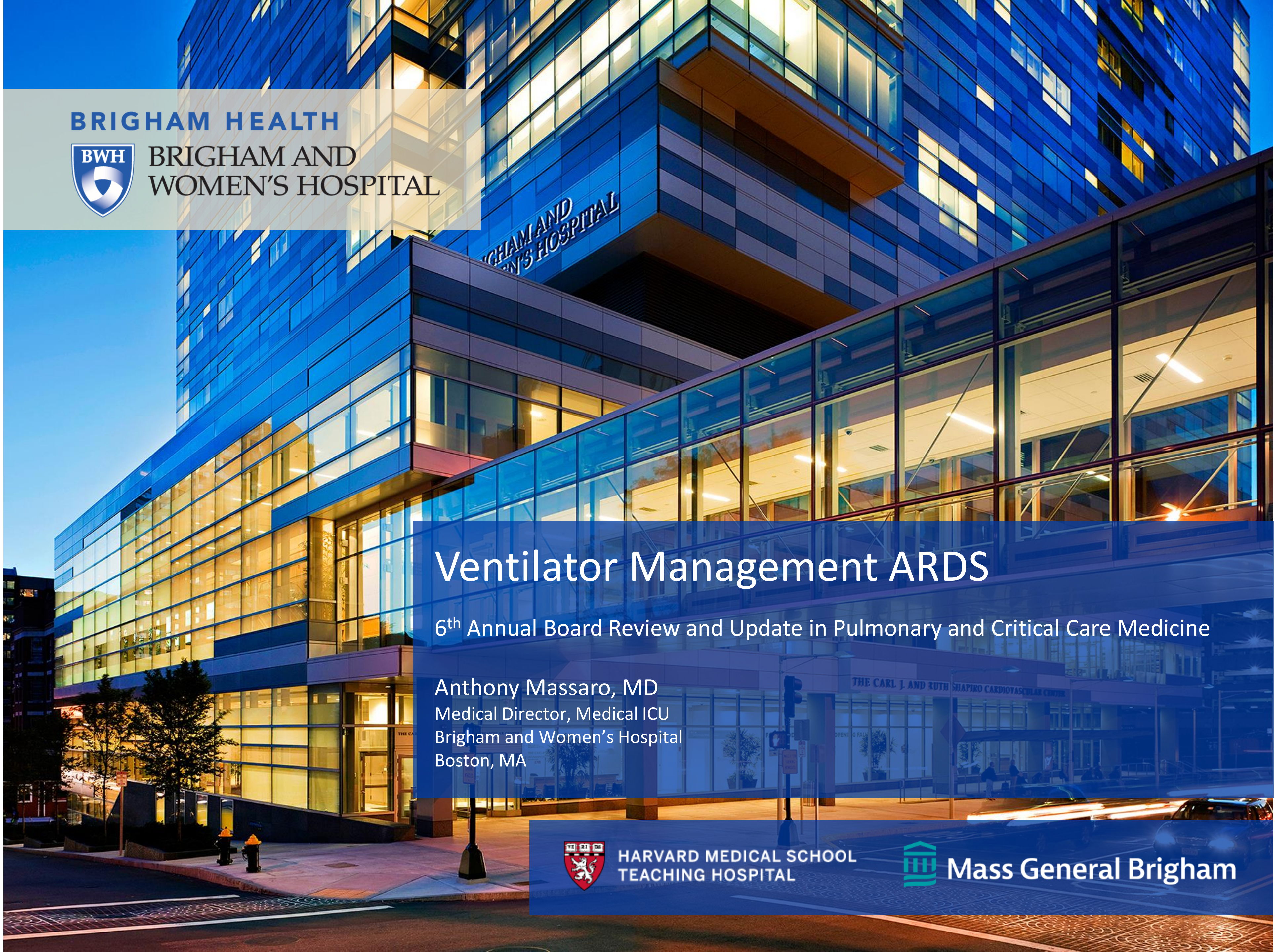

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Ventilator Management ARDS

6th Annual Board Review and Update in Pulmonary and Critical Care Medicine

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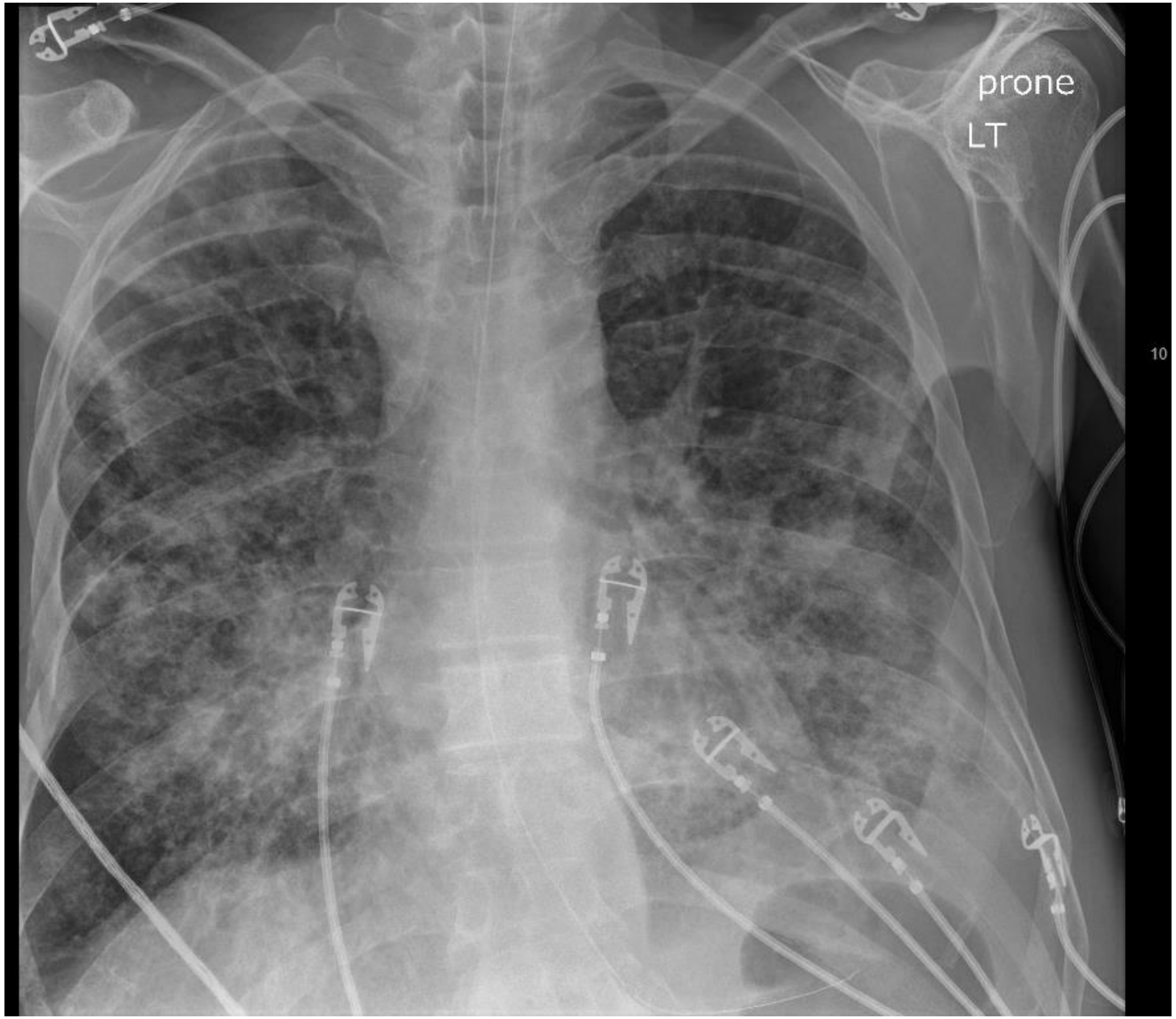
Mass General Brigham

Disclosures

- No disclosures

Aims

- ARDS
  - Definition of the syndrome
  - Incidence
  - Impact
- Covid ARDS
- What is "State of the Art" 2021?
  - Setting PEEP
  - Neuromuscular blockade
  - Prone Ventilation
  - ECMO
- Algorithm



Clinical Manifestations

- Oxygenation
- Ventilation

ARDS Berlin Definition

Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms	
Chest Imaging	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	
Oxygenation		
	Mild	200 mm Hg < PaO2/FiO2 < =300 mm Hg with PEEP or CPAP >=5 cm H2O
	Moderate	100 mm Hg < PaO2/FiO2 < =200 mm Hg with PEEP or CPAP >=5 cm H2O
	Severe	PaO2/FIO2 < =100 mm Hg with PEEP or CPAP >=5 cm H2O

Ranieri et al JAMA 2012; 307 (23) 2526-2533

ARDS

LUNG-SAFE[2]
(n=2377)

ARDS
10.4% of all ICU Admissions
23.4% of All Patients on MV

[1]Ranieri et al JAMA 2012; 307 (23) 2526-2533

[2]Bellani et al JAMA 2016; 315 (8) 788-800

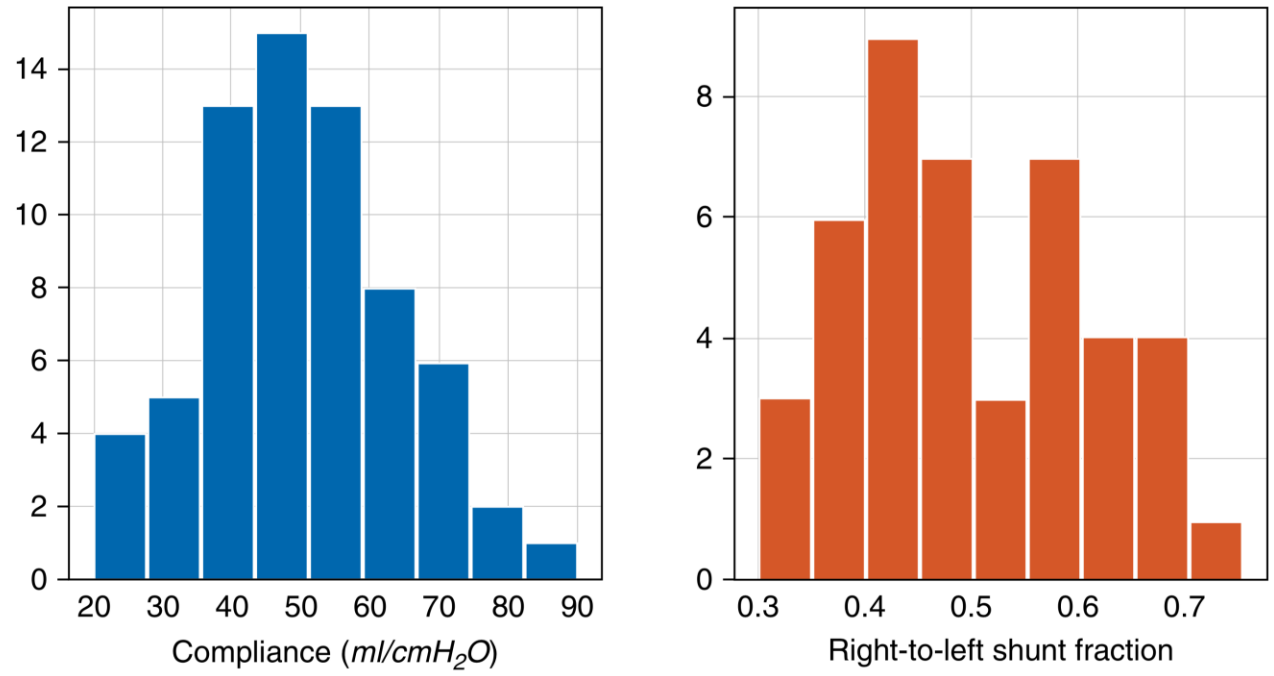
Ventilator Management in Covid-19 ARDS (CARDS) ?

Check for updates

COVID-19 Does Not Lead to a “Typical” Acute Respiratory Distress Syndrome

16 Patients

Compliance 50.2 + 1.6 ml/ cm H20
Shunt fraction 0.50+ 0.11



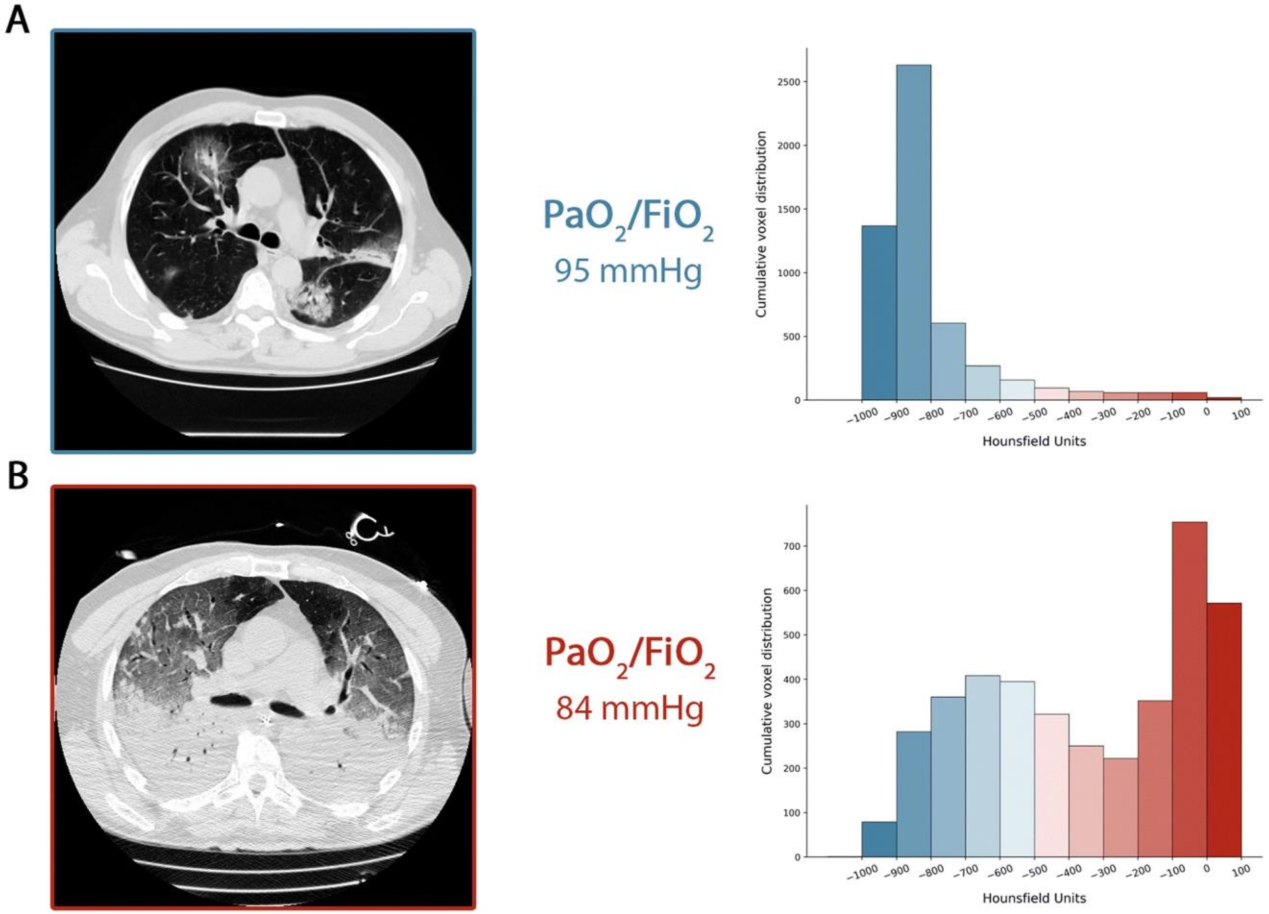
Gattinoni, L. et al.. COVID-19 Does Not Lead to a "Typical" Acute Respiratory Distress Syndrome. *AJRCCM, 201*(10), 1299-1300.

Is Covid-19 ARDS Unique?

Severe Hypoxemia with preserved Respiratory System Compliance ?

Difference between early and late in disease?

	Type L	Type H
Elastance	Low	High
	Low V/Q	High Shunt
Lung weight	Low	High
Lung Recruitability	Low	High



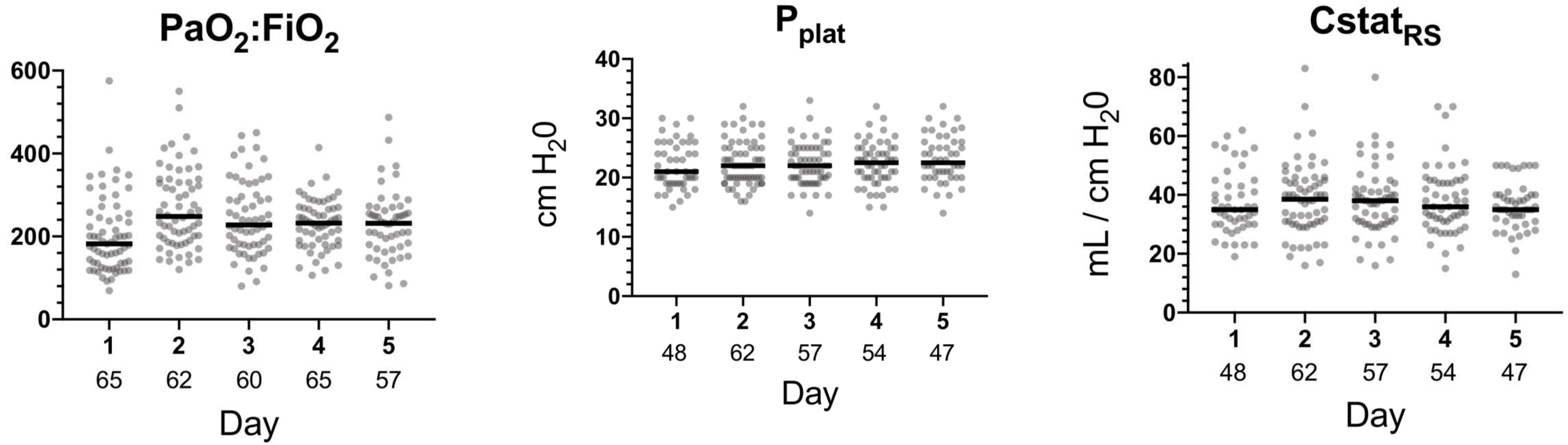
Gattinoni, L. *et al.* COVID-19 pneumonia: different respiratory treatments for different phenotypes?. *Intensive Care Med* (2020). https://doi.org/10.1007/s00134-020-06033-2

Different Respiratory Strategies ?

- Type L patients
  - An early intubation may avert the transition to Type H phenotype
  - If hypercapnic, ventilate with tidal volumes greater than 6 ml/kg (up to 8–9 ml/kg)
  - The PEEP should be reduced to 8–10 cmH_2O
    - recruitability is low and minimize hemodynamic consequences
  - Prone positioning should be used only as a rescue maneuver

Gattinoni, L. *et al.* COVID-19 pneumonia: different respiratory treatments for different phenotypes?. *Intensive Care Med* (2020). https://doi.org/10.1007/s00134-020-06033-2

Respiratory Mechanics In Covid-19



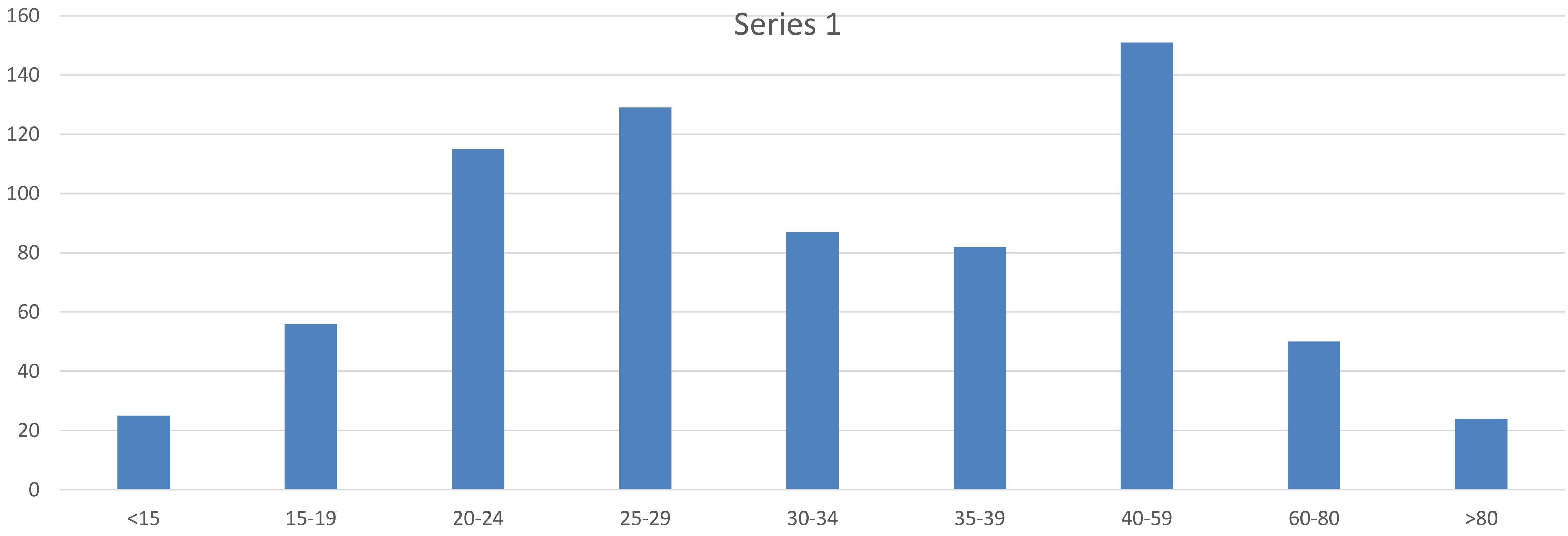
- 66 Patients
- 65% male
- Median Age = 58 yrs

Ziehr et al. AJRCCM https://doi.org/10.1164/rccm.202004-1163LE

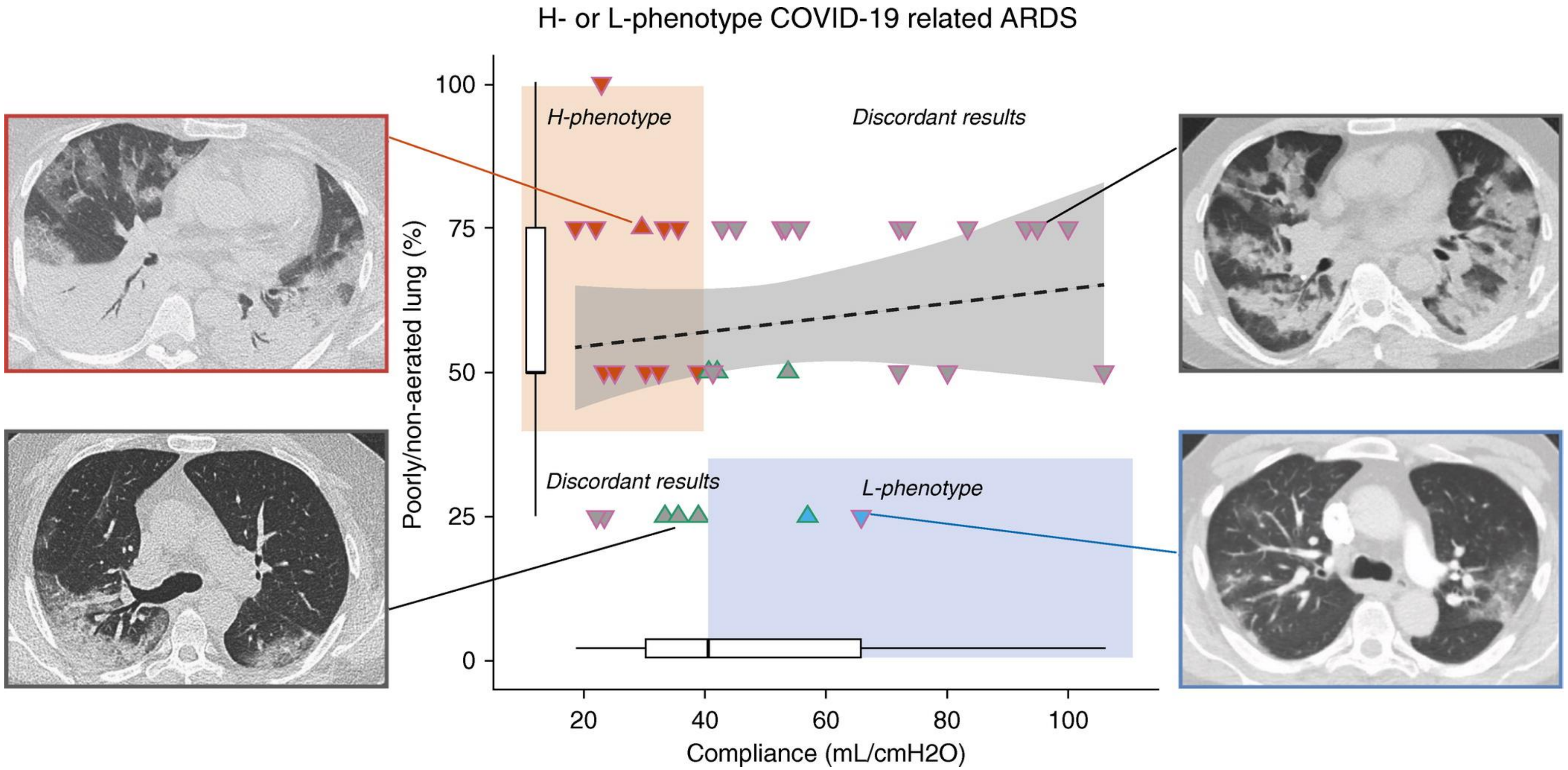
	# Patients	PaO2 / FiO2 ratio	Compliance	
Creteil, France	30	119 (97-163)	44 (35-51)	Haudebourg et al.
New York	222	129 (80-203)	27 (22-36)	Cummings et al.
Seattle	18		29 (25-36)	Bhatraju et al.
Boston	66	182 (135-245)	35 (30-43)	Ziehr et al.
Philadelphia	75	162	37.8	Pandya et al

Haudebourg et al. *Am J Respir Crit Care Med, 202*(2), 287-290. doi:10.1164/rccm.202004-1226LE
Cummings, M..J. et al. *The Lancet, 395*(10239), 1763-1770. doi:10.1016/S0140-6736(20)31189-2
Bhatraju, P. K. Et al. *New England Journal of Medicine, 382*(21), 2012-2022. doi:10.1056/NEJMoa2004500
Ziehr, D. R. et al. *Am J Respir Crit Care Med, 0*(ja), null. doi:10.1164/rccm.202004-1163LE
Pandya, A. et al. *Chest*. doi:10.1016/j.chest.2020.08.2084

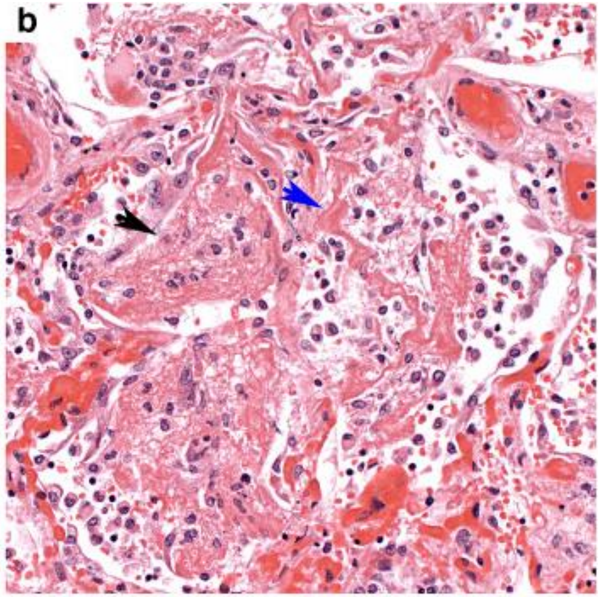
LUNG SAFE Compliance



Bellani, G. etal.(2016). *JAMA, 315*(8), 788-800. doi:10.1001/jama.2016.0291 Supplemental Material



Bos, L. et al. *Annals of the American Thoracic Society, 17*(9), 1161-1163. doi:10.1513/AnnalsATS.202004-376RL



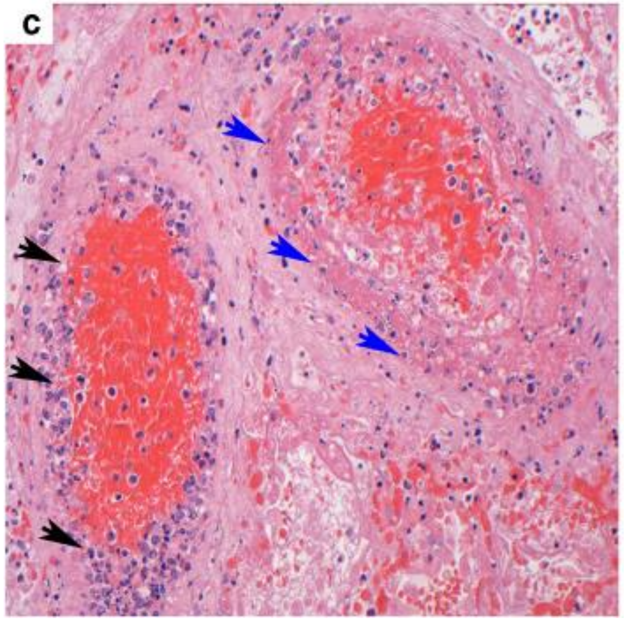
Covid-19 ARDS Pulmonary Pathology

Virus Detected
- Type I Pneumocytes
- Type II Pneumocytes
- Bronchial Epithelial Cells

Severe Endothelial Injury
Thrombus formation
Macroangiopathic Vasculopathy

Diffuse Alveolar Damage
- Acute Phase
- Organizing Phase

Acute fibrinous and Organizing Pneumonia
Acute neutrophilic Infiltrate



A, Klingel K, Fend F. Virchows Arch. 2020 Sep;477(3):349-357. doi: 10.1007/s00428-020-02881-x.

- At current time
  - No convincing data the Covid ARDS physiology is unique or separates into unique phenotypes
    - Non Covid ARDS is heterogeneous
    - Covid ARDS is heterogeneous
- Additional studies needed
  - Prospective, large cohort assessment
  - Well documented timepoints of symptom onset

Considerations in ARDS Treatment

- Low Tidal Volume Ventilation
- PEEP Optimization
- Recruitment Maneuvers
- Neuromuscular Blockade
- Prone Ventilation
- ECMO
- Inhaled Pulmonary Vasodilators
- Corticosteroids
- Volume Management

Minimize
Ventilator Induced Lung Injury
(VILI)

Adjust PEEP

Assess P/F Ratio

V_T = 6ml/kg IBW
Plateau Pressure < 30cm H_20

Low Vt Ventilation
PEEP = 5

Methods to Optimize PEEP

- PEEP / FiO2 table
- Maximize plateau pressure
- Assess Lung Recruitment
    - Radiographic
        - Sequential CT scan
        - Use of a Table based on CT scan
    - Helium Dilution or Nitrogen Washout
    - Maximize compliance
        - P/V curve – set PEEP above lower inflection point
        - Step PEEP titration
        - Driving Pressure (End inspiratory plateau – PEEP)
- Esophageal balloon
- Electrical Impedance Tomography
- Ultrasound

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Titrating Positive End-Expiratory Pressure (PEEP) With an Esophageal Pressure–Guided Strategy vs an Empirical High PEEP-FIO_2 Strategy on Death and Days Free From Mechanical Ventilation Among Patients With Acute Respiratory Distress Syndrome

A Randomized Clinical Trial

Jeremy R. Beitler, MD, MPH; Todd Sarge, MD; Valerie M. Banner-Goodspeed, MPH; Michelle N. Gong, MD, MSc; Deborah Cook, MD; Victor Novack, MD, PhD; Stephen H. Loring, MD; Daniel Talmor, MD, MPH; for the EPVent-2 Study Group

- P_{ES} guided vs PEEP-FiO2 table
- 14 sites (North America)
- Moderate-Severe ARDS (PaO2:FiO2 <200mm Hg)
- P_{ES}: 102 patients
- PEEP-FiO2: 100 patients

Beitler et al. JAMA 2019 Vol 321(9)

Ventilator Protocols EP Vent2

PEEP – FiO2

FiO2	0.3	0.3	0.3	0.4	0.4	0.4	0.4	0.4	0.5	0.5	0.6	0.7	0.8	0.8	0.9	1.0	1.0
PEEP	5	8	10	10	12	14	16	18	18	20	20	20	20	22	22	22	24

P_L – FiO2

FiO2	0.3	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_L	0	0	0	2	2	3	3	4	4	5	5	6	8			

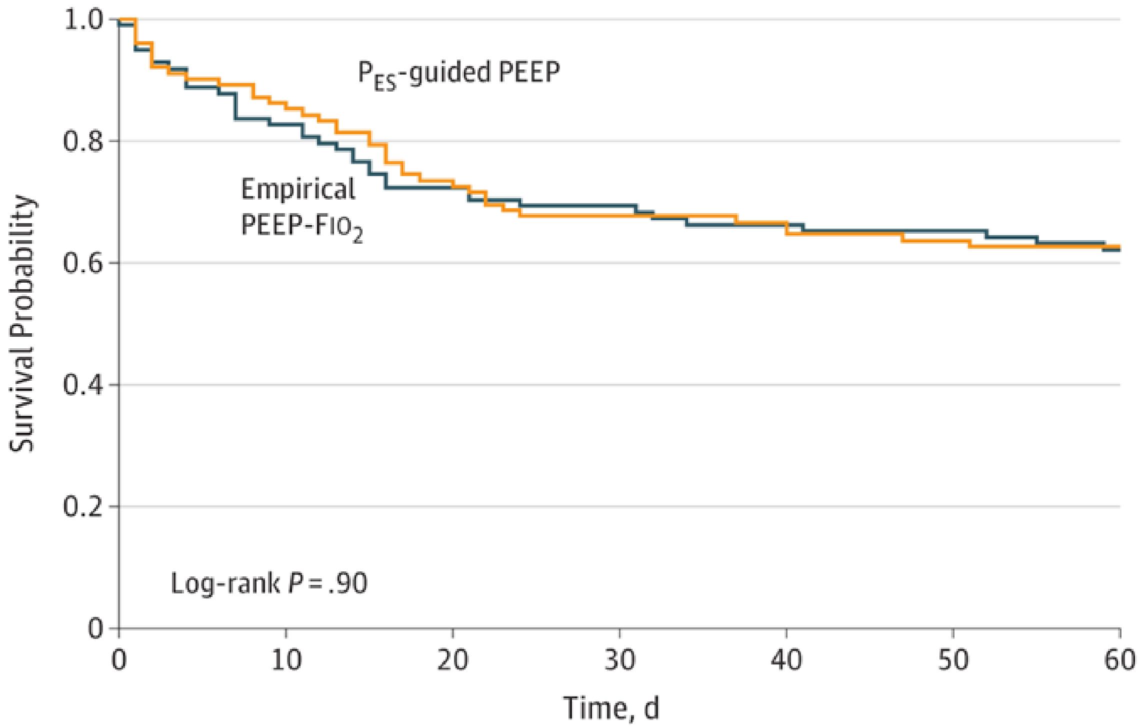
Beitler et al. JAMA 2019 Vol 321(9)

EP Vent 2 Outcomes

End Point	PES Guided	PEEP – FiO2	Absolute Diff,% (95% CI)	pValue
	(N=102)	(N=98)		
Primary				
Ranked Composite incorporating death and days free from mechanical ventilation	49.6 (41.7 to 57.5)	50.4 (42.5 to 58.3)		0.92
Secondary				
Mortality – Day 28 (%)	33 (32.4)	30 (30.6)	1.7 (-11.1 to 14.6)	0.88
Days free from MV - survivors (IQR)	22 (15 to 24)	21	0 (-1 to 2)	0.85
Mortality – Day 60 (%)	38/101 (37.6)	37/98 (37.8)	-0.1 (-13.6 to 13.3)	>0.99
ICU LOS median -thru day28 (IQR)	10 (6 to 17)	9.5 (5 to 14)	1 (-1 to 3)	0.24
Hospital LOS LOS-thru day 28 (IQR)	16 (9 to 26)	15 (8 to 24)	0 (-1 to 3)	0.58

Beitler et al. JAMA 2019 Vol 321(9)

EP Vent 2 Outcomes



No. at risk

P_{ES}-guided PEEP	102	88	75	68	67	64	63
Empirical PEEP-FIO_2	98	81	71	68	65	64	61

Beitler et al. JAMA 2019 Vol 321(9)

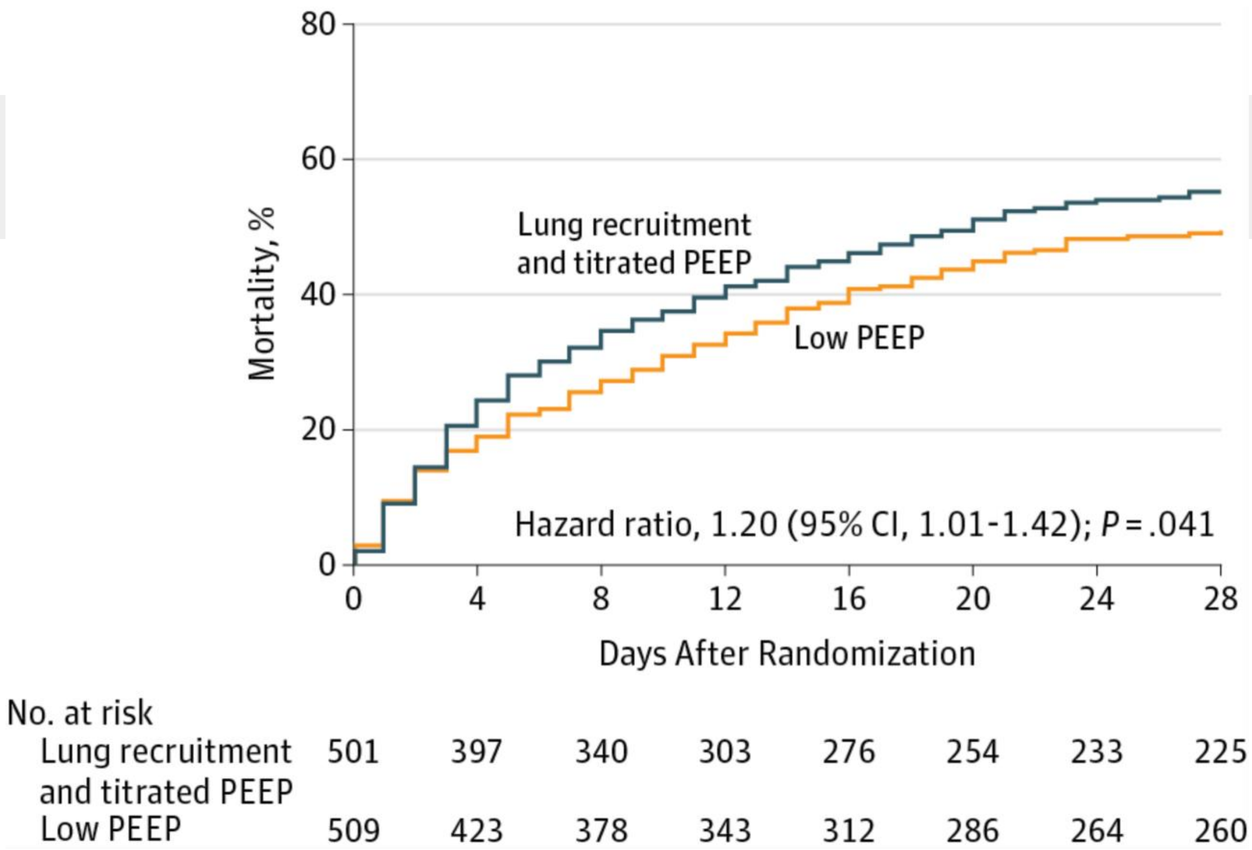
Higher vs Lower Positive End-Expiratory Pressure in Patients With Acute Lung Injury and Acute Respiratory Distress Syndrome

Systematic Review and Meta-analysis

	Clinical Outcomes								
	All Patients			ARDS (PaO_2:FiO_2<200)			Non ARDS		
	Low PEEP	High PEEP	P Value	Low PEEP	High PEEP	P Value	Low PEEP	High PEEP	P Value
# Patients	1163	1136		941	951		220	184	
Death in hospital %	35.2	32.9	0.25	39.1	34.1	0.049	19.4	27.2	0.070
Death in ICU %	32.8	28.5	0.01	36.6	30.3	.001	16.8	19.6	0.71
Days unassisted breathing	11	13	0.10	7	12	0.004	19	17	0.07
Rescue Therapy	18.6	12.2	<.001	21.3	13.7	<.001	16	8	0.25

Briel M, Meade M, Mercat A, et al. Higher vs Lower Positive End-Expiratory Pressure in Patients With Acute Lung Injury and Acute Respiratory Distress SyndromeSystematic Review and Meta-analysis. *JAMA*.2010;303(9):865–873. doi:10.1001/jama.2010.218

ART Trial – 28 Day Mortality



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

JAMA. 2017;318(14):1335-1345. doi:10.1001/jama.2017.14171

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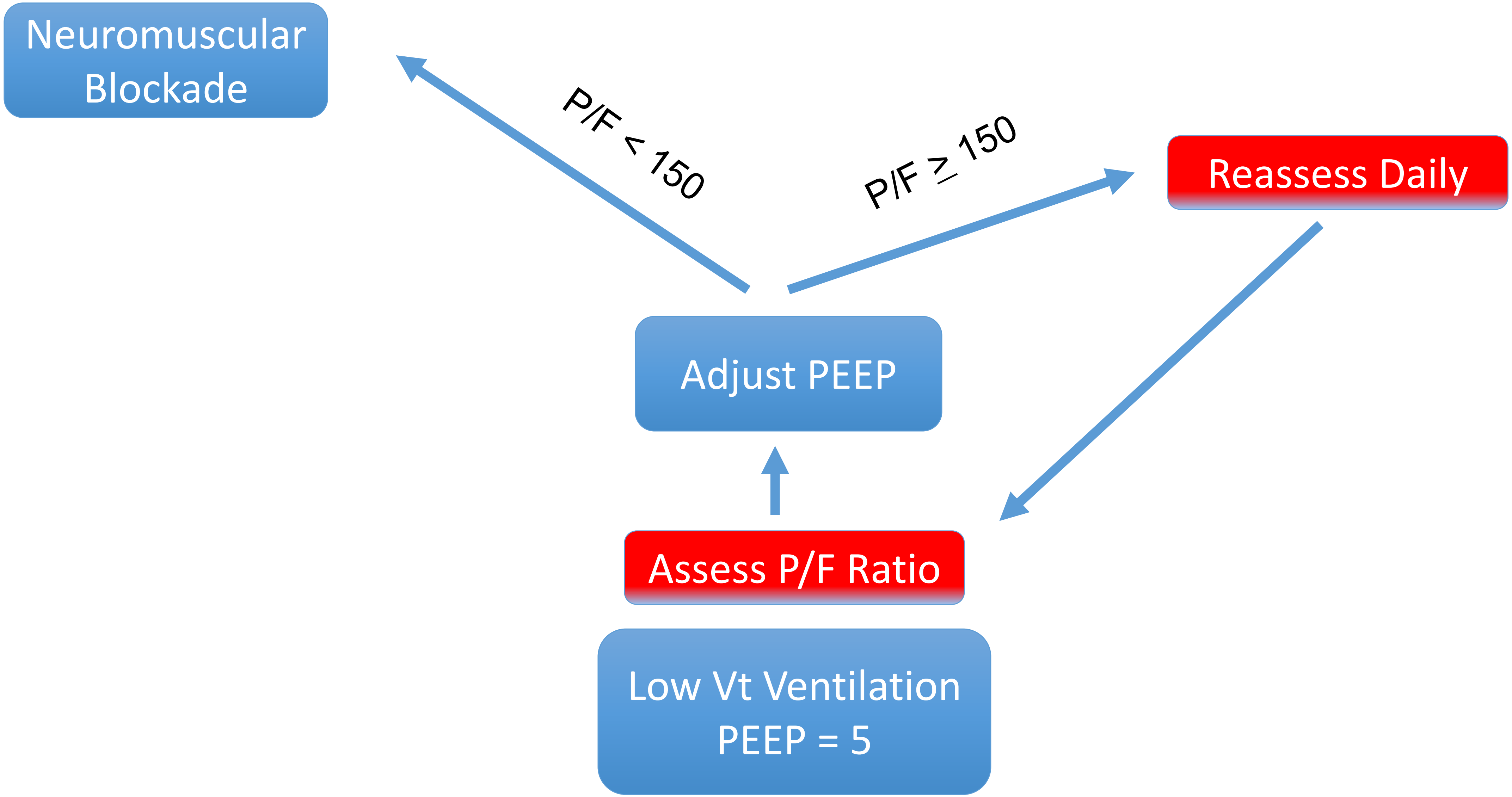
PEEP 2021 ?

- Literature does not support a particular method to determine optimal PEEP
- P/F >200 – Low or High PEEP Table probably OK
- P/F < 200 – High PEEP Table
- P/F < 200 - Consider Personalizing PEEP
  - You probably don't need to keep all alveoli open
  - Strike a balance: Avoid overdistention
  - Assess recruitability / Point of optimal compliance?
  - Data currently lacking.
- Future studies needed
  - Newer Technologies


Neuromuscular Blockade
P/F < 150
P/F ≥ 150
Reassess Daily
Adjust PEEP
Assess P/F Ratio
Low Vt Ventilation
PEEP = 5

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*

- Multicenter (20 ICU France)
- Double blind
- 340 patients
- Intervention: 48 hours of cisatricurium
  - Early (within 48 hours)
  - PaO2 : FiO2 <150
  - PEEP >5
  - Vt = 6-8ml /kg

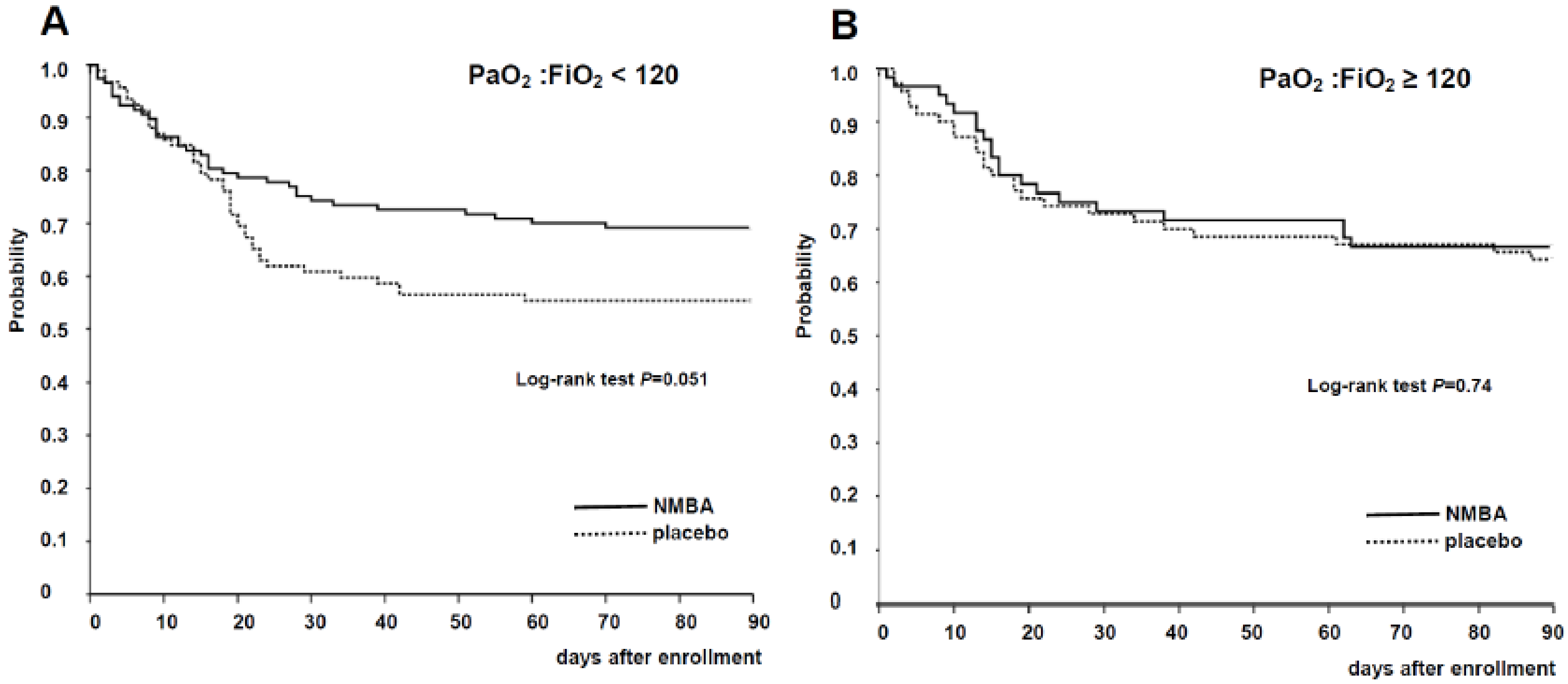
ACURASYS Primary Outcome

- Reduction of the hazard ratio of death at 90 days 0.68 (0.48-0.98; p=0.04)
  - Adjusted for PaO_2 / FiO_2
  - SAPS
  - Plateau Pressure
  - 90 Day crude mortality 31.6 vs 40.7 (p=0.08)

	NMB	Control		
	(n=177)	(n=162)	RR	P value
Death (@ 90 days)	31.6	40.7		0.08

Papazian et al. N Engl J Med. 2010 Sep 16;363(12):1107-16.

ACURASYS –Mortality and P/F ratio



Papazian et al. N Engl J Med. 2010 Sep 16;363(12):1107-16.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 | MAY 23, 2019 | VOL. 380 NO. 21

Early Neuromuscular Blockade in the Acute Respiratory Distress Syndrome

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

- ROSE Trial – Reevaluation of Systemic Early Neuromuscular Blockade
- Neuromuscular blockade (NMB) with Cisatracurium and deep sedation to usual care with lighter sedation.
- Moderate to Severe ARDS PaO_2: FiO_2 <150mmHg
- 1006 patients
- 48 US Hospitals

The National Heart, Lung, and Blood Institute PETAL Clinical Trials Network. N Engl J Med 2019;380:1997-2008

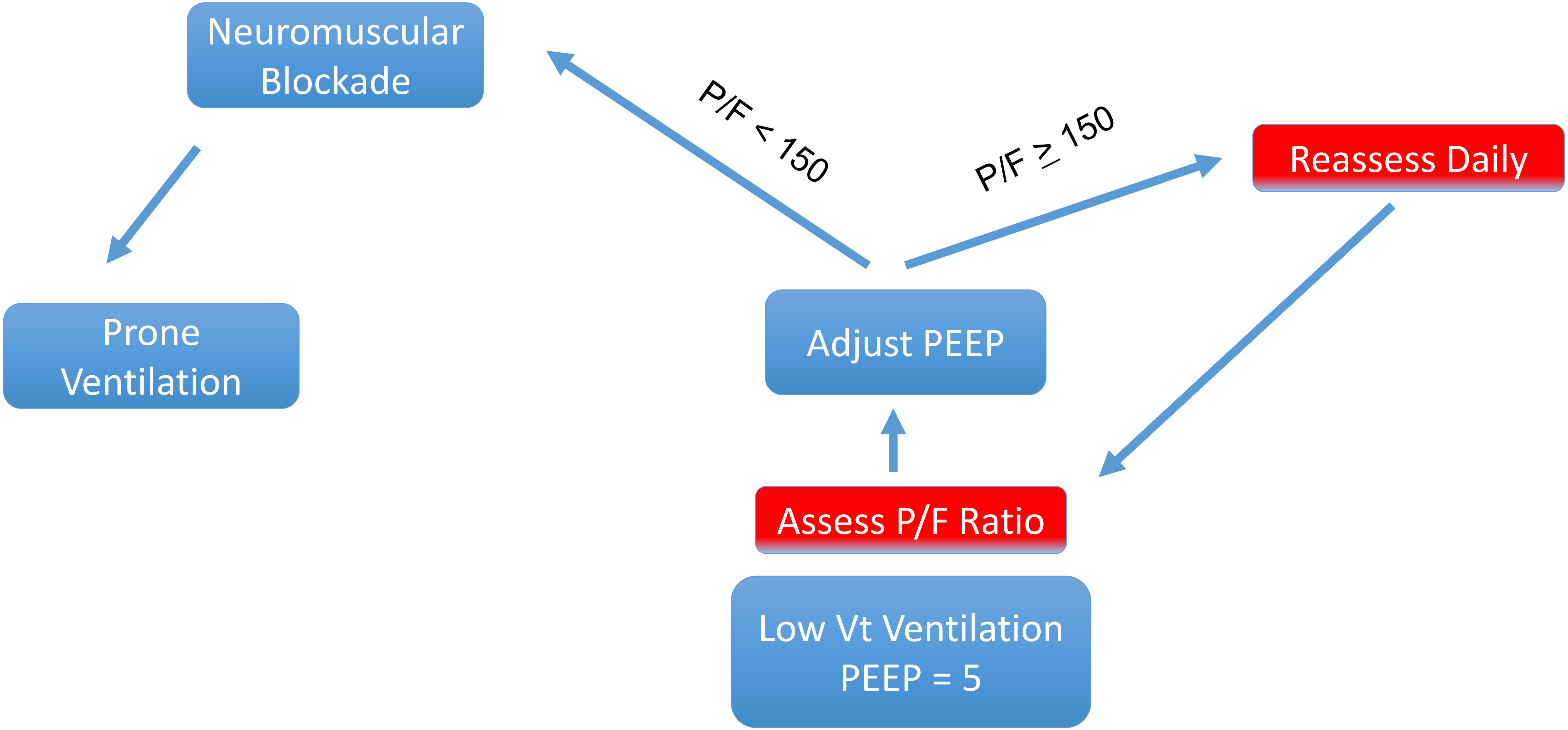
ROSE Trial Outcomes

End Point	NMB	Control	Between Group Difference (95% CI)	pValue
	(N=501)	(N=505)		
Primary				
In Hospital Death - Day 90 (%)	213 (42.5)	216 (42.8)	-0.3 (-6.4 to 5.9)	0.93
Secondary				
In Hospital Death – Day 28 (%)	184 (36.7)	187 (37.0)	-0.3 (-6.3 to 5.7)	
Days free from MV – Day 28	9.6 ± 10.4	9.9 ± 10.9	-0.3 (-1.7 to 1.0)	
Days Not in ICU – Day 28	9.0 ± 9.4	9.4 ± 9.8	-0.4 (-1.6 to 0.8)	
Days Not in Hospital – Day 28	5.7 ± 7.8	5.9 ± 8.1	-0.2 (-1.1 to 0.8)	

The National Heart, Lung, and Blood Institute PETAL Clinical Trials Network. N Engl J Med 2019;380:1997-2008

Neuromuscular Blockade 2021 ?

- Not to be used for all patients with Moderate – Severe ARDS
- May have role in patients in selected patients
  - Ongoing ventilator dyssynchrony despite optimization of ventilator settings and sedation


Neuromuscular Blockade
P/F < 150
P/F ≥ 150
Reassess Daily
Prone Ventilation
Adjust PEEP
Assess P/F Ratio
Low Vt Ventilation
PEEP = 5

Prone Ventilation

- Initial report 1976
  - Piehl and Brown Crit Care Med 1976;4;12-14
  - Increase PaO2 = 47 torr
- Multiple reports of improved oxygenation
- Mechanism of improved oxygenation
  - Recruitment of dorsal regions of lung
  - Improved ventilation – perfusion matching
  - Reduction of alveolar shunt
- Utilized as rescue therapy

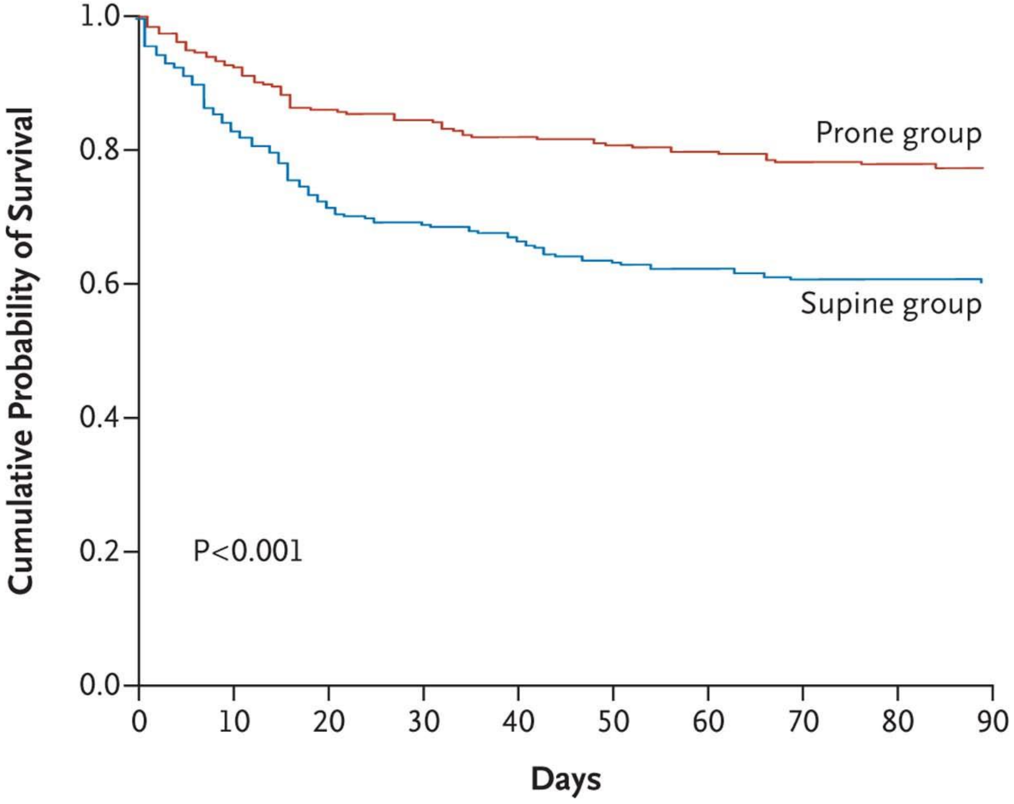
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 6, 2013 VOL. 368 NO. 23

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*

- Multicenter, Randomized
- Prone vs control (low VT and PEEP:FiO2 table)
- 466 patients
- Early application (within 36 hrs of initiation of MV); PaO2 / FiO2 <150
- Prone dose = 16 hours
- Outcome: Proportion of deaths from any cause within 28 days after enrollment



No. at Risk

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

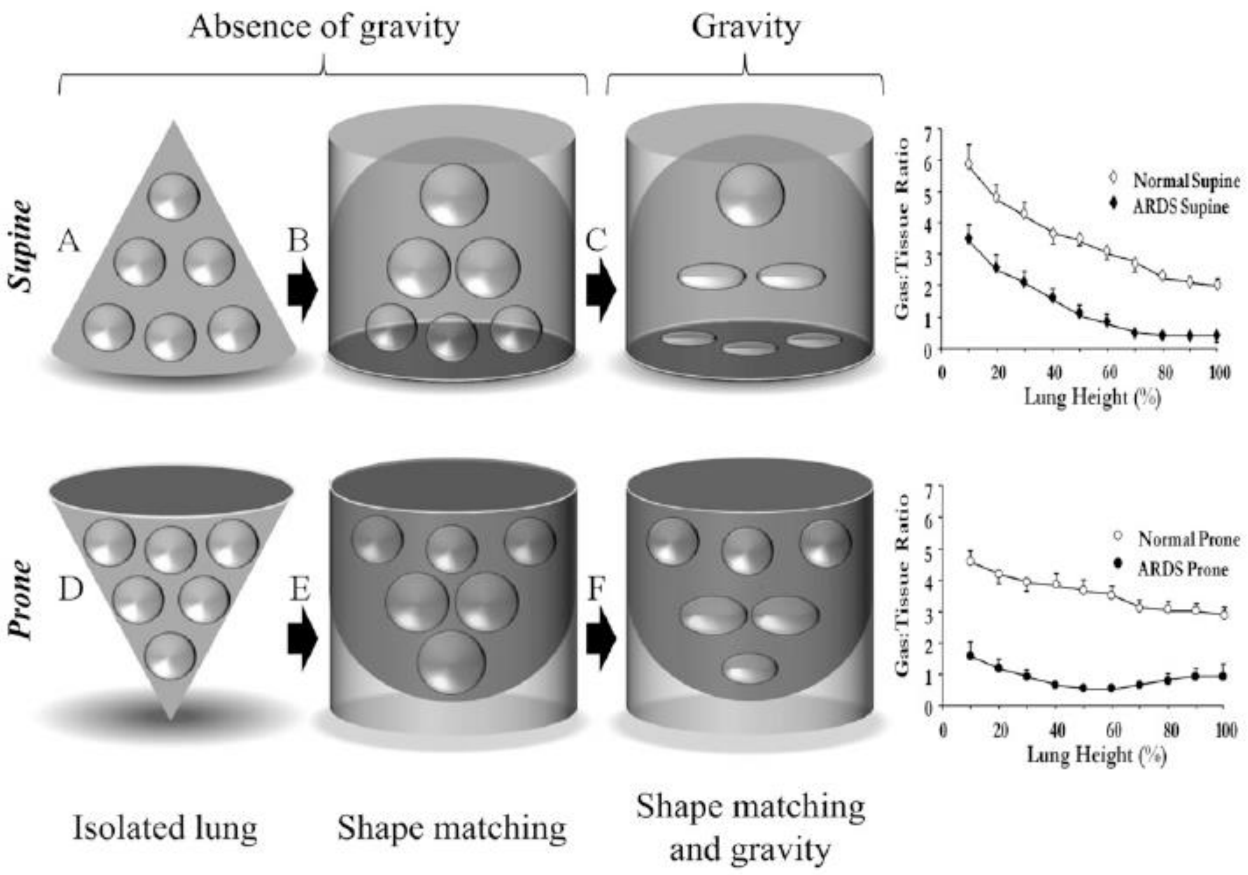
Guérin C et al. N Engl J Med 2013;368:2159-2168

Guerin et al. N Engl J Med 368;23

The NEW ENGLAND JOURNAL of MEDICINE

Prone Ventilation Studies

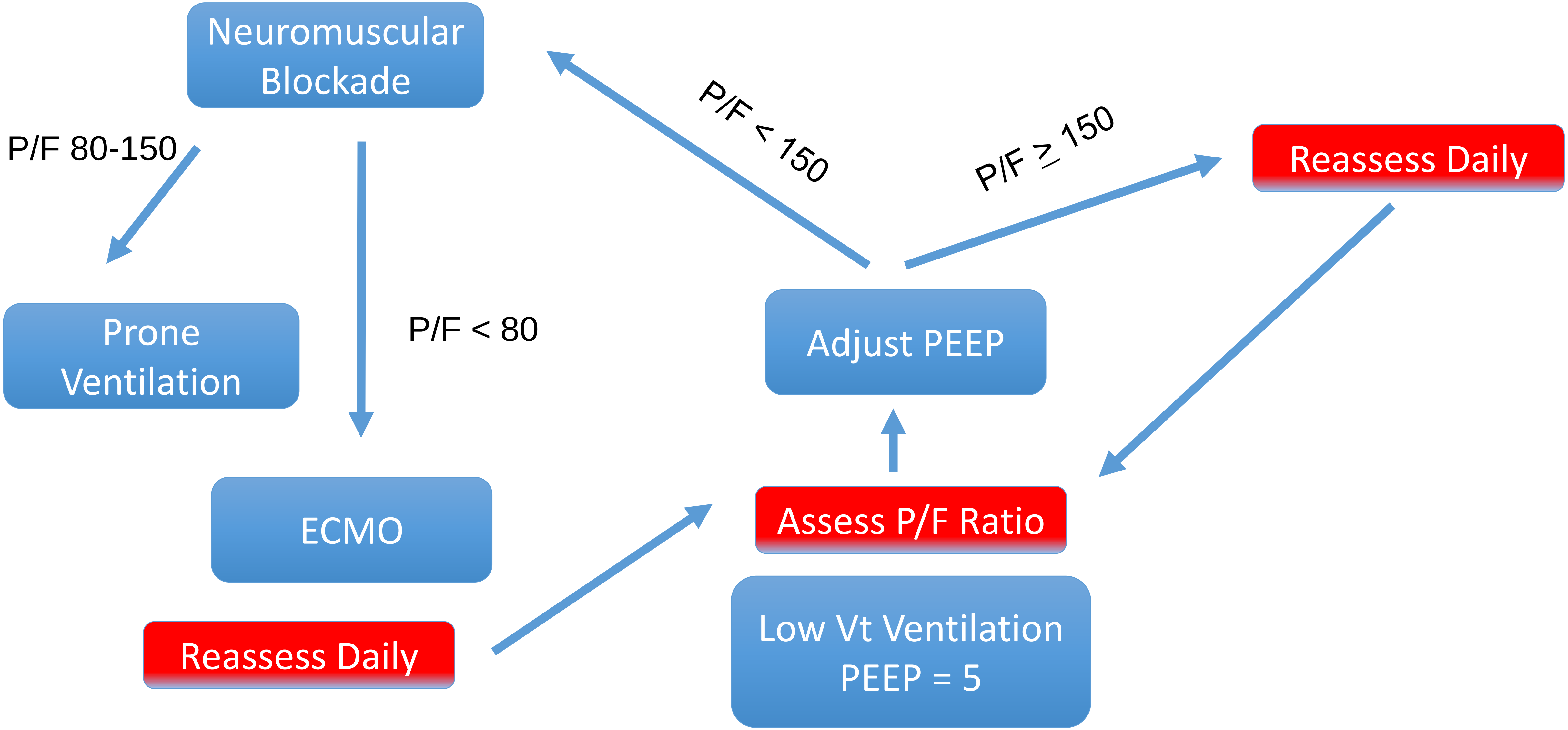
	2001	2004	2006	2009	2014
	Prone-Supine			Prone-Supine II	PROSEVA
	Gattinoni	Guerin	Mancebo	Taccone	Guerin
Patients	304	791	142	342	474
Proning Dose	>=6	>=8	20	>=20	>=16
PaO2:FiO2	<=300	<=300	<=200	100-200; <100	<150
Time Enrolled	Not early	Not early	<48 hrs	<72 hrs	<36 hrs
Mortality	ICU	28 day	ICU	28 day	28 day
Prone	50.7%	32.4%	43%	31%	16%
Control	48%	31.5%	58%	32.8%	32.8%
RR	1.05	1.02	0.74	0.97	0.48
		p=0.77	p=0.12	p=0.72	p<0.0001



Gattinoni et al. Prone Positioning in ARDS Am J Respir Crit Care Med 188 (11) 1286-1293

Prone Ventilation

- Indicated if PaO2:FiO2 ratio <150
  - Contraindications
    - Elevated intracranial pressure
    - Spinal instability
- Be prepared: Multidisciplinary team
- Perform early
- Proning duration of 16 hours



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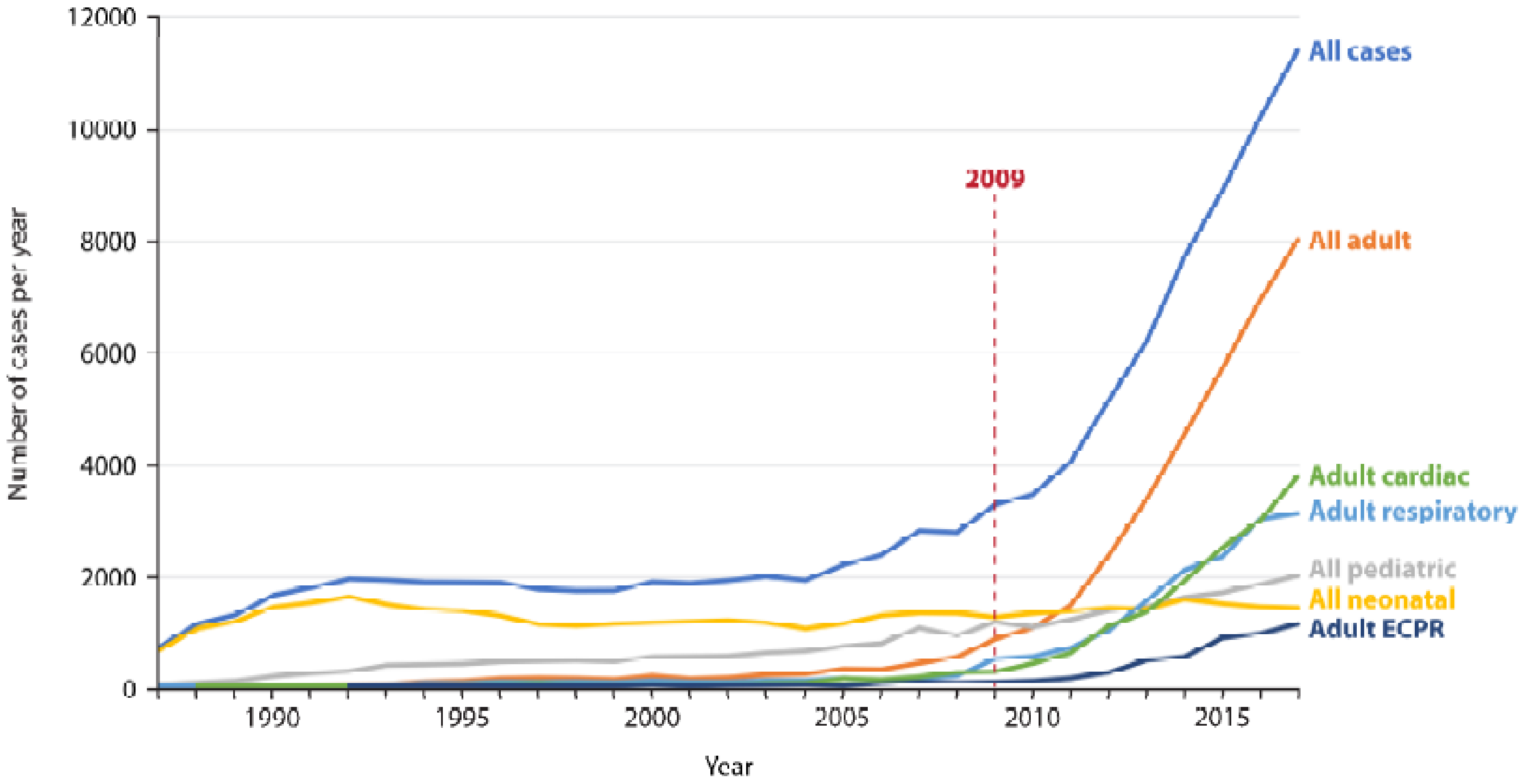
Is ECMO standard of care for ARDS?

ELSO Case Volume Trends 1987-2017



Brodie et al. JAMA 2019 Vol 322(6) eSupplement

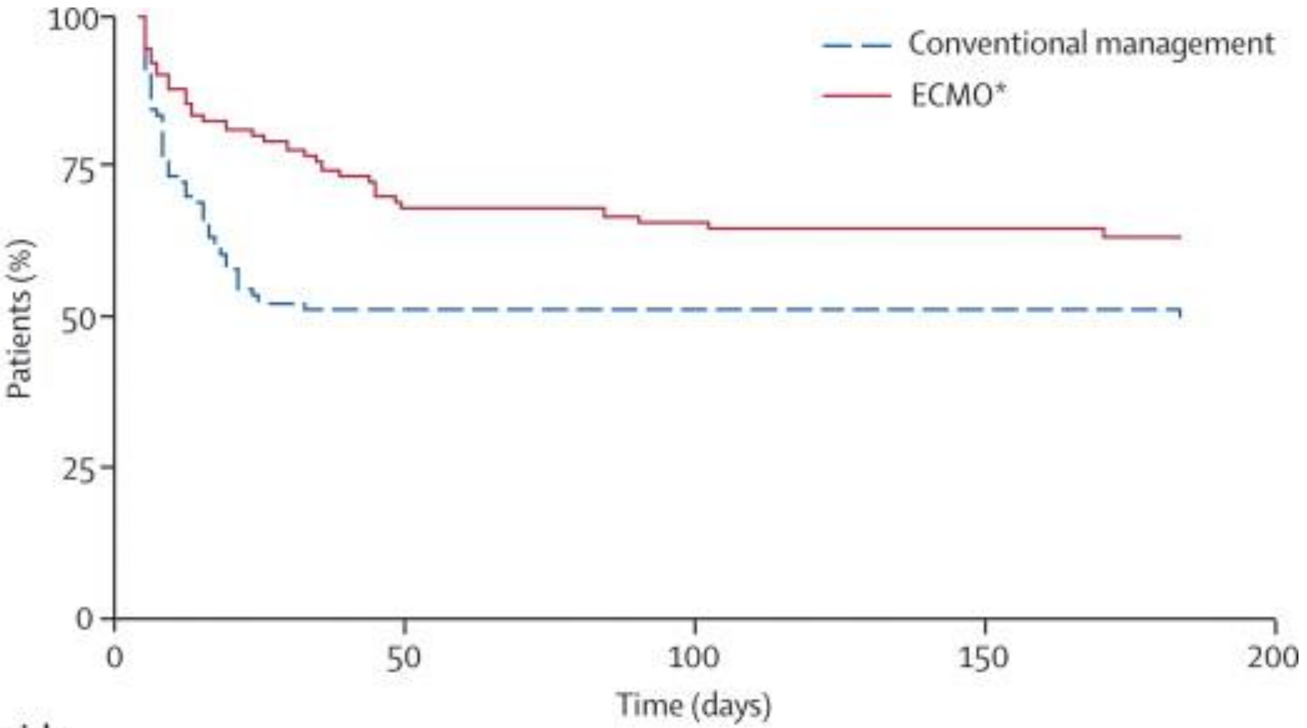
Extra-Corporeal Membrane Oxygenation (ECMO)

- 1979 – ECMO & MV vs. MV
  - 90 Patients, 9 centers, Randomized Prospective
  - Mortality ECMO = 90.5% vs MV= 91.7%
  - Zapol et al. JAMA 242: 2193-2196, 1979
- 1994 – PIRV & ECMO vs MV
  - 40 patients, 1 center, Randomized Porspective
  - 30 Day Mortality ECMO=42% vs 33% (p=0.8)
  - Morris et al. Am J Resp Crit Care Med 1994; 149:295-305

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

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

- Multicenter
- 180 Patients
- Conventional Management vs ECMO
- Primary Outcome – Death or Severe Disability at 6 months
- Peek et al. Lancet Volume 374, Issue 9698, 2009, 1351–1363



Patients at risk

	0	50	100	150	200
Conventional management	90	45	44	44	0
ECMO*	90	61	59	58	0

Kaplan-Meier survival estimates. Randomized to ECMO, but did not necessarily receive this treatment.

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

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

Volume 374, Issue 9698, 2009, 1351–1363

CESAR Criticisms

- Lack of specified protocol in control arm
- 30% of patients did not receive protective lung ventilation
- All ECMO at one center
- 75% of the intervention group received ECMO
- Early cessation of trial

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Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome

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

- Conventional support vs ECMO
  - Crossover allowed
- Very severe ARDS
- 240 Patients
- Primary Outcome: Mortality at 60 days

Combes et al. NEJM 2018 Vol 378(21)

EOLIA Trial

- Entry Criteria
  - Mechanical Ventilation < 7 days
  - "Very Severe ARDS"
    - PaO_2 / FiO_2 ratio <50mg Hg x 3 hours
    - PaO_2 / FiO_2 ratio <80mg Hg x 6 hours
    - pH <7.25 with $PaCO_2$ >=60 mmHg x 6hrs
- Cross Over for refractory hypoxemia
  - 35 patients in control arm (mean 6.5 days)
  - 57% mortality
- Endpoints
  - Mortality
  - Key Endpoint – Death and crossover to ECMO

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EOLIA Outcomes

End Point	ECMO Group	Control Group	Relative Risk	pValue
	(N=124)	(N=125)		
Primary				
Mortality at 60 days %	44 (35)	57 (46)	0.76 (0.55 to 1.04)	0.09
Key Secondary EndPoint				
Treatment Failure at 60 days	44 (35)	72 (58)	0.62 (0.47 to 0.82)	<0.001

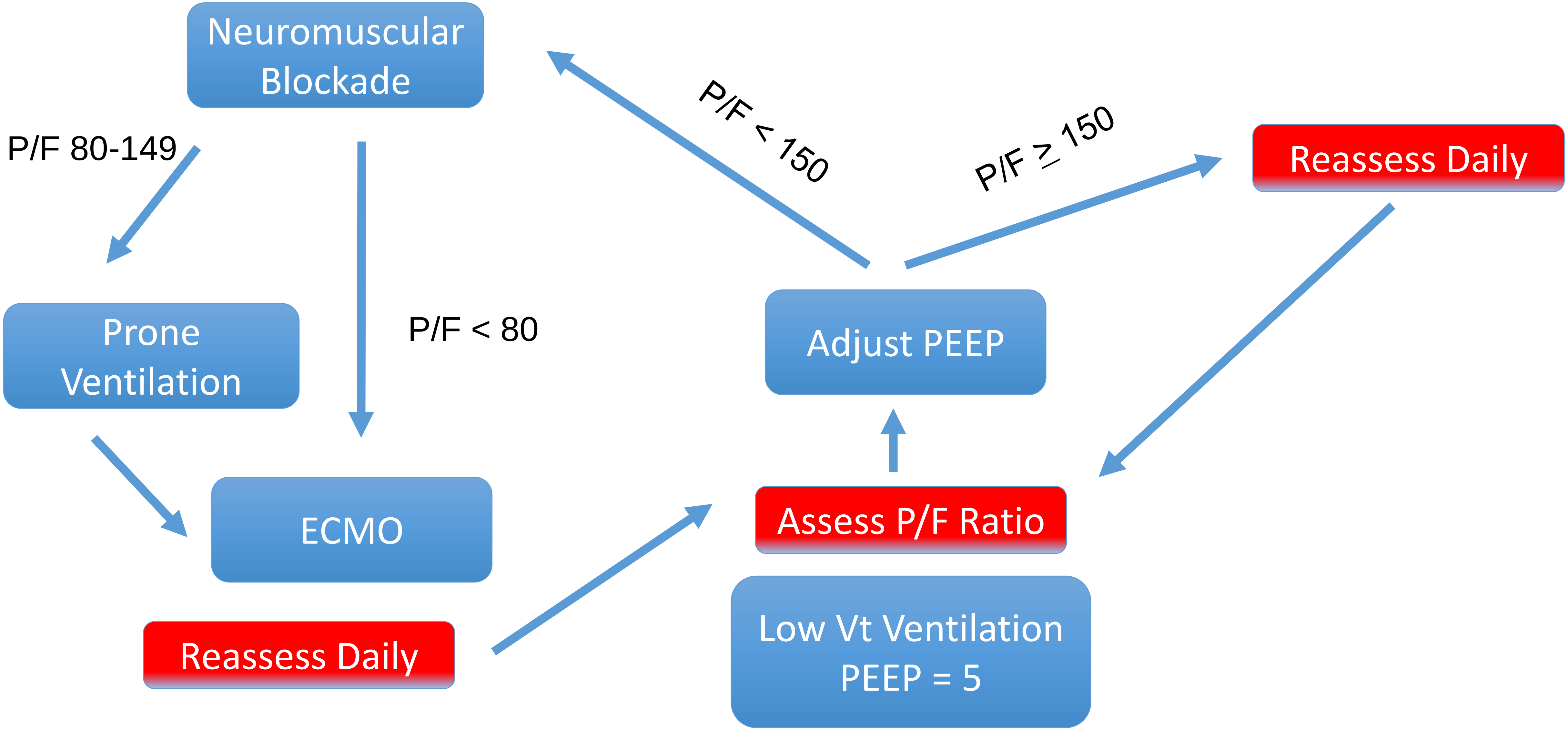
Combes et al. NEJM 2018 Vol 378(21)

EOLIA Outcomes

- Among patients with very severe ARDS, 60 day mortality was not significantly lower with ECMO than with a strategy of conventional mechanical ventilation that included ECMO as rescue therapy.

ECMO

- Consider for patients with very severe hypoxemic respiratory failure
- Patients failing NMB and prone ventilation


Neuromuscular Blockade
P/F 80-149
P/F < 150
P/F ≥ 150
Reassess Daily
Prone Ventilation
P/F < 80
Adjust PEEP
ECMO
Assess P/F Ratio
Reassess Daily
Low Vt Ventilation
PEEP = 5

Notes for Practice

- P/F ratio key for prognosis / rx.
- Optimize PEEP
  - For Moderate-Severe ARDS High PEEP:FiO2 table
- If PaO2/FiO2 < =150 consider neuromuscular blockade
  - If ongoing dyssynchrony
- If PaO2/FiO2 < =150 initiate prone ventilation
  - Early
  - Proning dose 16 hrs
- If very severe ARDS or failing above consider ECMO

Use of Supportive Modalities

	Patients (%)				
	All (n=2377)	Mild (n=498)	Moderate (n=1150)	Severe (n=729)	P value
Neuromuscular Blockade	21.7	6.8	18.1	37.8	<0.001
ECMO	3.2	0.2	2.4	6.6	<0.001
Prone Positioning	7.9	1.0	5.5	16.3	<0.001
		P value represents comparisons across ARDS severities			

Trends in Acute Respiratory Distress in 50 Counties
Bellani et al. JAMA 2016;315(8):788-800

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

Systematic Review and Meta-analysis

- Meta analysis of individual patient data
- 2200 patient (ALVEOLI, LOVS, EXPRESS)

	Respiratory Variables – First Week								
	Day 1			Day 3			Day 7		
	Low PEEP	High PEEP	P Value	Low PEEP	High PEEP	P Value	Low PEEP	High PEEP	P Value
PEEP (cm H_20)	9.0	15.3	<.001	8.2	13.3	<.001	7.8	10.8	<.001
Plateau (cm H_20)	23	29	<.001	23	27	<.001	24	27	<.001
P_aO2 (mmHg)	83	96	<.001	82	87	<.001	83	84	0.41

Briel M, Meade M, Mercat A, et al. Higher vs Lower Positive End-Expiratory Pressure in Patients With Acute Lung Injury and Acute Respiratory Distress SyndromeSystematic Review and Meta-analysis. *JAMA*.2010;303(9):865–873. doi:10.1001/jama.2010.218

Oxygenation Target Unclear

- Improved oxygenation does not always lead to improved survival
  - ARDSNet ARMA
- Morbidity
  - Low oxygenation associated with risk for long term neurologic sequela
    - Adult Respiratory Distress Cognitive Outcome Study (ACOS)
    - Surfactant, Positive Pressure and Oxygenation Randomized Trial (SUPPORT)

Prone Ventilation – Mechanisms of Benefit

- Reduced ventilator induced lung injury (VILI)
  - Minimize atelectatrauma
  - Minimize overdistention
- Improved oxygenation
- Decreased chest wall compliance
- Reverse of Right Heart Failure
- Decreased ventilator associated pneumonia

Prone Ventilation Risks

- Desaturation (transient)
- Hypotension (transient)
- Device removal
- Pressure ulcers
- Nerve compression
- Need for increased sedation