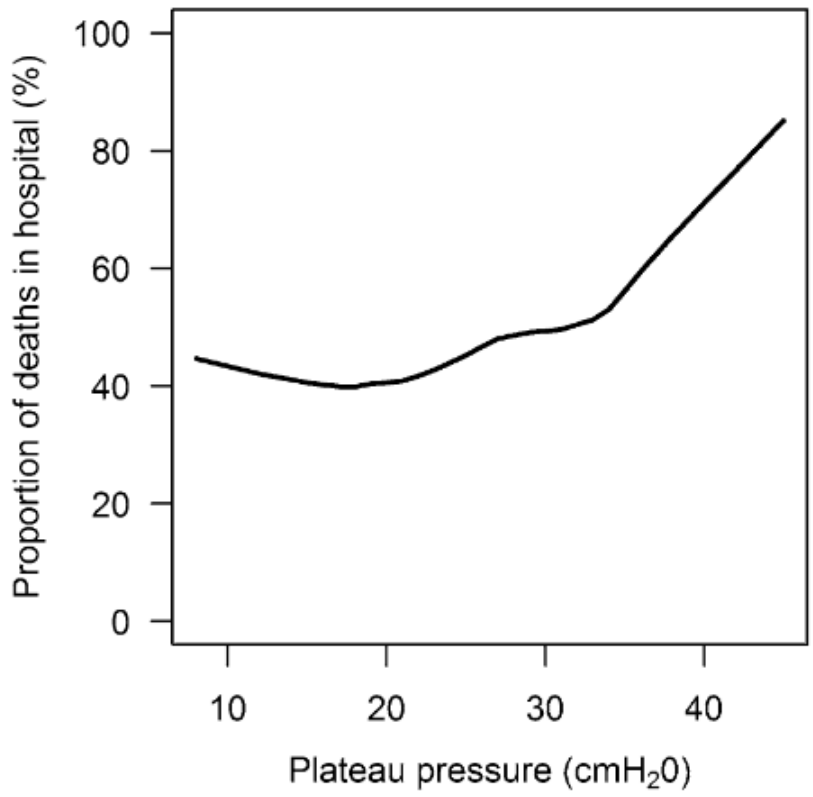
DIDIER DREYFUSS

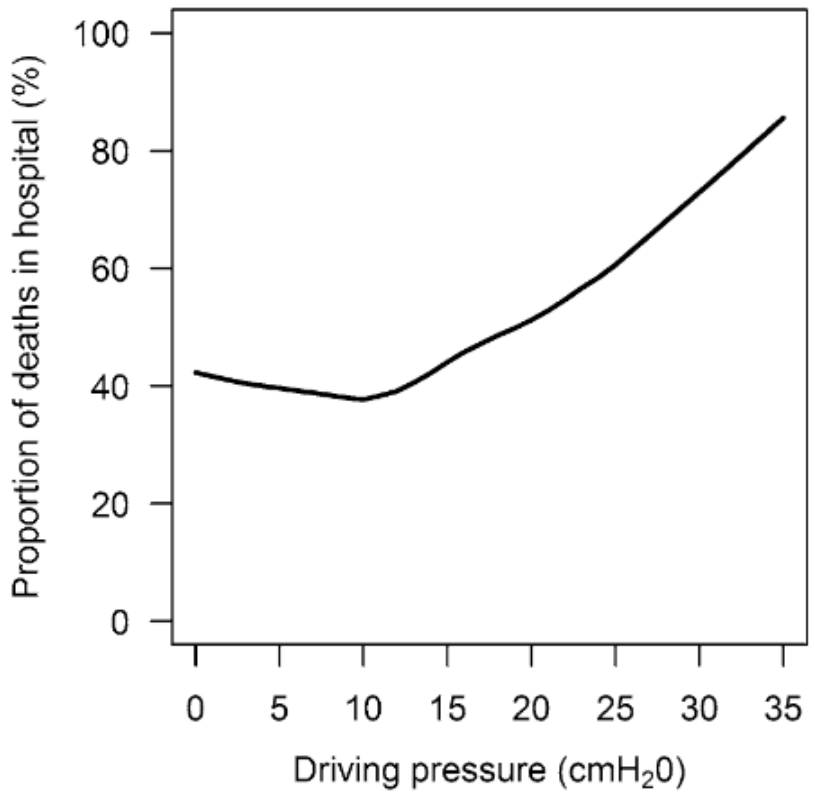
Am J Respir Crit Care Med Vol 157. pp 294–323, 1998



Potentially modifiable factors contributing to outcome from acute respiratory distress syndrome: the LUNG SAFE study

John G. Laffey[1,2*] and The LUNG SAFE Investigators





Intensive Care Med 2016

REVIEW

The standard of care of patients with ARDS: ventilatory settings and rescue therapies for refractory hypoxemia

Thomas Bein[1*], Salvatore Grasso[2], Onnen Moerer[3], Michael Quintel[3], Claude Guerin[4,5], Maria Deja[6], Anita Brondani[7] and Sangeeta Mehta[7]

Intensive Care Med (2016) 42:699–711

Table 1 Incidence of side effects and complications of mechanical ventilation in ARDS

Side effect/complication	Incidence	Comment
Ventilator-associated lung injury (VALI)	Not known	Incidence and intensity depend on invasiveness/duration of mechanical ventilation
Ventilation-associated pneumonia (VAP)	14–28 %	Problem: incidence depends on VAP definition; incidence increases with duration and invasiveness of mechanical ventilation
Right ventricular dysfunction, acute cor pulmonale	Up to 50 %	Often associated with severe hypercapnia/acidosis
Pleural effusions	Up to 80 %	Frequently related to fluid overload, hypo-oncotic states, cardiac dysfunction, and altered pleural pressure
Barotrauma/pneumothorax	6–12 %	Depends on the invasiveness (P_{Plat}) of mechanical ventilation
Damage of other organ systems via cross talk	Not known exactly	Lung, brain, and—renal cross talk via inflammation pathways
Prolonged sedation and immobilization	Not known	Incidence and intensity depend on sedation strategy, (early) wake up, and spontaneous breathing trials
Fibroproliferative response of the lung parenchyma	Up to 50 % in the "lung-protective era"	Decrements in lung function (vital capacity, forced expiratory volume) up to 5 years after discharge

Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries

Giacomo Bellani, MD,

JAMA February 23, 2016 Volume 315, Number 8

Parameter	All (N = 2377)	Mild (n = 714)	Moderate (n = 1106)	Severe (n = 557)	*P* Value[a]
FIO_2, mean (95% CI)	0.65 (0.64-0.65)	0.48 (0.47-0.50)	0.62 (0.61-0.63)	0.90 (0.88-0.91)	<.001
VT, mean (95% CI), mL/kg PBW	7.6 (7.5-7.7)	7.8 (7.6-7.9	7.6 (7.5-7.7)	7.5 (7.3-7.6)	.02
Set PEEP, mean (95% CI), cm H_2O	8.4 (8.3-8.6)	7.4 (7.2-7.6)	8.3 (8.1-8.5)	10.1 (9.8-10.4)	<.001
Peak pressure, mean (95% CI), cm H_2O[d]	27.0 (26.7-27.4)	24.7 (24.1-25.4)	26.9 (26.5-27.4)	30.3 (29.6-30.9)	<.001
Patients in whom P_{PLAT} measured, No. (%)					
Among all invasively ventilated patients, No. (%) [95% CI]	954 (40.1) [38.2-42.1]	260 (36.4) [32.9-40.1]	463 (41.9) [38.9-44.8]	231 (41.5) [37.3-45.7]	.05

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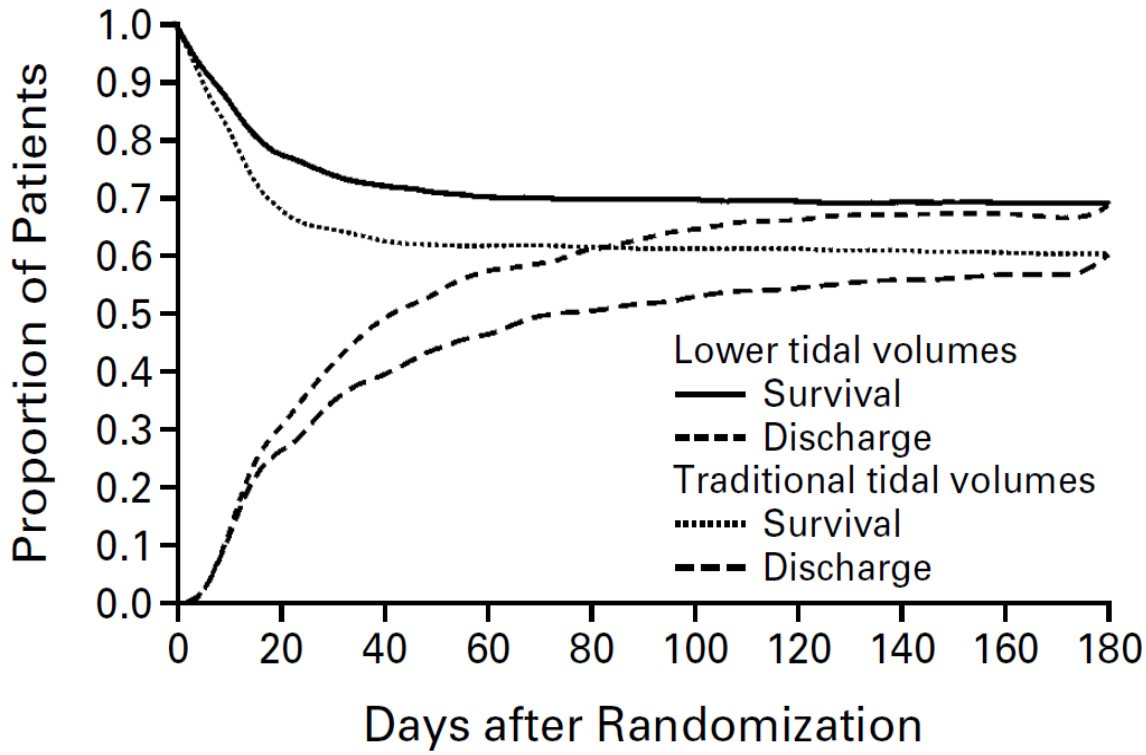
The New England
Journal of Medicine

VOLUME 342 MAY 4, 2000 NUMBER 18

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

THE ACUTE RESPIRATORY DISTRESS SYNDROME NETWORK*



Higher vs Lower Positive End-Expiratory Pressure in Patients With Acute Lung Injury and Acute Respiratory Distress Syndrome

JAMA, March 3, 2010

Matthias Briel, MD, MSc

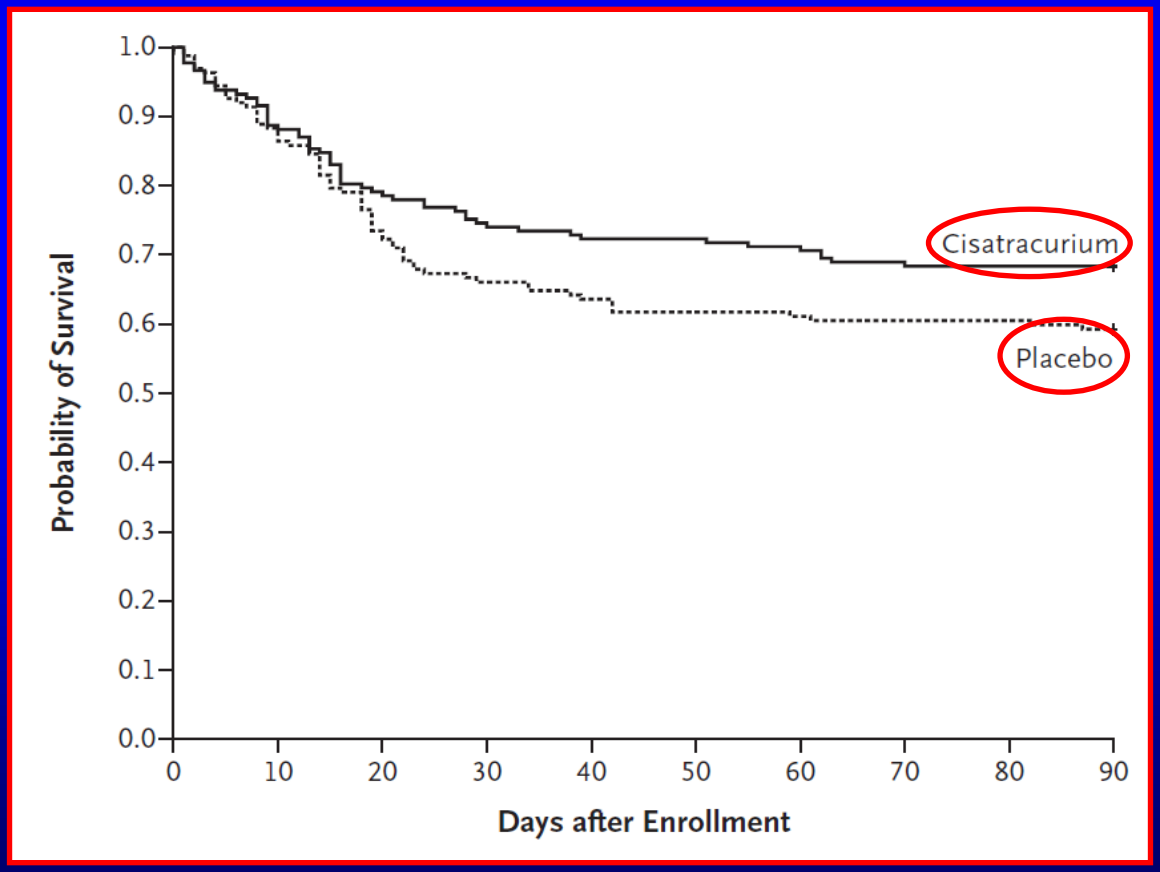
Outcomes	With ARDS			
	No. (%)			
	Higher PEEP (n = 951)	Lower PEEP (n = 941)	Adjusted RR (95% CI)[a]	*P* Value
Death in hospital	324 (34.1)	368 (39.1)	0.90 (0.81 to 1.00)	.049
Death in ICU[b]	288 (30.3)	344 (36.6)	0.85 (0.76 to 0.95)	.001
Days with unassisted breathing between day 1 and day 28, median (IQR)[d]	12 (0-21)	7 (0-20)	1.22 (0.39 to 2.05)[e]	.004
Total use of rescue therapies[f]	130 (13.7)	200 (21.3)	0.63 (0.53 to 0.75)	<.001

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.,

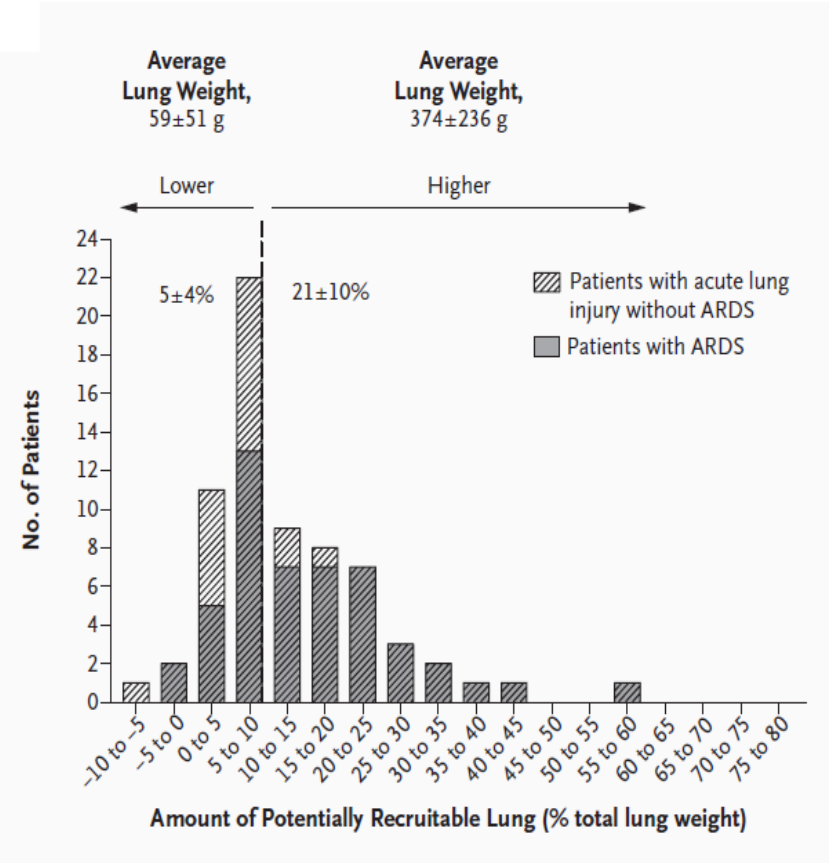


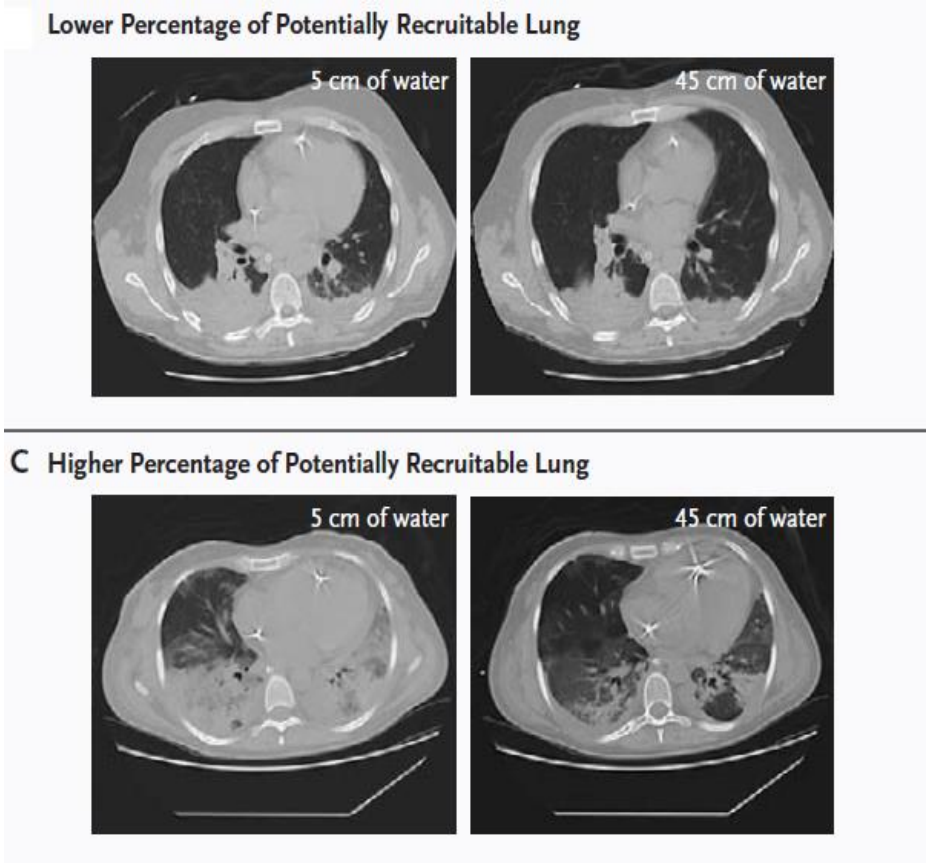
The Future of Critical Care Medicine: Integration and Personalization

Vincent J.-L.

Lung Recruitment in Patients with the Acute Respiratory Distress Syndrome

Luciano Gattinoni, M.D., F.R.C.P., Pietro Caironi, M.D., Massimo Cressoni, M.D., Davide Chiumello, M.D.,



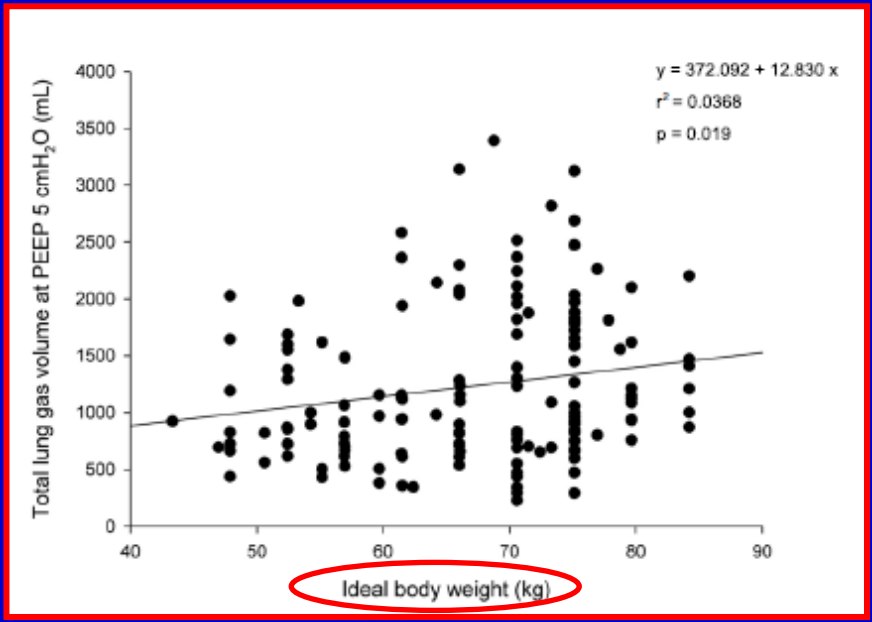


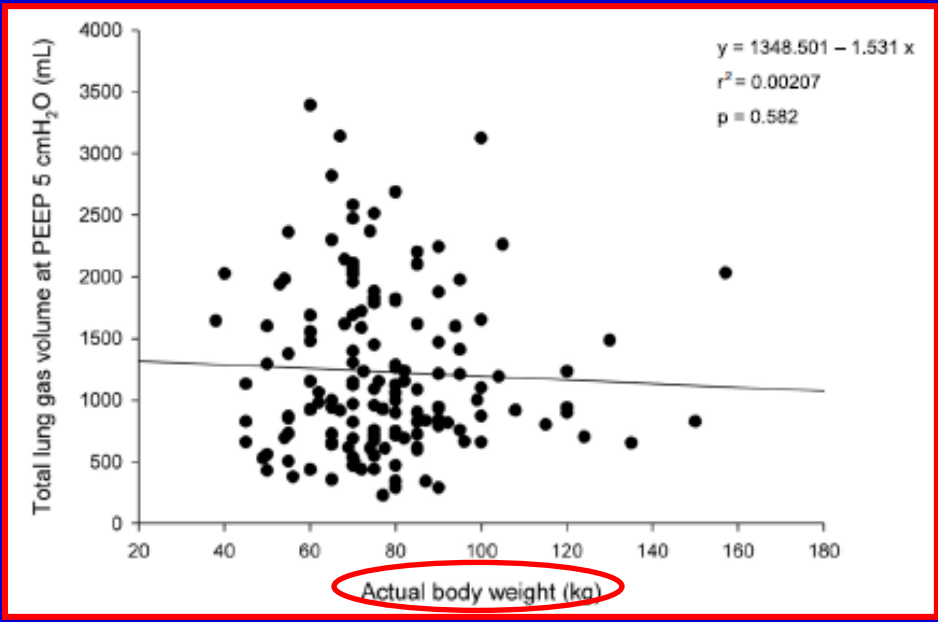
N Engl J Med 2006;354:1775-86.

Airway driving pressure and lung stress in ARDS patients

Davide Chiumello[1,2*], Eleonora Carlesso[3], Matteo Brioni[3] and Massimo Cressoni[3]

Critical Care (2016) 20:276



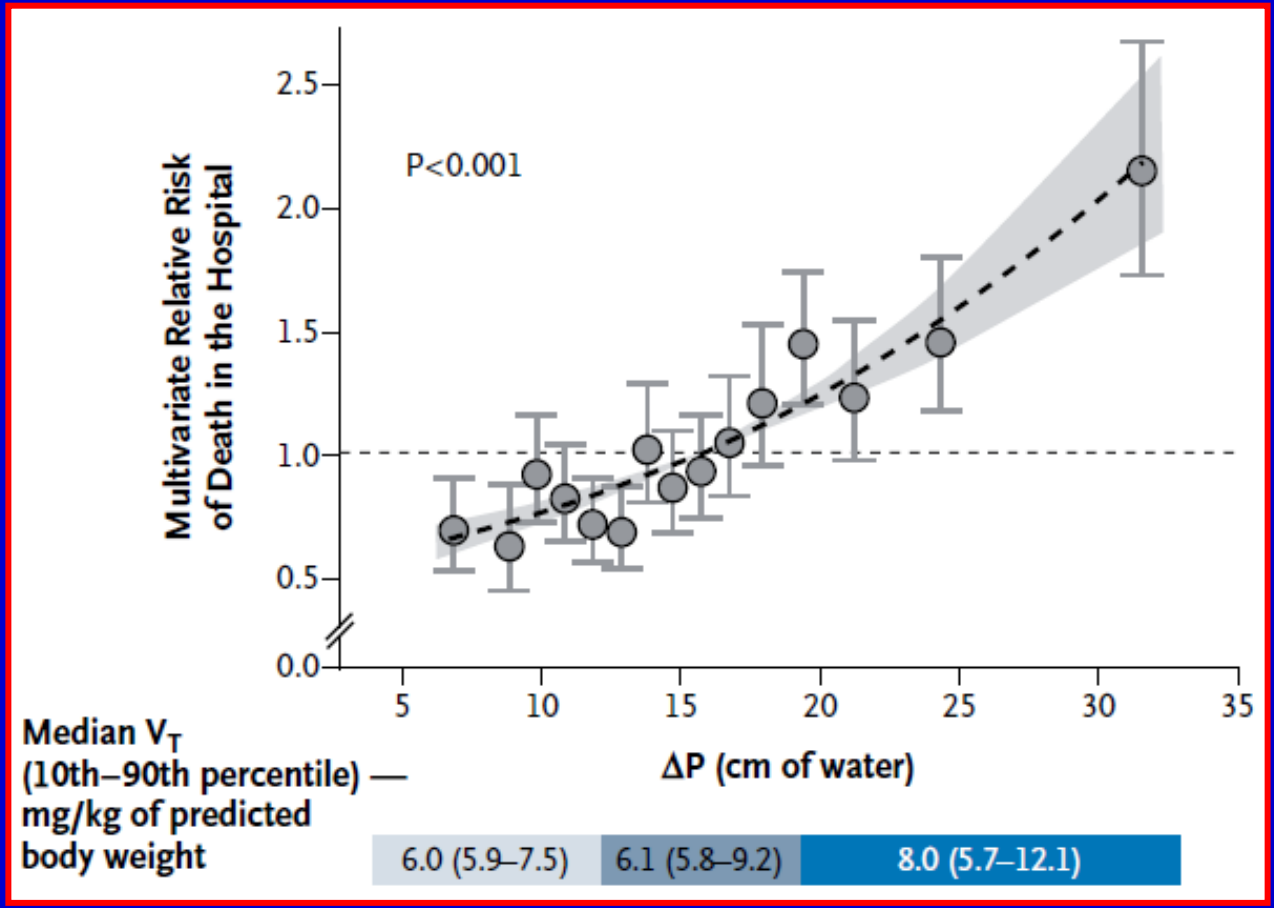


The NEW ENGLAND JOURNAL of MEDICINE

Driving Pressure and Survival in the Acute Respiratory Distress Syndrome

Marcelo B.P. Amato, M.D., Maureen O. Meade, M.D., Arthur S. Slutsky, M.D.,

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



Mechanical Power Determinants

- Tidal volume
- Respiratory rate
- PEEP
- Driving pressure
- Flow

Ventilator-related causes of lung injury: the mechanical power

Luciano Gattinoni

$$P = E_{RS} \bullet \Delta V + RAW \bullet F + PEEP$$

$E_{RS} \bullet \Delta V = \Delta P$

RAW • F = Peak - Plateau

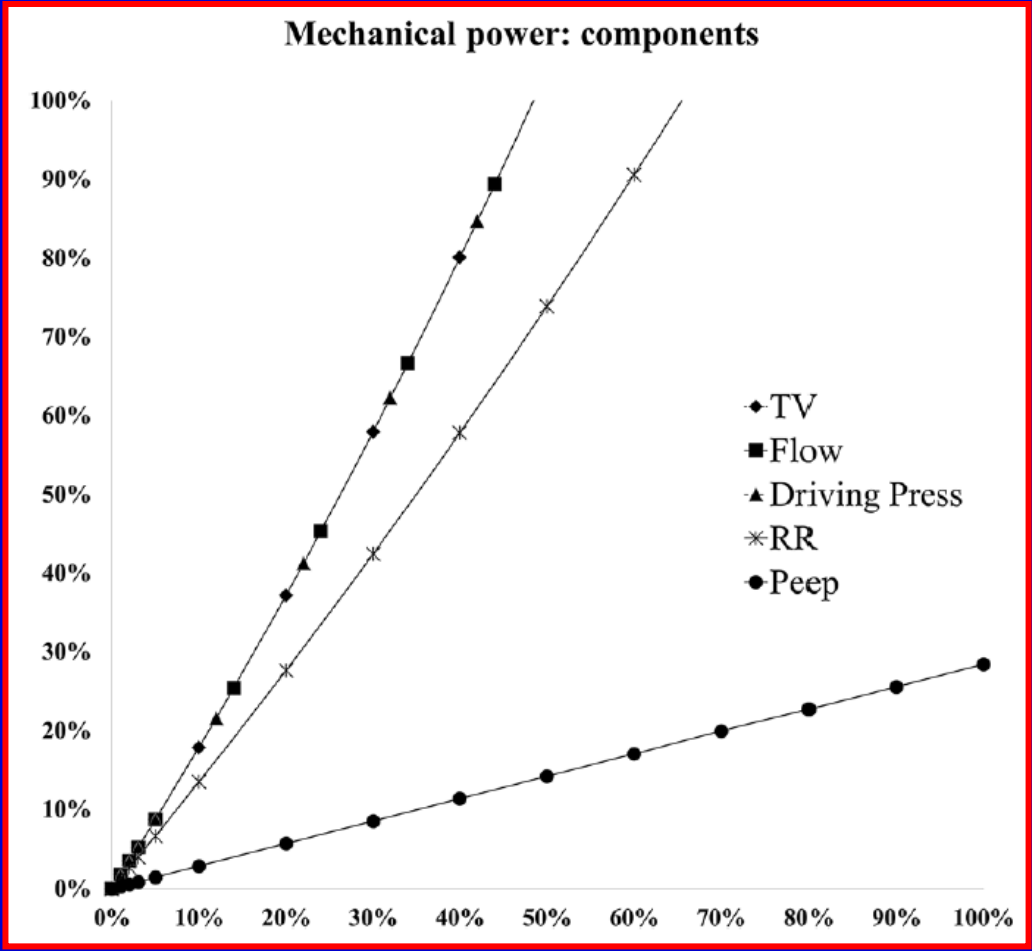
PEEP = Positive End-Expiratory Pressure

Intensive Care Med 2016

Ventilator-related causes of lung injury: the mechanical power

L. Gattinoni[1*], T. Tonetti[1], M. Cressoni[2], P. Cadringher[3], P. Herrmann[1], O. Moerer[1], A. Protti[3], M. Gotti[2], C. Chiurazzi[2], E. Carlesso[2], D. Chiumello[4] and M. Quintel[1]

Intensive Care Med (2016)



Mechanical power normalized to predicted body weight as a predictor of mortality in patients with acute respiratory distress syndrome

Zhongheng Zhang[1*], Bin Zheng[2], Nan Liu[3,4], Huiqing Ge[5] and Yucai Hong

Ventilator parameters	AUROC	Lower limit of 95% CI	Upper limit of 95% CI
Tidal volume (mL)	0.744	0.713	0.775
Tidal volume normalized to PBW (mL/kg)	0.746	0.715	0.777
Respiratory rate (/min)	0.743	0.713	0.774
PEEP (cmH_2O)	0.744	0.713	0.775
Plateau pressure (cmH_2O)	0.747	0.716	0.778
PIP (cmH_2O)	0.746	0.715	0.777
Driving pressure (cmH_2O)	0.743	0.712	0.774
MP (J/min)	0.747	0.717	0.778
norMP (10^{-3} J/min/kg)	0.751	0.720	0.781
MP normalized to compliance	0.753	0.722	0.783
Gradient boosting machine	0.748	0.717	0.779

IMPACT OF MECHANICAL POWER ON MORTALITY IN ARDS PATIENTS

Chiumello et. al

ICU mortality	IRR	95% CI	p
MP_PBW (J/min/Kg)	2.83	0.75 - 10.67	0.123
MP_well inflated tissue (J/min/g)	2.64	1.09 – 6.35	0.030
MP_Compliance$_{RS}$ (J/min/mL/cmH_2O)	1.78	1.17 – 2.71	0.007
MP_lung gas volume (J/min/mL)	1.01	0.99 – 1.01	0.165

Unpublished data

Conclusions

Global impact of ARDS is difficult to estimate.

Mortality continues to be in clinical trial greater than 40%.

Mechanical power could be important to titrate protective mechanical ventilation.

Many thanks