What is Lung Protective Ventilation?

NBART 2016

Disclosure

- Full time employee of Draeger

Outline

- 1. Why talk about Lung Protective Ventilation?
- 2. What is Lung Protective Ventilation?
- 3. How to apply Lung Protective Ventilation?

Outline

- **1. Why talk about Lung Protective Ventilation?**
- 2. What is Lung Protective Ventilation?
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Is the Ventilator Contributing to the Pathogenesis of ARDS?

Is acute respiratory distress syndrome an iatrogenic disease?

Jesús Villar[1,2,3] and Arthur S Slutsky*[3,4,5]   *Critical Care* 2010, 14:120

- "..injurious ventilation strategies have been shown to cause all of the pathology associated with ALI/ARDS."
- "..should we begin to consider that ALI/ARDS is a consequence of our efforts rather than progression of the underlying disease?"
- "..ALI/ARDS is largely a 'man-made' syndrome."
- "..ALI/ARDS is no longer a syndrome that must be treated, but is a syndrome that should be prevented."

No Reduction in ARDS Mortality since 1998

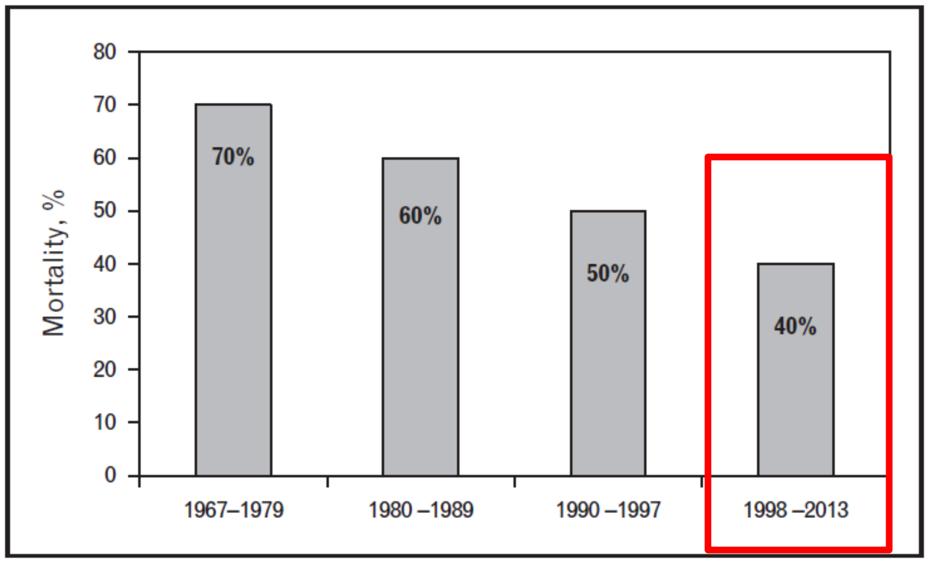


FIGURE 1. Schematic representation of average reported mortality in observational and randomized controlled trials in adult patients with acute respiratory distress syndrome since 1967. Data have been compiled from [6■■,11,12■,26,27■].

Villar et al. Curr Opin Crit Care 2014;20:3-9

How Does the Ventilator Cause Injury?
Ventilator Induced Lung Injury (VILI)

Mechanisms:

- **Volutrauma & Barotrauma (Stress/Strain)**
  - **Stress = High ΔTranspulmonary Pressure, not necessarily high PIP!**
  - **Strain = High tidal volume (Volume above the FRC) & may occur even with low VT of 4-6 ml/kg IBW in heterogenous lung disease (ARDS Baby Lung)**
- **Atelectrauma**
  - **Repetitive opening and closing of Alveoli (recruitment/derecruitment injury)**
  - **Disruption of surfactant monolayer → Shear stress injury**
  - **Altered A/C membrane → permeability to proteins and other solutes → pulmonary edema and intrapulmonary floating**
- **Biotrauma (Systemic Organ Failure)**
  - **Resultant effect of initial insult and above injuries**

Outline

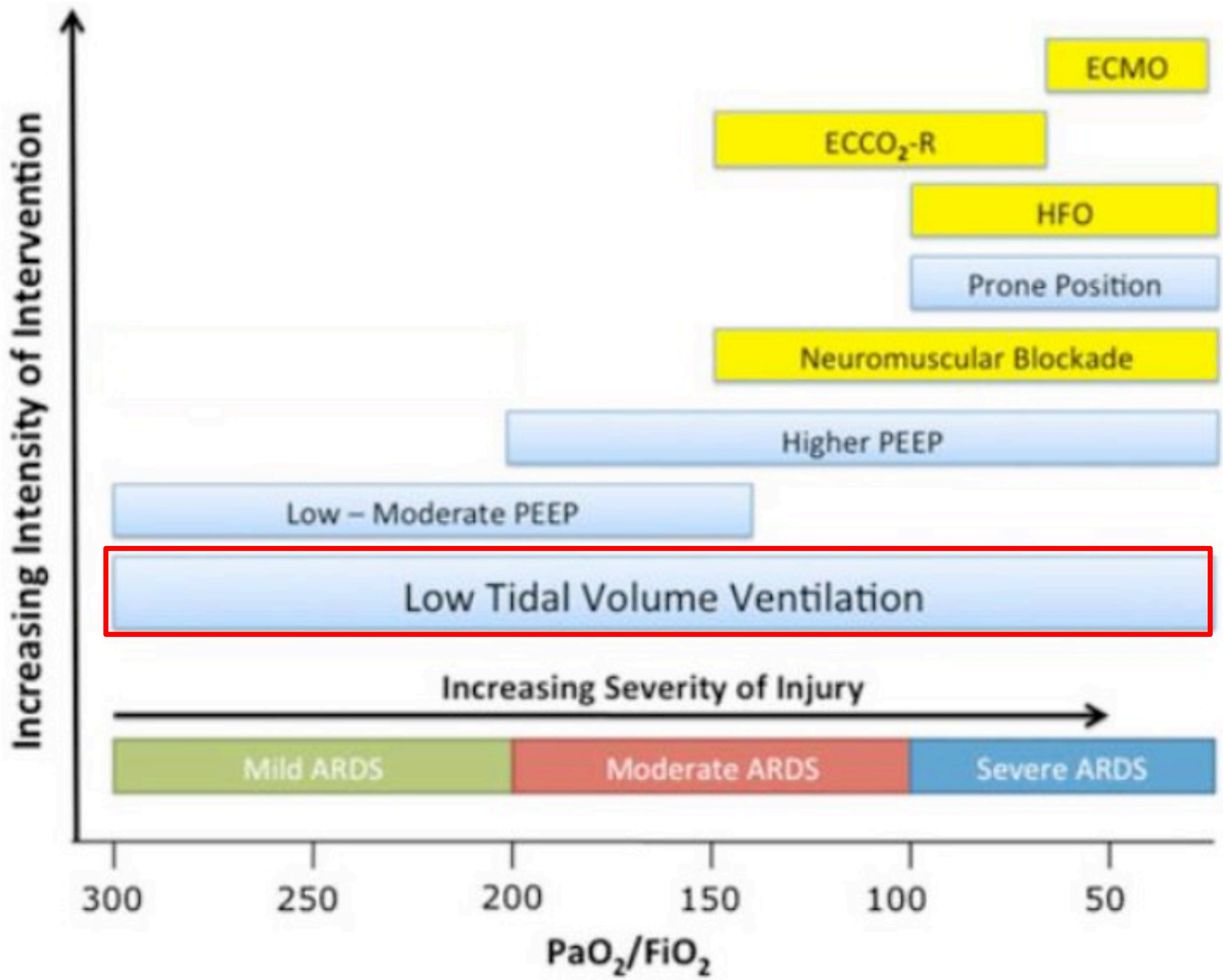
- 1. Why talk about Lung Protective Ventilation?
- **2. What is Lung Protective Ventilation?**
- 3. How to apply Lung Protective Ventilation?

What is lung protective ventilation?

- Any ventilation strategy that aims to minimize or prevent VILI
- ARDSnet Low VT, Pplateau < 30 & PEEP/FiO2 table
- Open Lung Ventilation (Recruitment, HFO, APRV, Optimal PEEP)
- Prone Ventilation
- Adjunctive Therapies: Pulmonary vasodilators, ECLS, gene therapy, pharmacological, etc…..

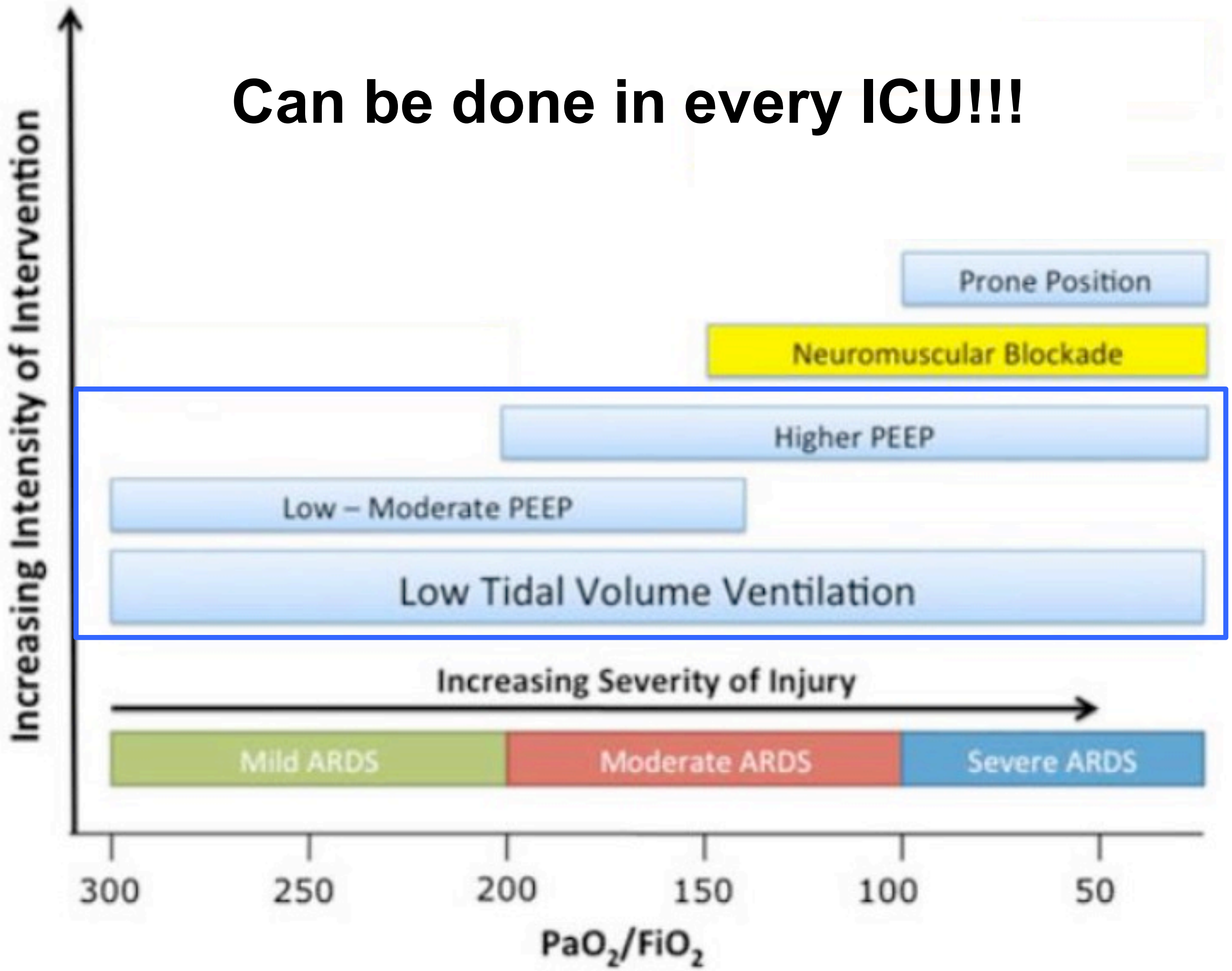
  - Mechanical ventilation strategies that minimizes Lung Strain and Stress, as well as prevention of recruitment-derecruitment injury

What is LPV?



Intensive Care Med. (2012) 38:1573-1582

What is LPV?



Intensive Care Med. (2012) 38:1573-1582

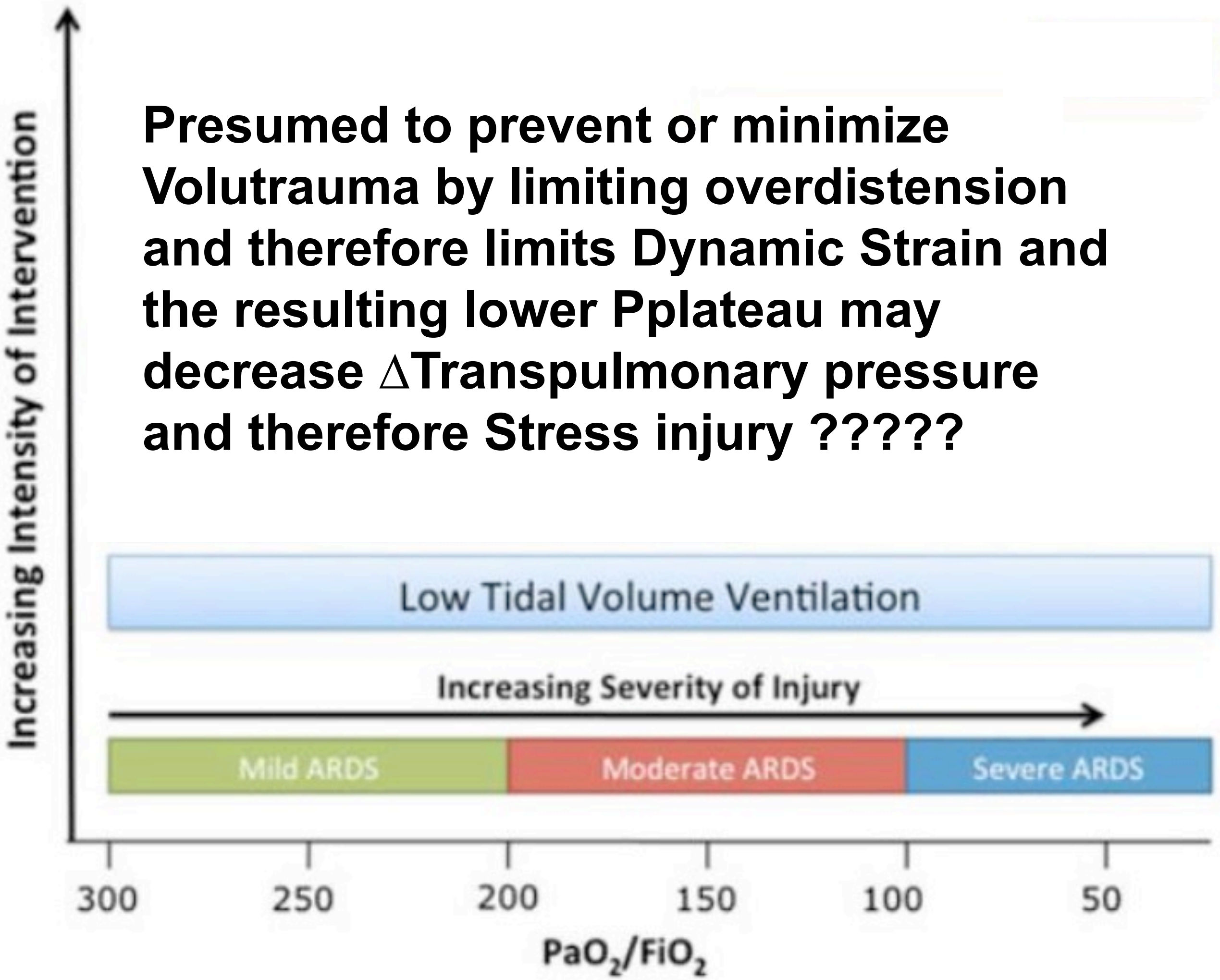
How Does the Ventilator Cause Injury?
Ventilator Induced Lung Injury (VILI)

Mechanisms:

- **Volutrauma & Barotrauma (Stress/Strain)**
- **Atelectrauma (shear injury)**
- **Biotrauma (Systemic Organ Failure)**

What is LPV?
Low Tidal Volume (LTV)

Presumed to prevent or minimize Volutrauma by limiting overdistension and therefore limits Dynamic Strain and the resulting lower Pplateau may decrease ∆Transpulmonary pressure and therefore Stress injury ?????



Intensive Care Med. (2012) 38:1573-1582

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*

TABLE 1. SUMMARY OF VENTILATOR PROCEDURES.*

VARIABLE	GROUP RECEIVING TRADITIONAL TIDAL VOLUMES	GROUP RECEIVING LOWER TIDAL VOLUMES
Ventilator mode	Volume assist–control	Volume assist–control
Initial tidal volume (ml/kg of predicted body weight)†	12	6
Plateau pressure (cm of water)	≤50	≤30
Ventilator rate setting needed to achieve a pH goal of 7.3 to 7.45 (breaths/min)	6–35	6–35
Ratio of the duration of inspiration to the duration of expiration	1:1–1:3	1:1–1:3
Oxygenation goal	PaO_2, 55–80 mm Hg, or SpO_2, 88–95%	PaO_2, 55–80 mm Hg, or SpO_2, 88–95%
Allowable combinations of FiO_2 and PEEP (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 1.0 and 24	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 1.0 and 24
Weaning	By pressure support; required by protocol when FiO_2≤0.4	By pressure support; required by protocol when FiO_2≤0.4

TABLE 4. MAIN OUTCOME VARIABLES.*

VARIABLE	GROUP RECEIVING LOWER TIDAL VOLUMES	GROUP RECEIVING TRADITIONAL TIDAL VOLUMES	P VALUE
Death before discharge home and breathing without assistance (%)	31.0	39.8	0.007
Breathing without assistance by day 28 (%)	65.7	55.0	<0.001
No. of ventilator-free days, days 1 to 28	12±11	10±11	0.007
Barotrauma, days 1 to 28 (%)	10	11	0.43
No. of days without failure of nonpulmonary organs or systems, days 1 to 28	15±11	12±11	0.006

LTV in ALI and ARDS

Meta-Analysis of Acute Lung Injury and Acute Respiratory Distress Syndrome Trials Testing Low Tidal Volumes

Peter Q. Eichacker, Eric P. Gerstenberger, Steven M. Banks, Xizhong Cui, and Charles Natanson

TABLE 1. NUMBER OF PATIENTS, TIDAL VOLUMES STUDIED, AND MORTALITY RATES IN FIVE RANDOMIZED CLINICAL TRIALS

	Number of Patients		Tidal Volume		Mortality Rate		
Author (Ref.)	Low Tidal Volume	Control	Low Tidal Volume* (*ml/kg*)	Control* (*ml/kg*)	Low Tidal Volume (%)	Control (%)	Reported Mortality Difference (*p Value*)
Amato and coworkers (3)	29	24	6.1 ± 0.2†‡	11.9 ± 0.5†‡	38	71	< 0.001
Stewart and coworkers (5)	60	60	7.2 ± 0.8§	10.6 ± 0.2§	50	47	0.72
Brochard and coworkers (6)	58	58	7.2 ± 0.2‖	10.4 ± 0.2‖	47	38	0.38
Brower and coworkers (7)	26	26	7.3 ± 0.1¶	10.2 ± 0.1¶	50	46	0.60
ARDSNet (4)	432	429	6.3 ± 0.1¶	11.7 ± 0.1¶	31	40	0.007

Am J Respir Crit Care Med. 2002, Vol. 166, P. 1510-1514

LTV for everyone?

Ventilation with lower tidal volumes for critically ill patients without the acute respiratory distress syndrome: a systematic translational review and meta-analysis

Ary Serpa Neto[a,b,c], Liselotte Nagtzaam[c], and Marcus J. Schultz[c,d]

Curr Opin Crit Care 2014, 20; 25-32

Author	Year	Tidal volume (ml/kg)		Effect of low tidal volume			
		Low tidal volume	High tidal volume	Duration mechanical ventilation	Mortality	Inflammatory markers	Development of ARDS
Lee *et al.* [39]	1990	6.0	12.0	↓	↔	NR	↓
Gajic *et al.* [40]	2004	9.0	12.0	NR	↔	NR	↓
Wolthuis *et al.* [41]	2007	8.0	10.0	↔	↔	NR	NR
Yilmaz *et al.* [42]	2007	8.0	11.0	↓	↓	NR	↓
Determann *et al.* [8]	2010	6.0	10.0	↔	↔	↓	↓
Pinheiro de Oliveira *et al.* [43]	2010	5.0	12.0	↔	↔	↓	NR

LTV for everyone?

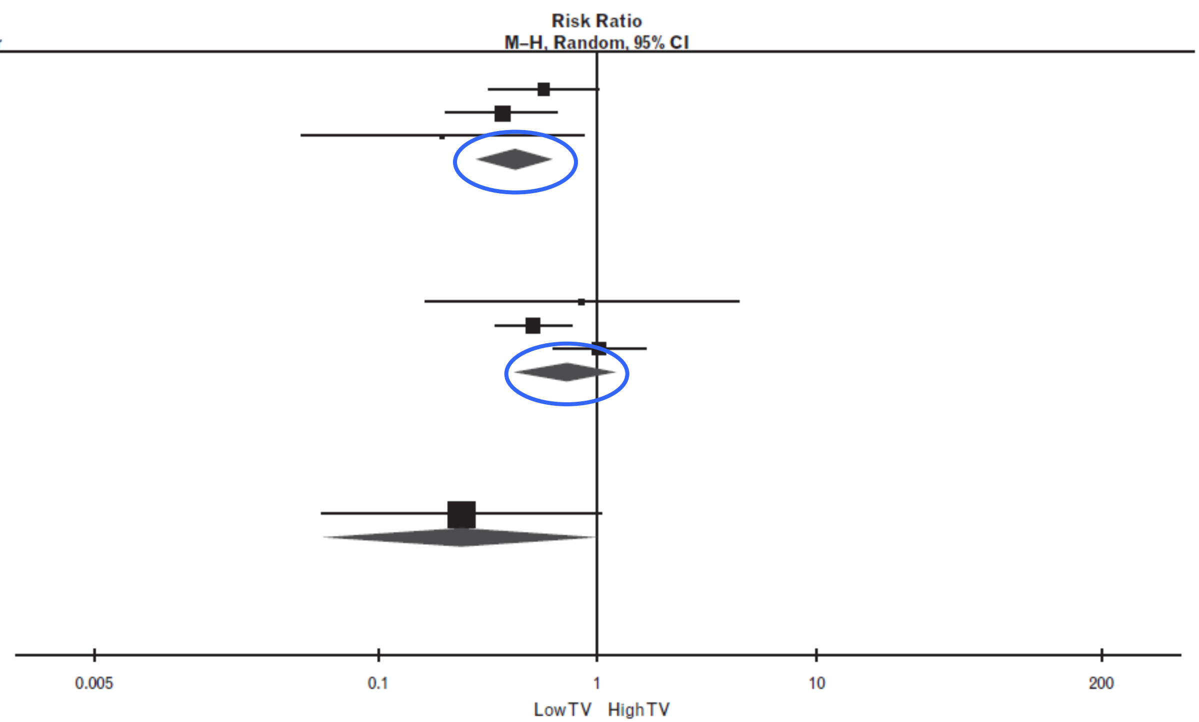
CURRENT OPINION

Ventilation with lower tidal volumes for critically ill patients without the acute respiratory distress syndrome: a systematic translational review and meta-analysis

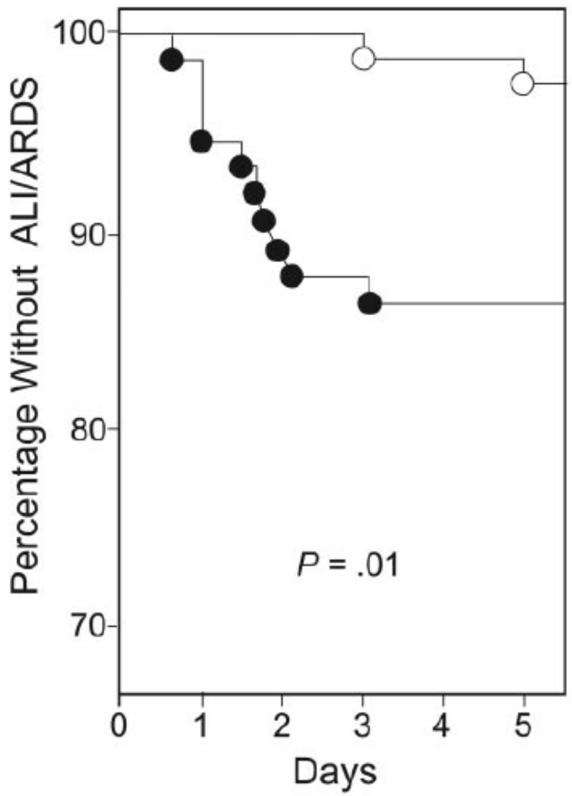
Ary Serpa Neto[a,b,c], Liselotte Nagtzaam[c], and Marcus J. Schultz[c,d]

Curr Opin Crit Care 2014, 20; 25-32

Study or Subgroup	Low TV Events	Low TV Total	High TV Events	High TV Total	Weight	Risk Ratio M–H,Random,95%CI	Year
1.2.1 Lung Injury							
Gajic 2004 [40]	12	66	32	100	40.4%	0.57 [0.32. 1.02]	2004
Yilmaz 2007 [42]	17	163	60	212	52.0%	0.37 [0.22. 0.61]	2007
Determann 2010 [8]	2	76	10	74	7.6%	0.19 [0.04. 0.86]	2010
Subtotal (95%CI)		**305**		**386**	**100.0%**	**0.42 [0.28, 0.63]**	
Total events	31		102				
Heterogeneity: Tau^2 = 0.02; chi^2 = 2.35, df = 2 (P = 0.31); I^2 = 15%							
Test for overall effect: Z = 4.10 (P < 0.0001)							
1.2.2 Mortality							
Wolthuis 2007 [41]	3	23	2	13	9.7%	0.85 [0.16. 4.44]	2007
Yilmaz 2007 [42]	27	163	69	212	47.4%	0.51 [0.34. 0.76]	2007
Determann 2010 [8]	24	76	23	74	42.9%	1.02 [0.63. 1.63]	2010
Subtotal (95%CI)		**262**		**299**	**100.0%**	**0.72 [0.41, 1.26]**	
Total events							
Heterogeneity: Tau^2 = 0.13; chi^2 = 4.95, df = 2 (P = 0.08); I^2 = 60%							
Test for overall effect: Z = 1.15 (P < 0.25)							
1.2.3 Pulmonary Infection							
Lee 1999 [39]	2	47	10	56	100.0%	0.24 [0.05, 1.03]	1999
Subtotal (95%CI)		**47**		**56**	**100.0%**	**0.24 [0.05, 1.03]**	
Total events	2		10				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.92 (P < 0.06)							

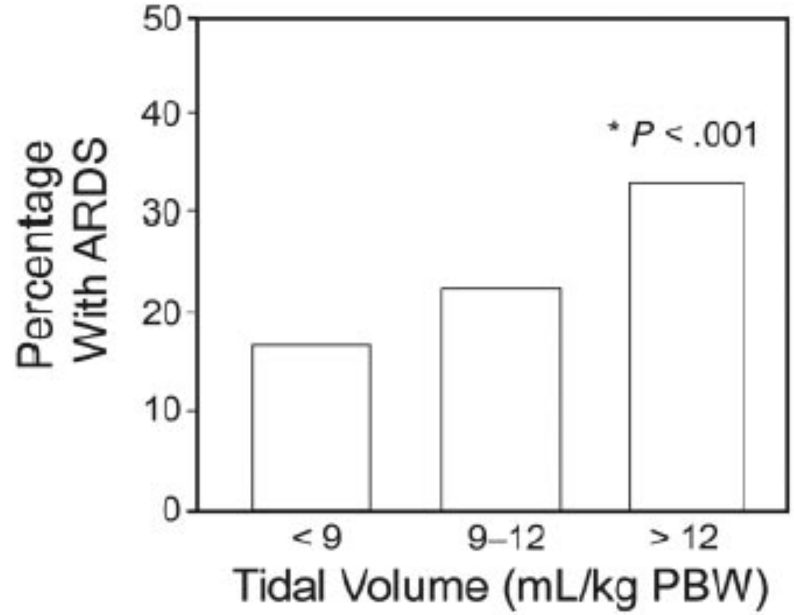


Improper Ventilation Settings in Healthy Can Propagate ARDS



● = 10ml/kg
o = 6ml/kg

Critical Care 2010, 14:R1



Critical Care 2004, 32(9):1817-1824

LTV for everyone?

Association Between Use of Lung-Protective Ventilation With Lower Tidal Volumes and Clinical Outcomes Among Patients Without Acute Respiratory Distress Syndrome

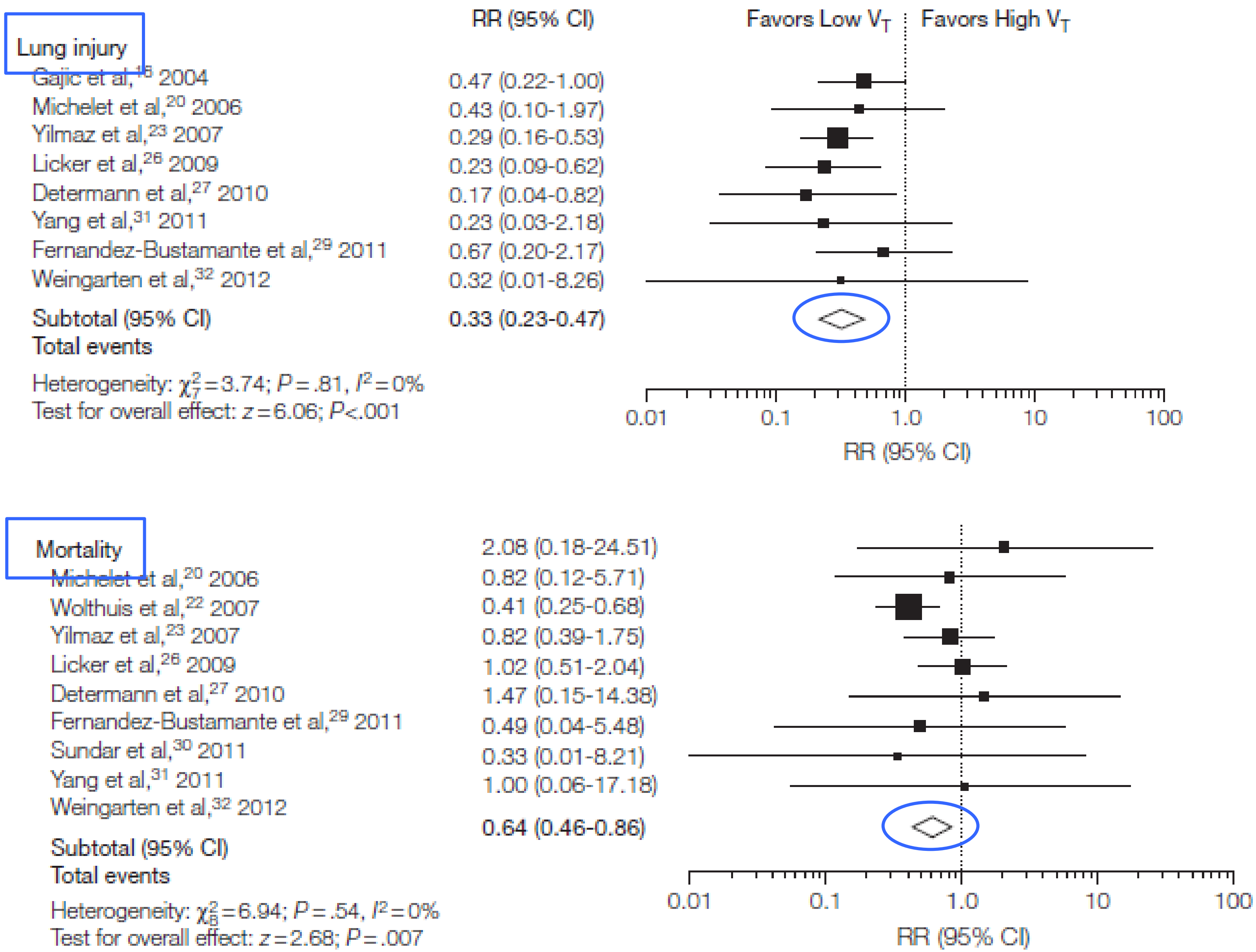
A Meta-analysis

Neto el al. JAMA 2012, 308, No. 16, p.1651-1659

- **20 Articles Included**

Table 2. Demographic, Ventilation, and Laboratory Characteristics of the Patients at the Final Follow-up Visit

	Mean (SD)		
	Protective Ventilation (n = 1416)	Conventional Ventilation (n = 1406)	*P* Value
Age, y	59.97 (7.92)	60.22 (7.36)	.93
Weight, kg	72.71 (12.34)	72.13 (12.16)	.93
Tidal volume, mL/kg IBW[a]	6.45 (1.09)	10.60 (1.14)	<.001
PEEP, cm H_2O[a]	6.40 (2.39)	3.41 (2.79)	.01
Plateau pressure, cm H_2O[a]	16.63 (2.58)	21.35 (3.61)	.006
Respiratory rate, breaths/min[a]	18.02 (4.14)	13.20 (4.43)	.01
Minute-volume, L/min[a,b]	8.46 (2.90)	9.13 (2.70)	.72
PaO_2/FIO_2[a]	304.41 (65.74)	312.97 (68.13)	.51
$PaCO_2$, mm Hg[a]	41.05 (3.79)	37.90 (4.19)	.003
pH[a]	7.37 (0.03)	7.40 (0.03)	.11



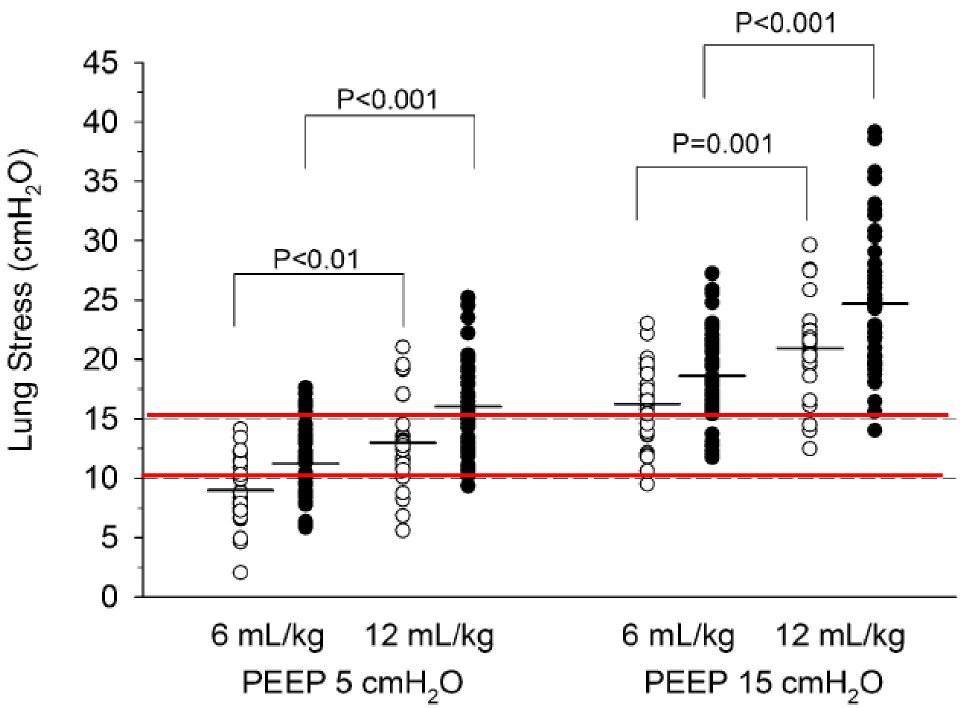
Neto el al. JAMA 2012, 308, No. 16, p.1651-1659

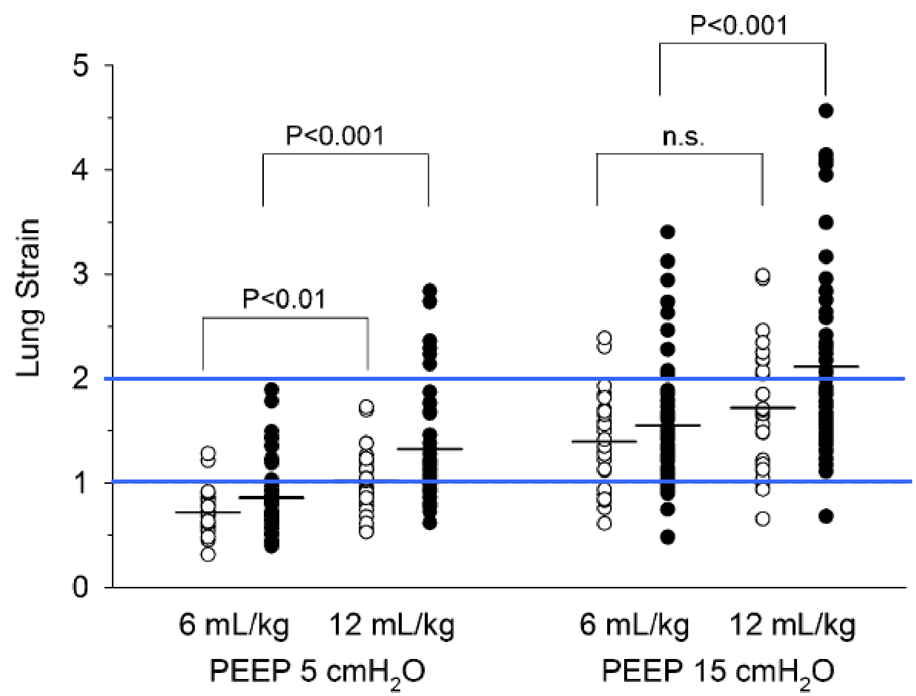
Does LTV and Pplateau < 30 Alone Prevent VILI?

Lung Stress and Strain during Mechanical Ventilation for Acute Respiratory Distress Syndrome

Davide Chiumello[1], Eleonora Carlesso[2], Paolo Cadringher[2], Pietro Caironi[1,2], Franco Valenza[1,2], Federico Polli[2], Federica Tallarini[2], Paola Cozzi[2], Massimo Cressoni[2], Angelo Colombo[1], John J. Marini[3], and Luciano Gattinoni[1,2]

Am J Respir Crit Care Med Vol 178. pp 346–355, 2008





LTV For Mitigating Volutrauma & Barotrauma

What do we actually know?:

1. VT ≤ 8ml/kg decreases develoment of ALI and ARDS (Maybe 9 - 10ml/kg?????)
2. VT ≤ 8ml/kg decreases ARDS mortality.
3. Plateau of ≤ 30cmH2O may still cause VILI, especially in ARDS and with high ΔTranspulmonary pressure.
4. May still see VILI with LTV, especially in ARDS.

- **Still disagreement on exactly how low of VT is lung protective?**
- **Normal Mammal Vt = 6.3ml/kg IBW +/-~30%, so 4 – 8 ml/kg IBW**

How Does the Ventilator Cause Injury?
Ventilator Induced Lung Injury (VILI)

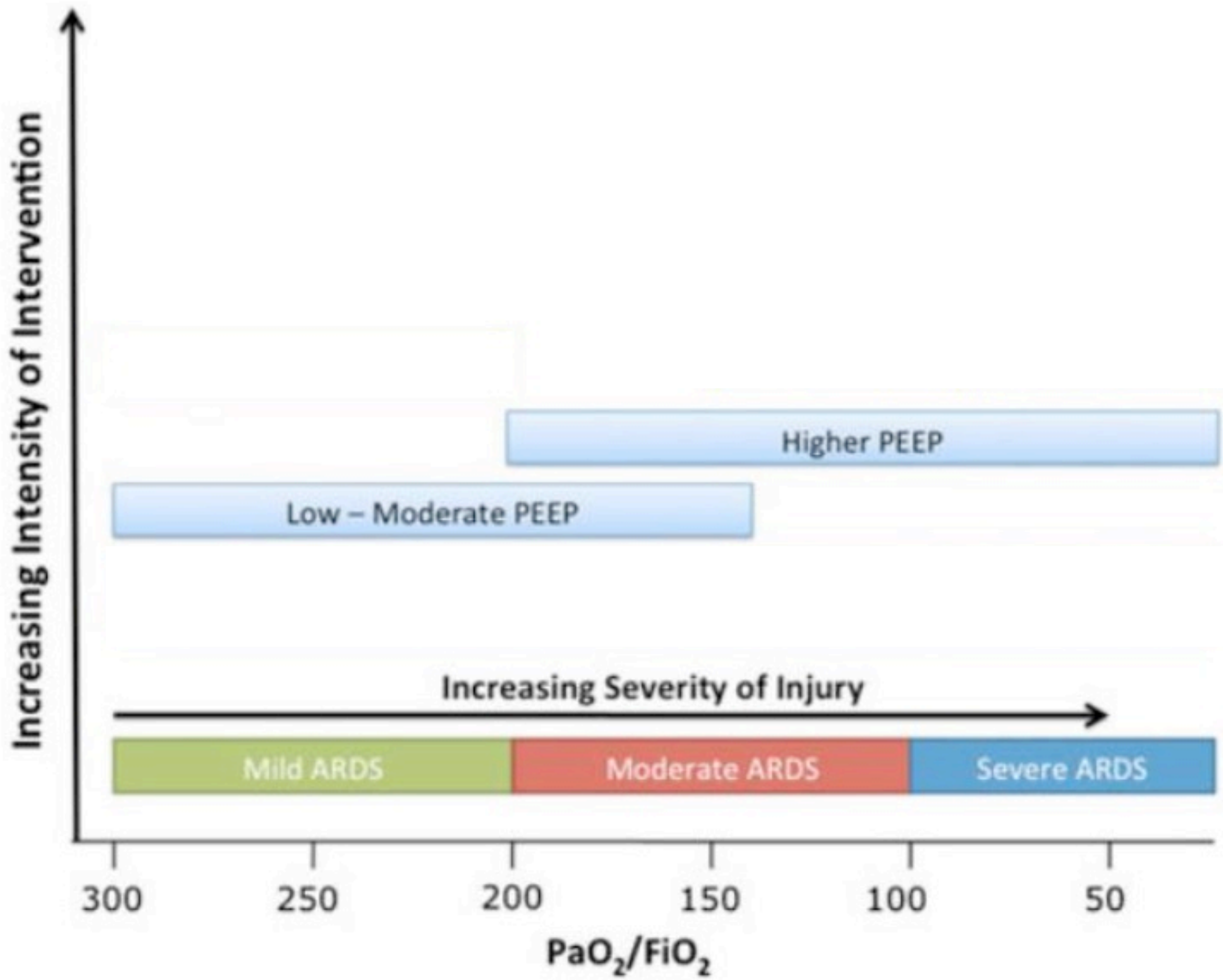
Mechanisms:

- **Volutrauma & Barotrauma (Stress/Strain)**
- **Atelectrauma (Shearing injury)**
- **Biotrauma**

Addressing Atelectrauma

- Preventing alveolar collapse and development of heterogeneous lung disease
- Recruit collapse alveoli and prevent derecruitment at end exhalation
- **Open Lung Ventilation?:**
  - PEEP?
  - Recruitment?
  - HFO?
  - APRV?

What is LPV – Preventing Atelectrauma?
Low versus High PEEP



Intensive Care Med. (2012) 38:1573-1582

Preventing Atelectrauma

- Does PEEP prevent atelectrauma?
- How to establish required PEEP level?

Does PEEP really matter?

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

Systematic Review and Meta-analysis

Briel et al. JAMA 2010, Vol.303; 3:865-873

	Trial		
Characteristic	**ALVEOLI,[8] 2004**	**LOVS,[9] 2008**	**EXPRESS,[10] 2008**
Inclusion criteria	Acute lung injury with $PaO_2:FIO_2 \leq 300$[a]	Acute lung injury with $PaO_2:FIO_2 \leq 250$[a]	Acute lung injury with $PaO_2:FIO_2 \leq 300$[a]
Recruitment period	1999-2002	2000-2006	2002-2005
Recruiting hospitals (country)	23 (United States)	30 (Canada, Australia, Saudi Arabia)	37 (France)
Patients randomized to higher vs lower PEEP	276 vs 273	476 vs 509[b]	385 vs 383[c]
Validity			
Concealed allocation	Yes	Yes	Yes
Follow-up for primary outcome, %	100	100	100
Blinded data analysis	Yes	Yes	Yes
Stopped early	Stopped for perceived futility	No	Stopped for perceived futility
Experimental intervention	Higher PEEP according to FIO_2 chart, recruitment maneuvers for first 80 patients	Higher PEEP according to FIO_2 chart, required plateau pressures ≤40 cm H_2O, recruitment maneuvers	PEEP as high as possible without increasing the maximum inspiratory plateau pressure >28-30 cm H_2O
Control intervention	Conventional PEEP according to FIO_2 chart, required plateau pressures ≤30 cm H_2O, no recruitment maneuvers	Conventional PEEP according to FIO_2 chart, required plateau pressures ≤30 cm H_2O, no recruitment maneuvers	Conventional PEEP (5-9 cm H_2O) to meet oxygenation goals

Does PEEP really matter?

	Mean (SD)								
	Day 1			Day 3			Day 7		
Variable	Higher PEEP	Lower PEEP	*P* Value	Higher PEEP	Lower PEEP	*P* Value	Higher PEEP	Lower PEEP	*P* Value
Tidal volume, mL/kg of predicted body weight	6.3 (1.0) [n = 1051]	6.3 (0.8) [n = 1051]	.33	6.3 (1.0) [n = 793]	6.3 (1.0) [n = 852]	.47	6.5 (1.4) [n = 443]	6.4 (1.3) [n = 494]	.25
Plateau pressure, cm H_2O	29 (5.4) [n = 1043]	23 (5.6) [n = 991]	<.001	27 (5.6) [n = 781]	23 (5.9) [n = 825]	<.001	27 (6.2) [n = 408]	24 (6.9) [n = 443]	<.001
FIO_2	0.51 (0.18) [n = 1053]	0.61 (0.19) [n = 1051]	<.001	0.44 (0.15) [n = 812]	0.56 (0.18) [n = 862]	<.001	0.45 (0.15) [n = 502]	0.54 (0.19) [n = 550]	<.001
PEEP, cm H_2O	15.3 (3.4) [n = 1053]	9.0 (3.1) [n = 1051]	<.001	13.3 (4.3) [n = 812]	8.2 (3.0) [n = 863]	<.001	10.8 (5.0) [n = 503]	7.8 (3.3) [n = 548]	<.001
Oxygenation index[a]	13.2 (8.7) [n = 949]	12.7 (7.8) [n = 944]	.16	11.2 (7.0) [n = 705]	11.6 (7.1) [n = 755]	.29	11.2 (7.1) [n = 392]	11.8 (8.4) [n = 421]	.34
PaO_2, mm Hg	96 (38) [n = 1024]	83 (29) [n = 1026]	<.001	87 (31) [n = 792]	82 (28) [n = 835]	<.001	84 (25) [n = 484]	83 (26) [n = 532]	.41
$PaCO_2$, mm Hg	44 (11) [n = 1025]	44 (11) [n = 1026]	.42	44 (9.9) [n = 792]	44 (11) [n = 835]	.68	45 (12) [n = 485]	46 (12) [n = 532]	.06
Arterial pH	7.35 (0.09) [n = 1025]	7.36 (0.09) [n = 1026]	.02	7.38 (0.08) [n = 793]	7.38 (0.08) [n = 836]	.49	7.41 (0.08) [n = 485]	7.40 (0.08) [n = 532]	.08

Briel et al. JAMA 2010, Vol.303; 3:865-873

Does PEEP matter?

FIO2 %	30	40	40	50	50	60	70	70	70	80	90	90	90	100
PEEP cmH_2O	5	5	8	8	10	10	10	12	14	14	14	16	18	20–24

Step	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
FiO_2	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

	All Patients				With ARDS				Without ARDS			
	No. (%)				No. (%)				No. (%)			
Outcomes	Higher PEEP (n = 1136)	Lower PEEP (n = 1163)	Adjusted RR (95% CI)[a]	P Value	Higher PEEP (n = 951)	Lower PEEP (n = 941)	Adjusted RR (95% CI)[a]	P Value	Higher PEEP (n = 184)	Lower PEEP (n = 220)	Adjusted RR (95% CI)[a]	P Value
Death in hospital	374 (32.9)	409 (35.2)	0.94 (0.86 to 1.04)	.25	324 (34.1)	368 (39.1)	0.90 (0.81 to 1.00)	.049	50 (27.2)	44 (19.4)	1.37 (0.98 to 1.92)	.07
Death in ICU[b]	324 (28.5)	381 (32.8)	0.87 (0.78 to 0.97)	.01	288 (30.3)	344 (36.6)	0.85 (0.76 to 0.95)	.001	36 (19.6)	37 (16.8)	1.07 (0.74 to 1.55)	.71

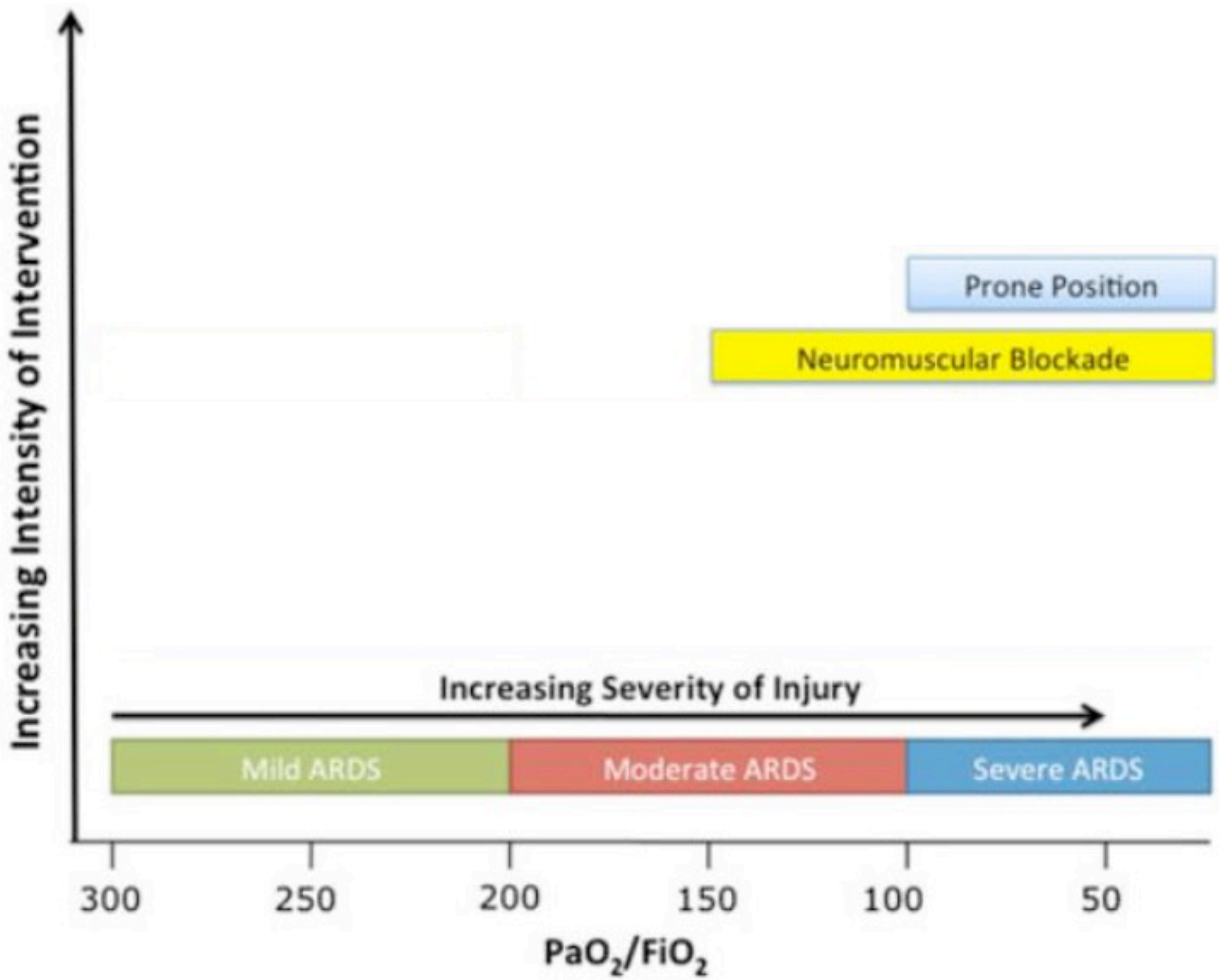
Briel et al. JAMA 2010, Vol.303; 3:865-873

So, What Do We Know From This?

- Higher PEEP may confer a mortality benefit in Moderate to Severe ARDS patients with P/F ratio of < 200mmHg.
- In these patients, may actually decrease the need for rescue therapies
- Improves thoracic compliance
- Improves oxygenation
-
- **BUT**

- Higher PEEP may actually be detrimental in patients without ARDS or Mild ARDS

What is LPV?



Intensive Care Med. (2012) 38:1573-1582

Study Summary: Prone Positioning

CURRENT OPINION

Prone position

Claude Guérin

Curr opin crit care. 2014, 20;92-97

First author	Gattinoni *et al.* [3]	Guérin *et al.* [16]	Mancebo *et al.* [17]	Taccone *et al.* [18]	Guérin *et al.* [19■■]
No. of patients (SP/PP)	152/152	378/413	60/76	174/168	229/237
% of ARDS (SP/PP)	93.3/94.7	28/33.9	100/100	100/100	100/100
PaO_2/FIO_2 (mmHg)[a]	127	150	147	113	100
Tidal volume (ml/kg)[a]	10.3 MBW	8 MBW	8.4 PBW	8 PBW	6.1 PBW
PEEP (cmH_2O)[a]	10	8	12	10	10
PP session duration (average hours per session)	7	8	17	18	17
Mortality (SP/PP) (%)	25/21.1	31.5/32.4	58/43	32.8/31	32.8/16

Paralysis????

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*

Paralysis

Age — yr	58±16	58±15
Tidal volume — ml/kg of predicted body weight	6.55±1.12	6.48±0.92
$PaO_2:FIO_2$‡	106±36	115±41

- N = 339, Study = 177
- Cisatracurium = 15 mg bolus followed by 37.5 mg/hour infusions X 48 hours

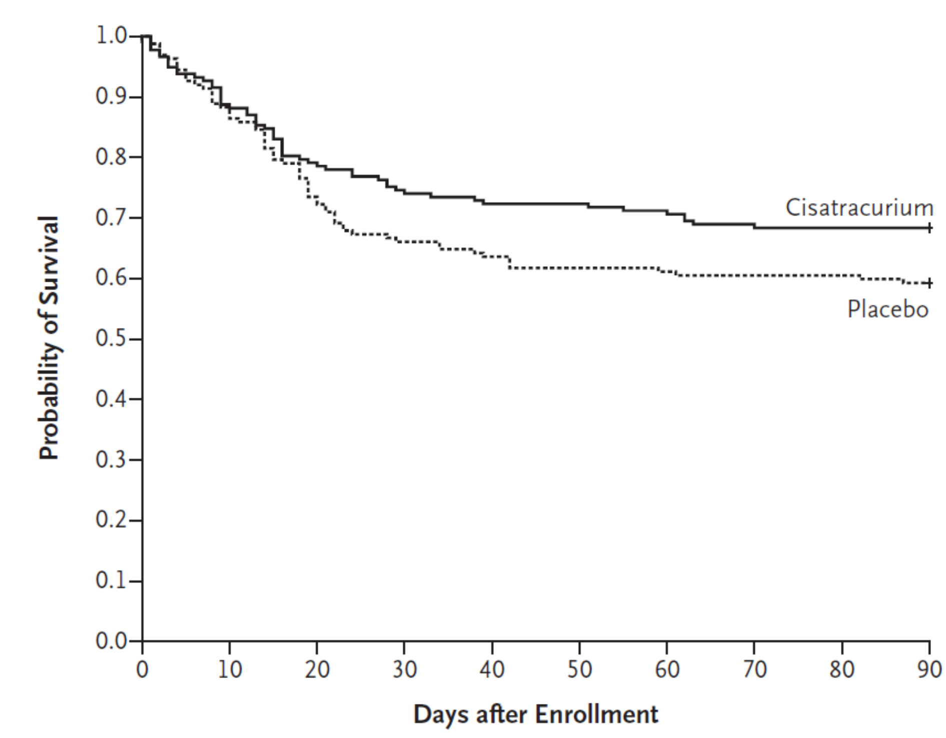


Figure 2. Probability of Survival through Day 90, According to Study Group.

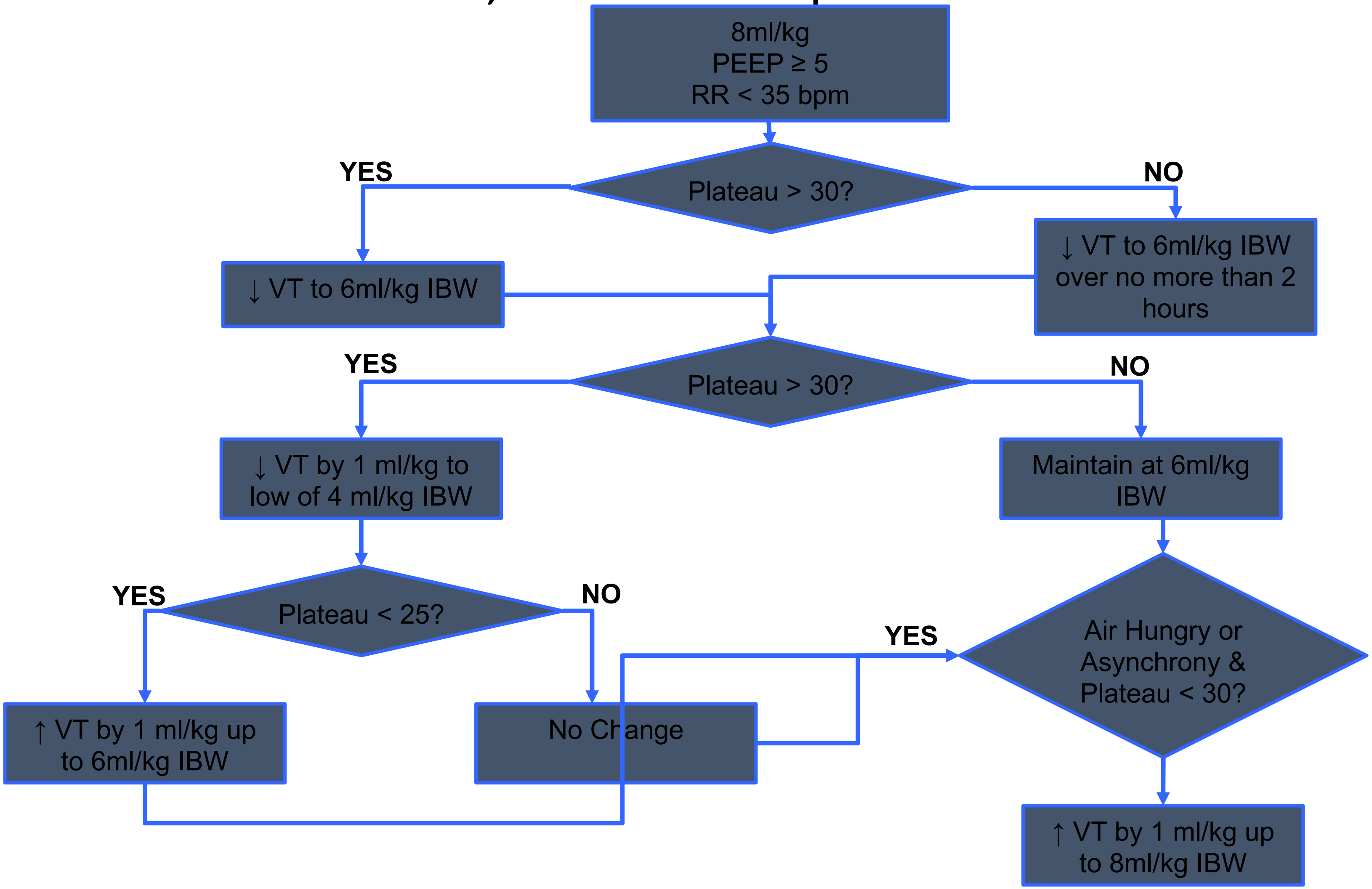
Outline

- 1. Why talk about Lung Protective Ventilation?
- 2. What is Lung Protective Ventilation?
- 3. **How to apply Lung Protective Ventilation?**

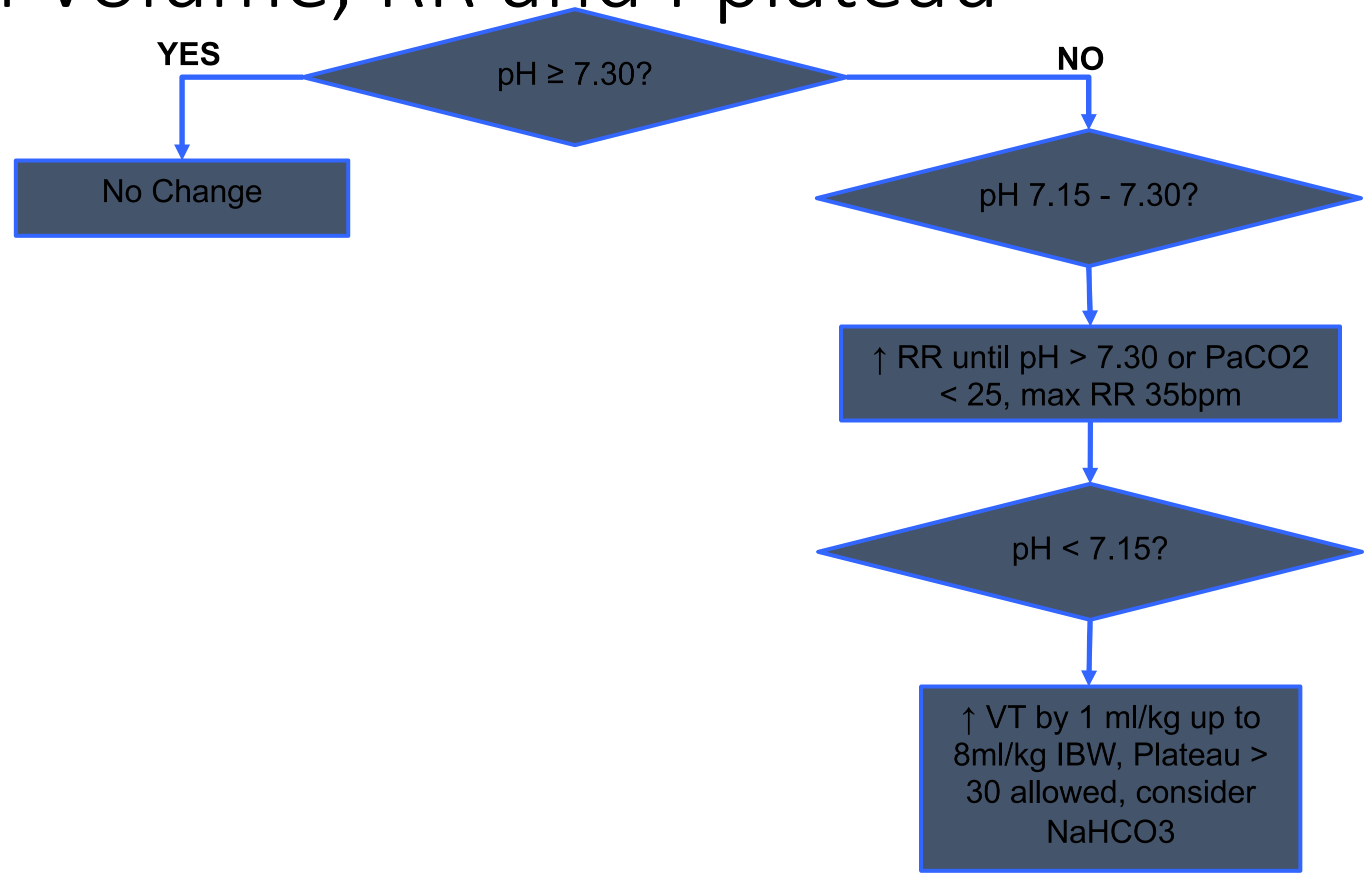
How to apply Lung Protective Ventilation?

- **Paralysis:**
  - Establish true baseline pulmonary status
  - Optimize mechanical ventilation settings
  - **Need a static state with no patient respiratory efforts!!!**

NIH ARDSnet LPV Protocol At The Bedside: Tidal Volume, RR and Pplateau



ARDSnet LPV Protocol At The Bedside: Tidal Volume, RR and Pplateau



ARDSnet LPV Protocol At The Bedside: PEEP

P/F ≥ 200 mmHg = Mild ARDS as per Berlin Definition

FIO2 %	30	40	40	50	50	60	70	70	70	80	90	90	90	100
PEEP cmH_2O	5	5	8	8	10	10	10	12	14	14	14	16	18	20–24

P/F ≤ 200 mmHg = Moderate to severe ARDS as per the Berlin Definition

Step	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
FiO_2	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

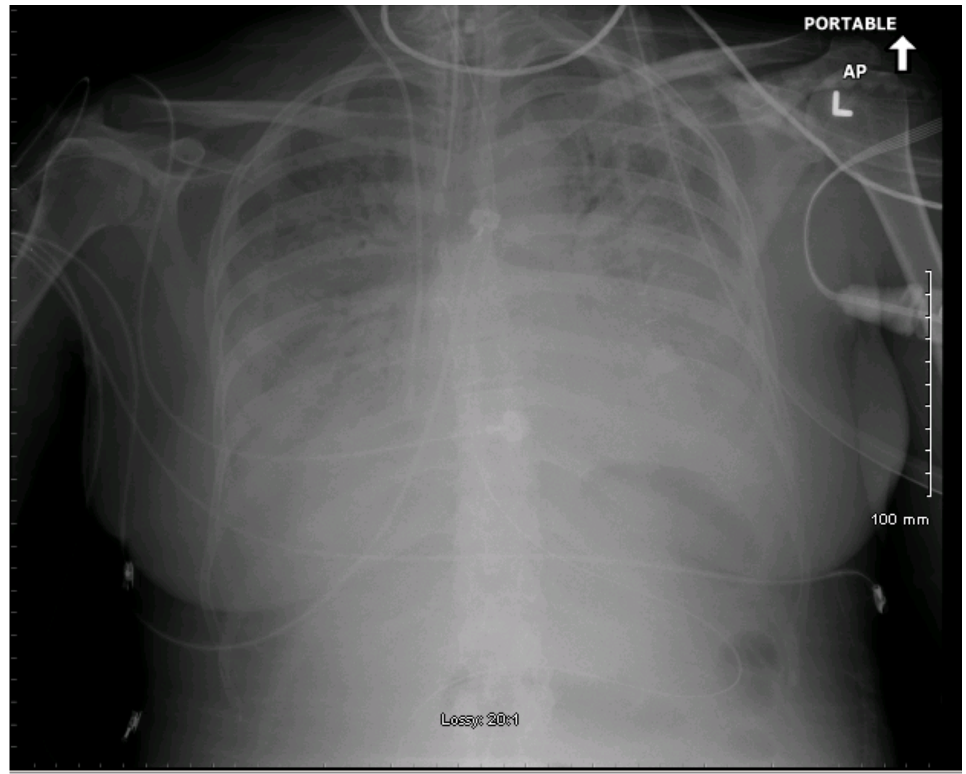
Lung Protective Ventilation: ARDSnet Approach

- ▪ Prevent Volumtrauma & Barotrauma
- ▪ Prevent Atelectrauma
- ▪ Minimize O2 toxicity
- ▪ Minimize Biotrauma

- ▪ VT 4-6ml/kg with Pplateau of ≤ 30 and permissive hypercapnia, as long as pH is ≥ 7.30
- ▪ FiO2/PEEP table (non-physiological).
- ▪ Looked at High v. Low PEEP table, concluded no benefit but, subgroup analysis showed benefit for sicker pt. with P/F < 200
- ▪ Minimize FiO2 to maintain PaO2 55 to 80mmHg or SpO2 88 to 95%
- ▪ 1/3 of pt. still had increase inflammatory markers

LPV at the bedside: ARDSnet approach

- Dx with MRSA Pneumonia
- Intubated for respiratory failure after trial 1 day of Optiflow 50 LPM, FiO2 0.60:
- Pre-intubation ABG with
- pH 7.13
- PaCO2 75
- HCO3-22
- PaO2 60
- SpO2 93%



Initial ventilator setttings:

- VC-AC (constant flow)
- VTset 500
- RR 16
- PEEP 8
- FiO2 0.60

- PIP 37
- Pplat 32
- MV 8.3
- SpO2 98%

First ABG:

pH	7.23
PCO2	65
HCO3-	18
PaO2	150
SpO2	98%
P/F	250

ARDSnet LPV Protocol At The Bedside

- 1. Calculate IBW:
    - Males IBW(kg) = 50 + 2.3 (Height(inches) – 60)
    - Females IBW(kg) = 45.5 + 2.3 (Height(inches) – 60)

2. Volume or Pressure Control (Original study was VC, with no plateau time)

- Pplateau measures minimum Q4h

- IBW = 54.7 kg

MEASURE PATIENT HEIGHT

ARDSnet LPV Protocol At The Bedside

1. What VT to set?
   - 8ml/kg ~ 438 ml
2. What RR to set?
   - MV for pH > 7.30 ~ MV 10, therefore RR ~ 22
3. What PEEP and FiO2 to set?
   - PaO2 150, therefore decrease FiO2 to 50%
   - P/F > 200, so low PEEP/FiO2 Table

FIO2 %	30	40	40	50	50	60	70	70	70	80	90	90	90	100
PEEP cmH_2O	5	5	8	8	10	10	10	12	14	14	14	16	18	20–24

ARDSnet LPV Protocol At The Bedside

- What are you going to do over the next 2 hours?
  1. Decrease VT towards 6ml/kg IBW ~ 328 ml
  2. RR is increased to match MV 10 ~ RR – 30bpm
  3. PEEP 8, FiO2 0.50

Pplateau 27
SpO2 97%

  - Any changes?

ARDSnet LPV Protocol At The Bedside

- Patient resp. status worsens and now is on the following settings:
    - VT = 4ml/kg
    - RR = 35
    - FiO2 = 0.90
    - PEEP = 22
    - Pplateau = 35

What are you going to do next?????

Is ARDSnet the only way to do LPV?

HFO?

OSCILLATE [36■■]	275	HFOV	40.0	273	Conventional ventilation	29.0	1.41 (1.12–1.61)
OSCAR [37■■]	398	HFOV	41.7	397	Conventional ventilation	41.1	1.03 (0.75–1.40)

- Is it really not beneficial?
- Poor study design?
- Based on old AECC definition of ARDS, so patients had P/F ratios of < 150 and therefore already had moderate ARDS as per the new Berlin Definition of ARDS. Therefore, was it just started too late?

Is ARDSnet the only way to do LPV?
APRV?

A Randomized Prospective Trial of Airway Pressure Release Ventilation and Low Tidal Volume Ventilation in Adult Trauma Patients With Acute Respiratory Failure

- Maxwell R et al. Journal of Trauma Injury, Infection and Critical Care, Sept. 2010
- N = 63 (31 APRV and 32 LOVT)
- **Results:**
- No differences in ventilator days, ICU length of stay, mortality and associated complications
- **Conclusion:**
- “APRV seems to have a similar safety profile as the LOVT”

Moving Towards Prevention: Evidence from Human Studies

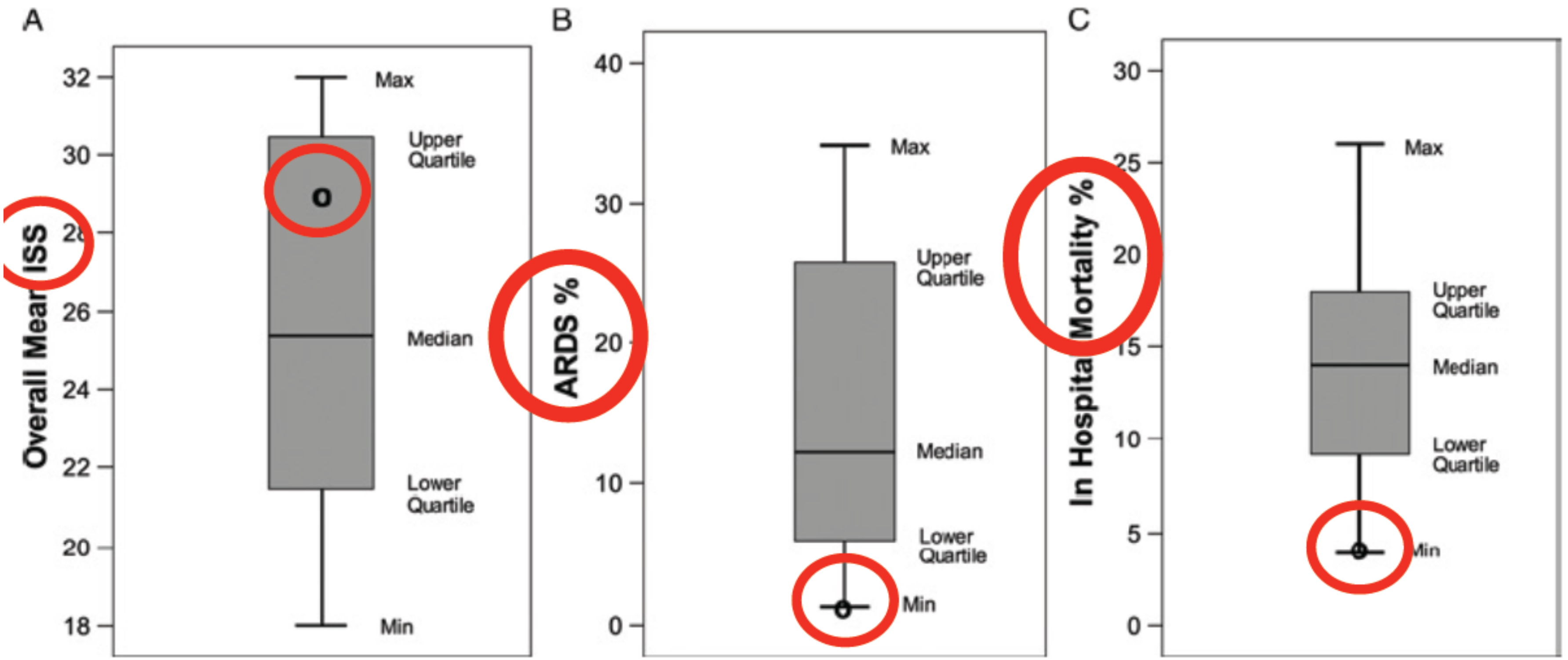
Early application of airway pressure release ventilation may reduce mortality in high-risk trauma patients: A systematic review of observational trauma ARDS literature

Penny L. Andrews, RN, BSN, Joseph R. Shiber, MD, Ewa Jaruga-Killeen, PhD, Shreyas Roy, MD, CM, Benjamin Sadowitz, MD, Robert V. O'Toole, Louis A. Gatto, PhD, Gary F. Nieman, BA, Thomas Scalea, MD, *and* **Nader M. Habashi, MD,** *Baltimore, Maryland*

Andrews et al. *J Trauma Acute Care Surg* 2013;75:635

Moving Towards Prevention: Evidence from Human Studies

Pre-emptive Use of APRV in Humans



Andrews et al. *J Trauma Acute Care Surg* 2013;75:635

Moving Towards Prevention: Evidence from Animal Studies

SHOCK, Vol. 39, No. 1, pp. 28–38, 2013

EARLY AIRWAY PRESSURE RELEASE VENTILATION PREVENTS ARDS—A NOVEL PREVENTIVE APPROACH TO LUNG INJURY

Shreyas Roy,[*] Nader Habashi,[†] Benjamin Sadowitz,[*] Penny Andrews,[†] Lin Ge,[*] Guirong Wang,[*] Preyas Roy,[‡] Auyon Ghosh,[*] Michael Kuhn,[§] Joshua Satalin,[*] Louis A. Gatto,[||] Xin Lin,[¶] David A. Dean,[¶] Yoram Vodovotz,[**] and Gary Nieman[*]

Moving Towards Prevention: Evidence from Animal Studies

Experimental Design:

APRV (n=4)

- Phigh = P_{plat}
- Plow = 0
- Tlow PEFR = 75%
- Thigh ≥ 90% CPAP
- Vt= 12 mL/kg

Sham (n=5)

- PEEP = 5
- Vt = 10mL/kg
- No Sepsis + I/R

ARDSnet (n=3)

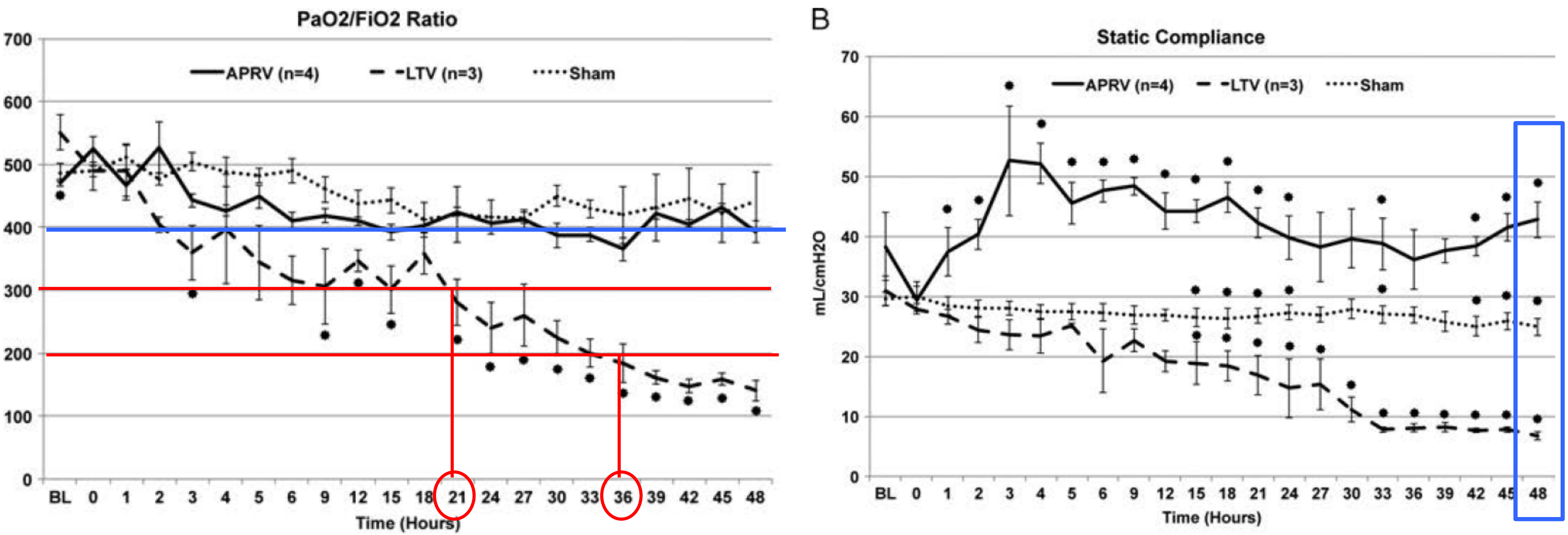
- High PEEP table
- Vt = 6mL/kg

Broad Spectrum Antibiotics

Early Goal Directed Therapy Based Fluid Resuscitation and Vasopressors

All Animals Continously Monitored according to ICU Standards of Care

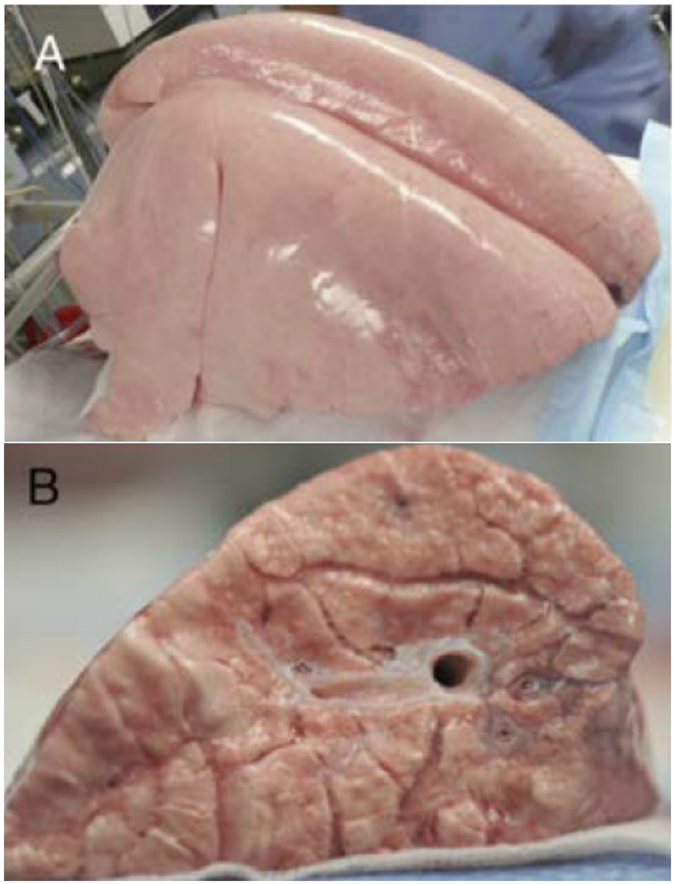
Moving Towards Prevention: Evidence from Animal Studies



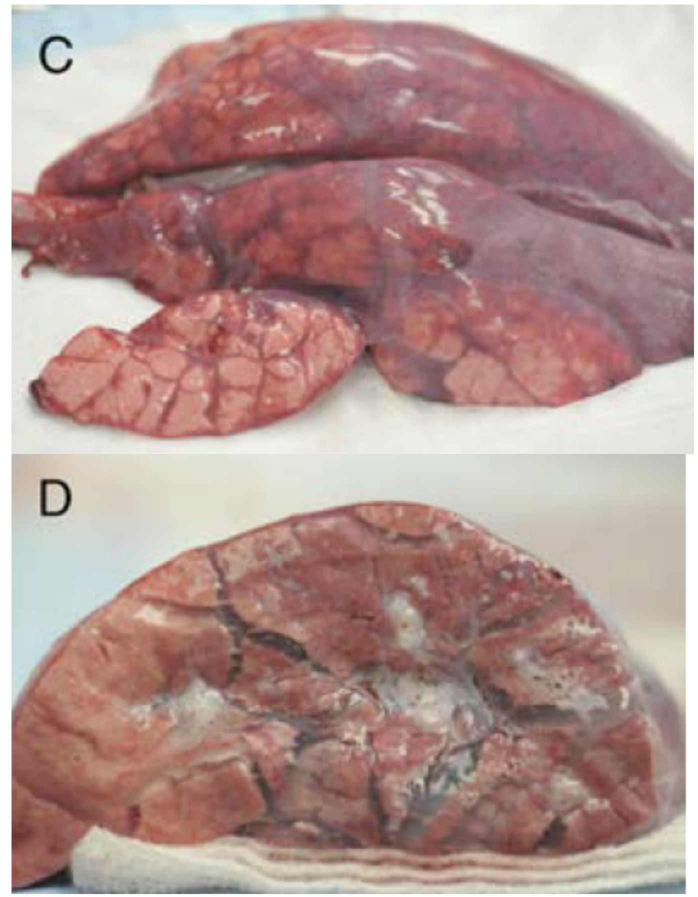
Moving Towards Prevention: Evidence from Animal Studies

Gross Anatomy

APRV



ARDSnet



Is APRV a viable LPV strategy?

- Animal and small human trials suggest it’s as effective or more effective than ARDSnet, but
- No large randomized trials on mortality benefit
- Still treated by many as a rescue therapy just like HFO

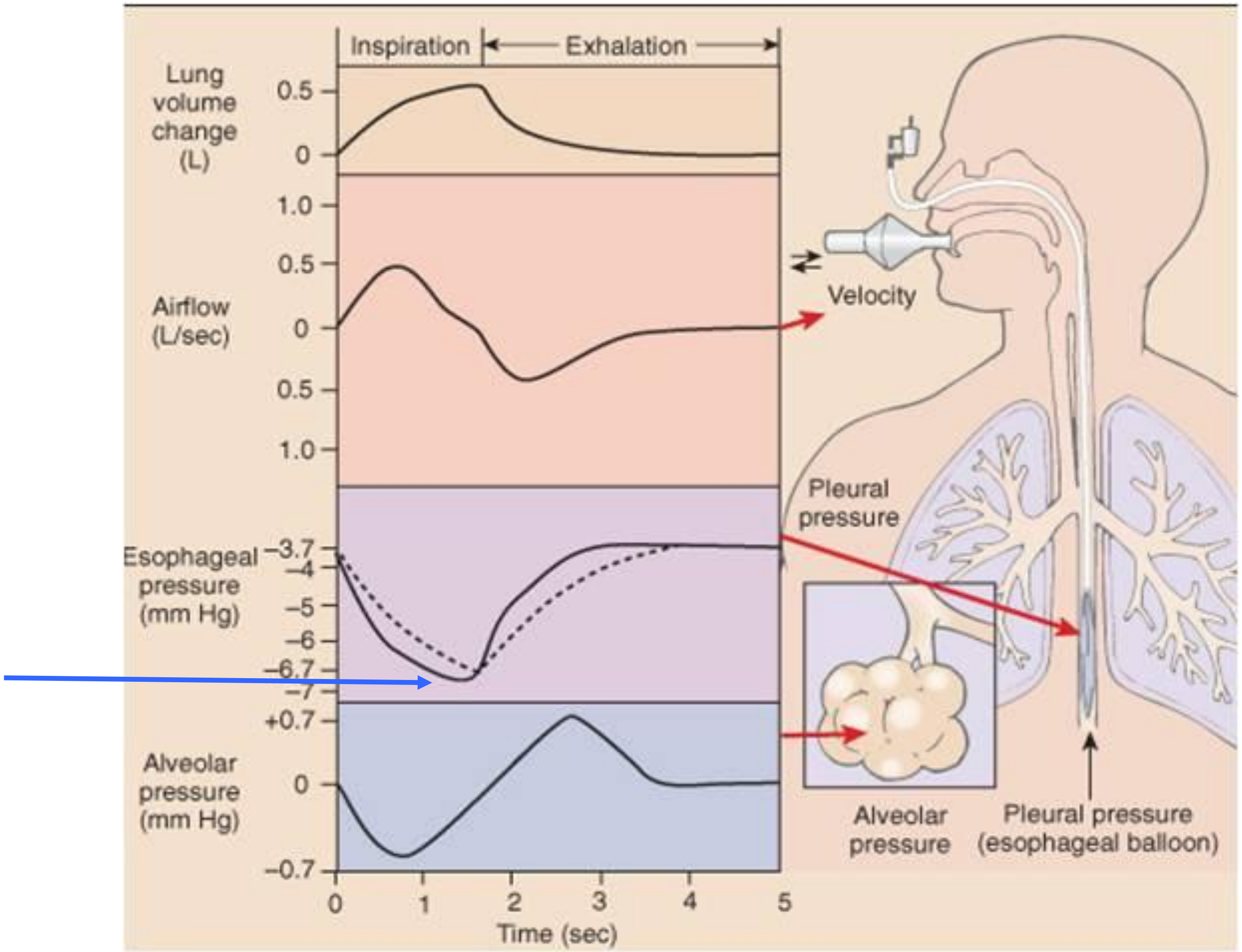
Low VT and Pplateau < 30 the only lung protective strategy?

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., Laurent Brochard, M.D., Eduardo L.V. Costa, M.D., David A. Schoenfeld, Ph.D., Thomas E. Stewart, M.D., Matthias Briel, M.D., Daniel Talmor, M.D., M.P.H., Alain Mercat, M.D., Jean-Christophe M. Richard, M.D., Carlos R.R. Carvalho, M.D., and Roy G. Brower, M.D.

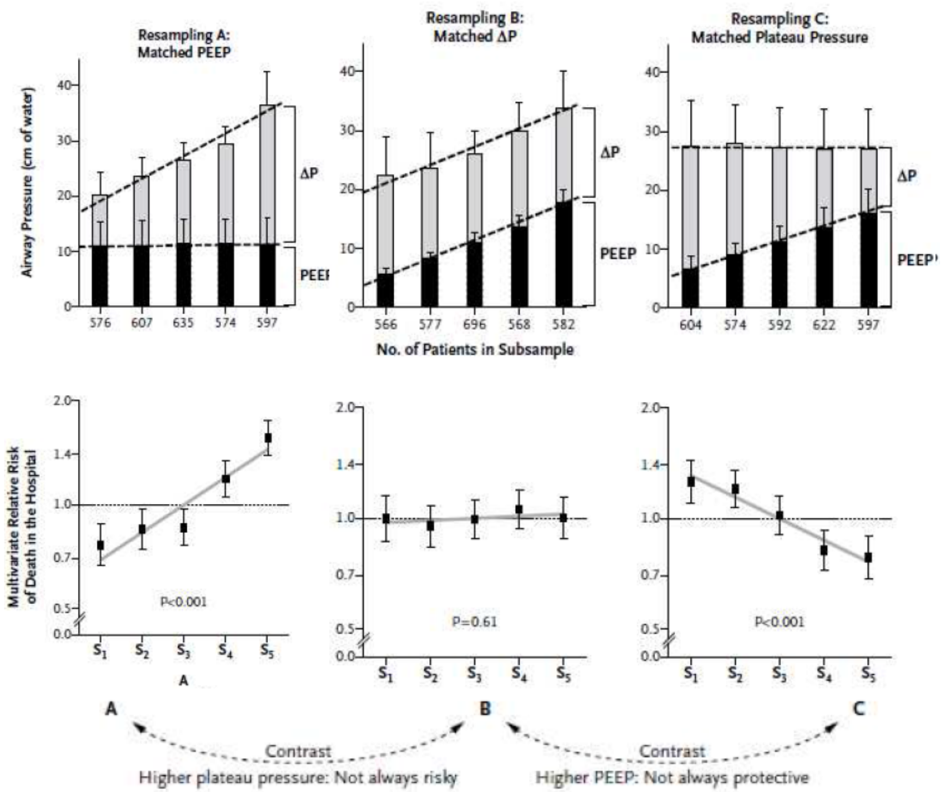
- Multilevel Mediation Analysis
- 3562 patients from 9 published randomized controlled trials
- Increase in ΔP by 7 cmH20 → ↑ Mortality, not VT or Pplateau

Why 7 cmH2O?
Changes in pleural pressures with normal ventilation



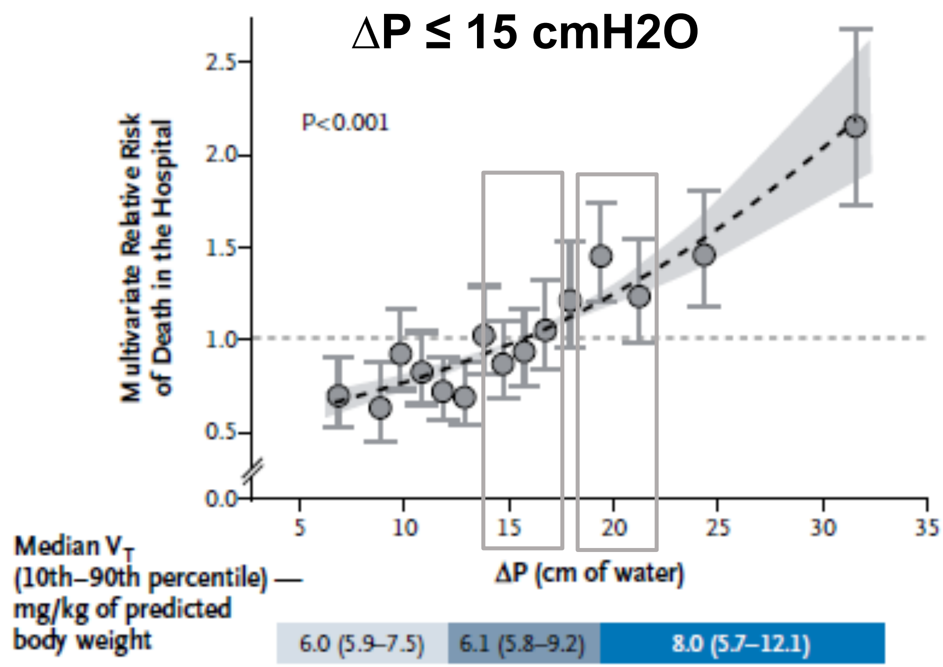
Lung Protective Ventilation: Minimizing Dynamic Strain

Is it just low VT and Pplateau < 30 that decreases mortality???????



Amato et al. N Engl J Med. (2015)372;8:747-755

N = 3652, from 9 previous studies



Individualizing Lung Protective Ventilation: Using conventional Ventilation

- Starting a breath from a lower pressure to a higher pressure, with changes in VT > anatomical deadspace
  - Make the lungs as homogenous as possible
    - Recruit collapsed alveoli
    - What's the best way to do this and how do we know at the bedside?
- Keep the alveoli open at end exhalation (Alveolar Stability)
  - Prevent derecruitment and therefore atelectrauma or shearing injury
  - No agreement on how to do this!!!!!!
  - VT ≤ 8ml/kg is likely a good thing
  - The lower the airway pressure the better??
    - or is it the driving pressure or transpulmonary pressure that's important?
    - Basically we need to minimize Dynamic Strain and Stress

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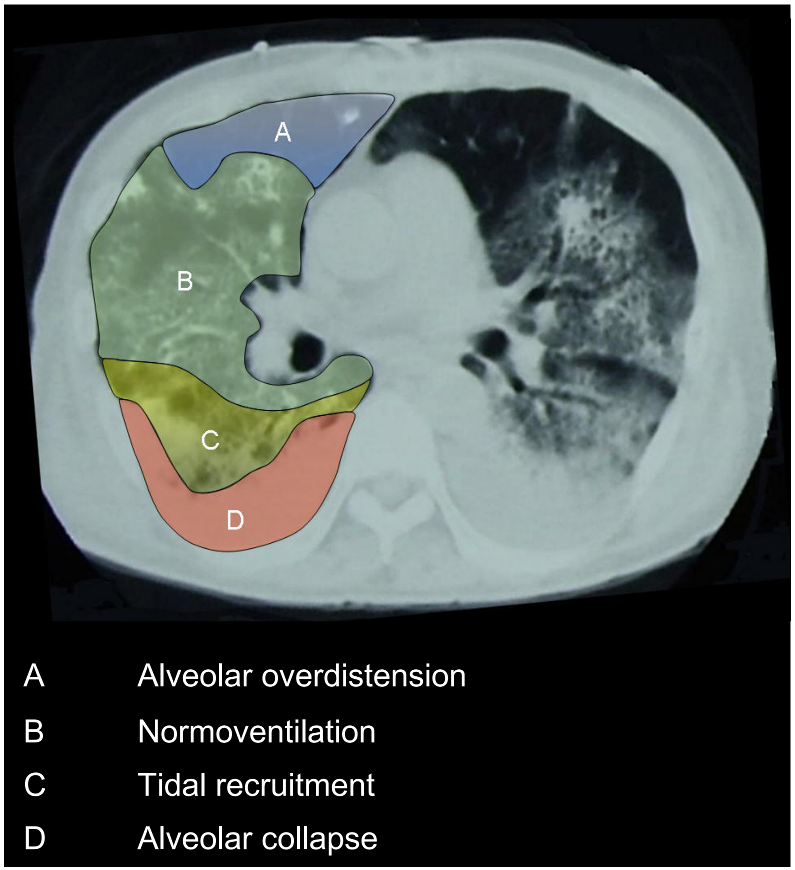
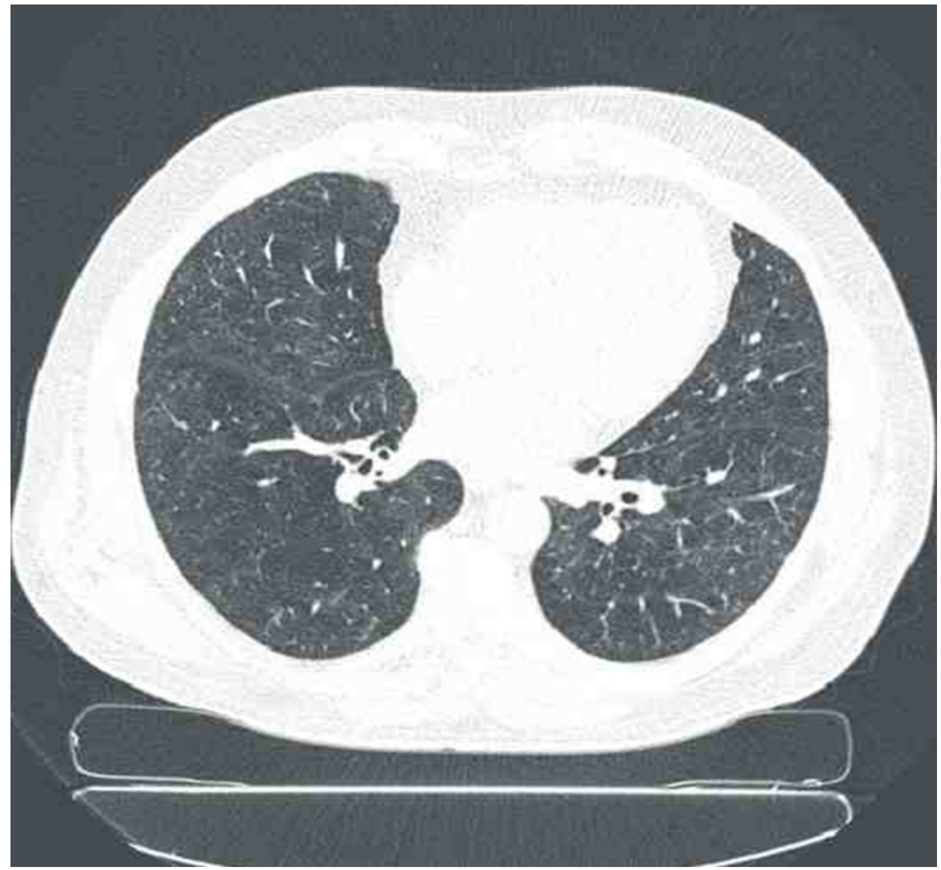
Individualizing Lung Protective Ventilation: Using conventional Ventilation

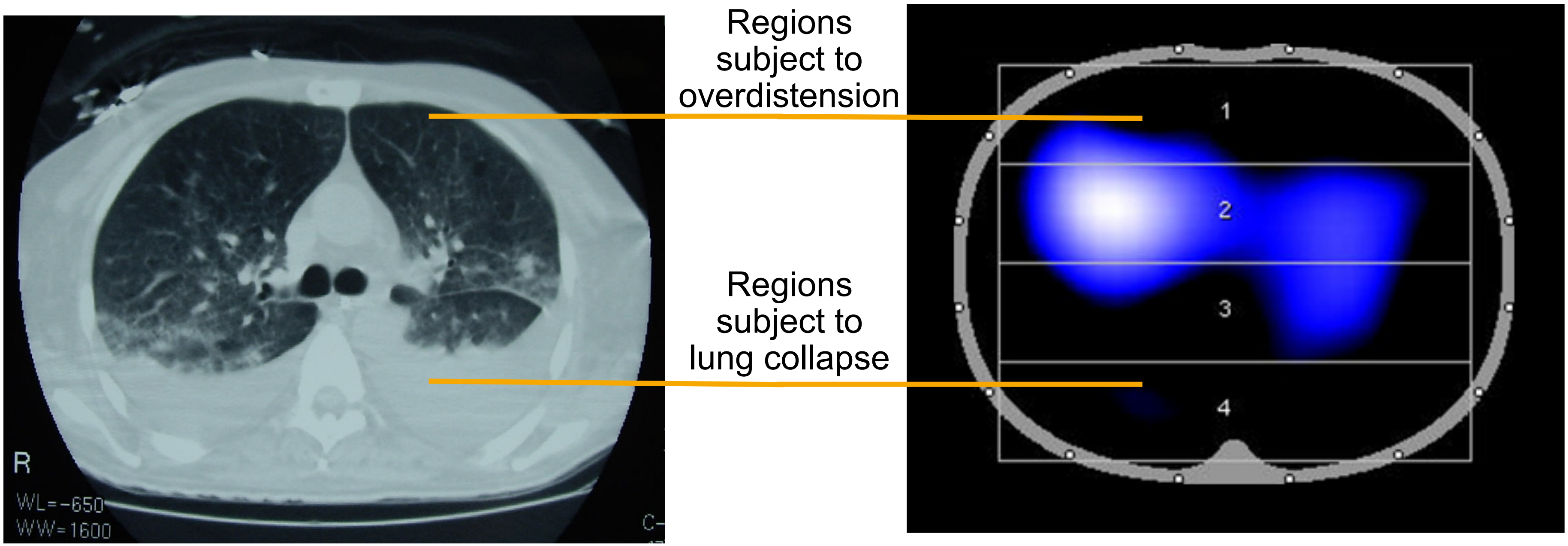
CT Scan = Gold standard for assessing extend of Collapse and Recruitability





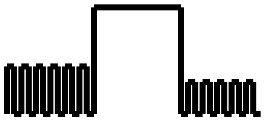
New and Newer Technological Approach

Dorsal atelectasis – CT and PulmoVista500



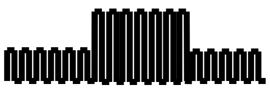
How to Recruit on a Ventilator

Lung recruitment - patterns



- Sustained inflations / Continuous distending pressure
  - 40 cmH20 for 40sec

- Incremental PEEP + Pinsp / Pplat increase
  - Keeping same ΔP



- Incremental Pinsp - increase leaving PEEP the same

- Incremental PEEP increase leaving Pinsp the same

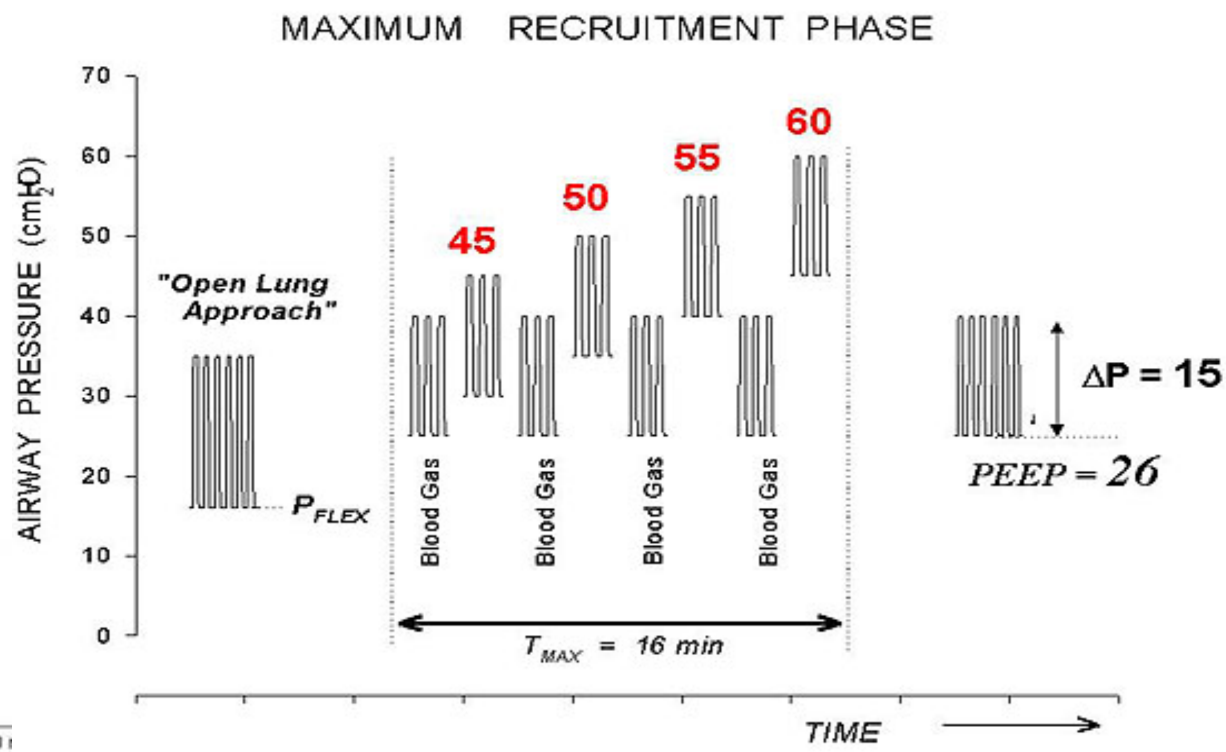
- Intermittent sighs / intermittent high level PEEP

Clinical situation

Lung recruitment – incremental PEEP + Pinsp

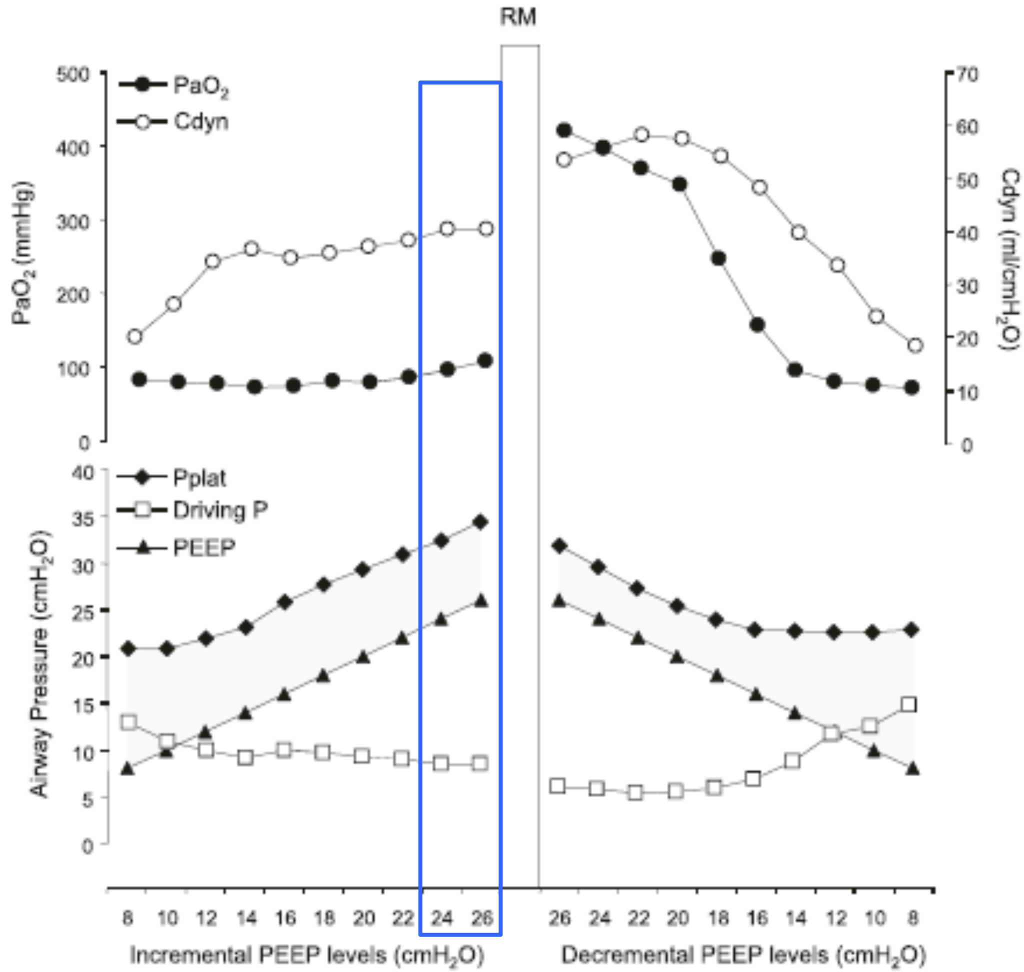
Conclusions:

Can reverse hypoxemia in majority (95%) of patients with primary or secondary ARDS



Amato et al. 2006 Aug;174(3):268-78)

Possible Clinical Application:
Trendin rol



Conclusions

- Different opinions on what Recruitment Maneuvers should be applied, IF AT ALL:
- ▪ Variety of Recruitment Maneuvers currently discussed
- ▪ Available studies show mainly positive outcomes, especially oxygenation
- ▪ Few adverse effects published
- **BUT:**
- ▪ Small numbers of patients/poorly controlled studies
- ▪ More effective early in disease process
- ▪ Most publications state that Recruitment Maneuvers are more effective in
- ARDS of extrapulmonary origin(Gattinoni et al., Villagra et al. , Pelosi et al.,Lim et al. , Valente Barbas, Kacmarek et al.)

▪ Results short lived if appropriate PEEP is not applied afterwards

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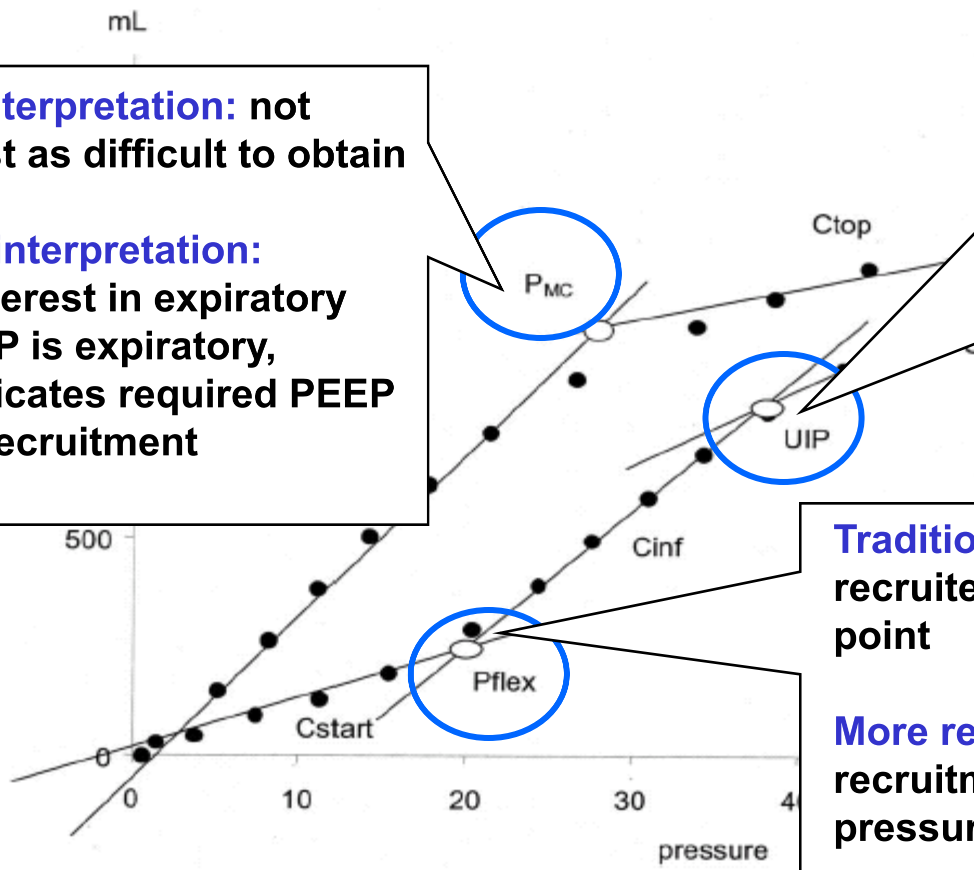
Characteristical Points on a PV curve and their suggested meaning



Traditional interpretation: not much interest as difficult to obtain

More recent interpretation: increased interest in expiratory limb as PEEP is expiratory, probably indicates required PEEP to maintain recruitment

Traditional interpretation: beginning of lung overdistention, stay below this point with Pinsp / Pplat!

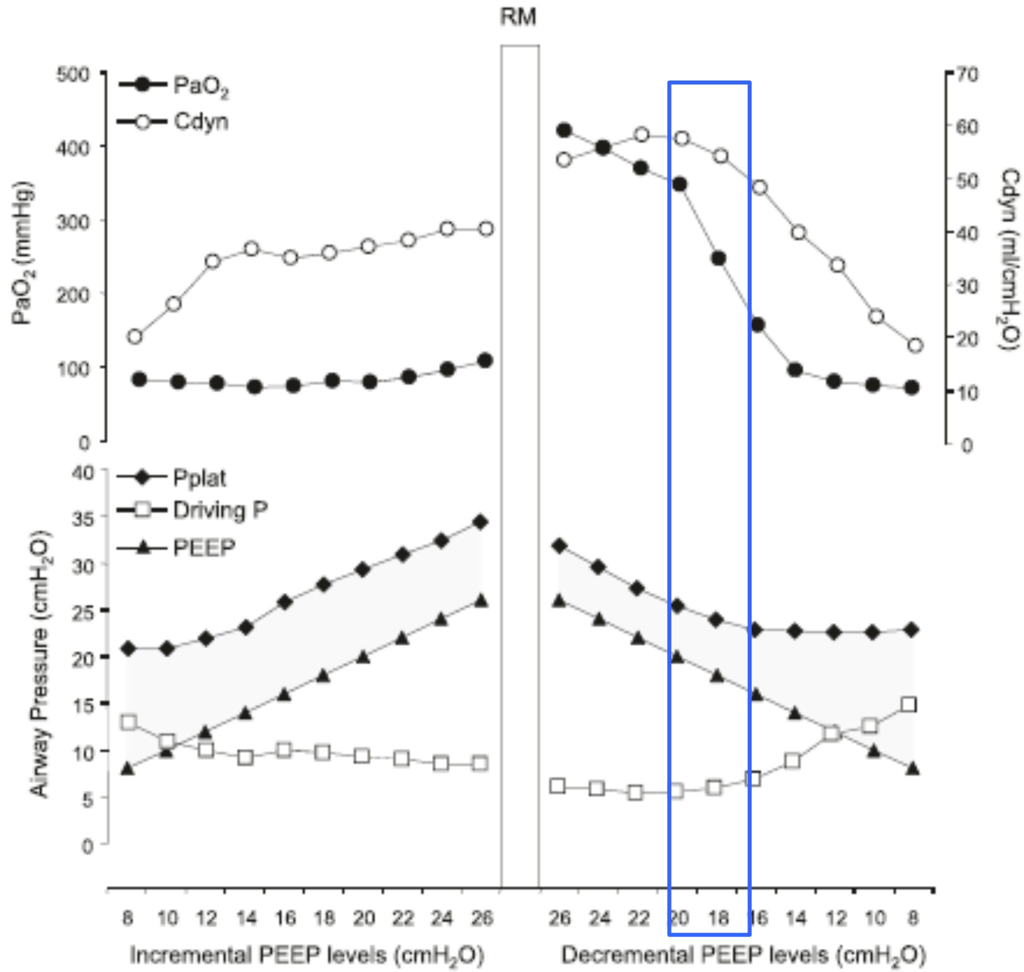
More recent interpretation: could be both end of recruitment and / or regional alveolar overdistention depending on this, limit Pplat

Traditional interpretation: lung fully recruited at this point, set PEEP above this point

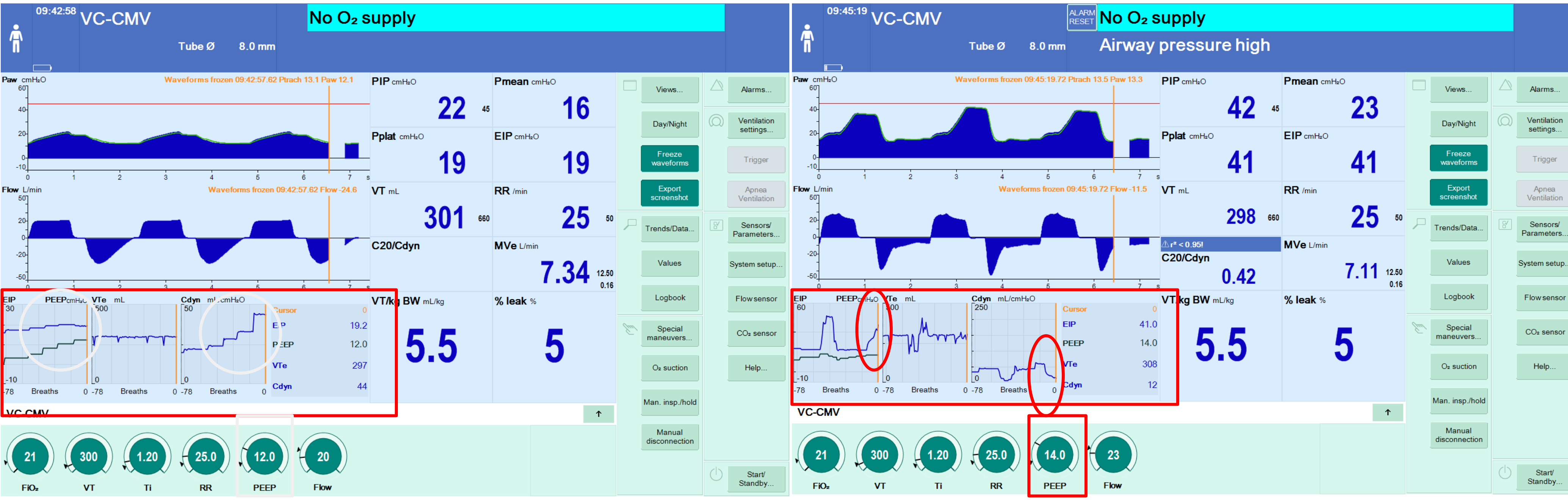
More recent interpretation: start of recruitment of alveoli with similar opening pressures, influenced by chestwall

Reference: Nishida T, Suchodolski K, Schettino GP, Sedeek K, Takeuch M, Kacmarek RM. Peak volume history and peak pressure-volume curve pressures independently affect the shape of the pressure-volume curve of the respiratory system. Crit Care Med. 2004 Jun;32(6):1358-64.

Possible Clinical Application: Trending Cdyn and ΔP

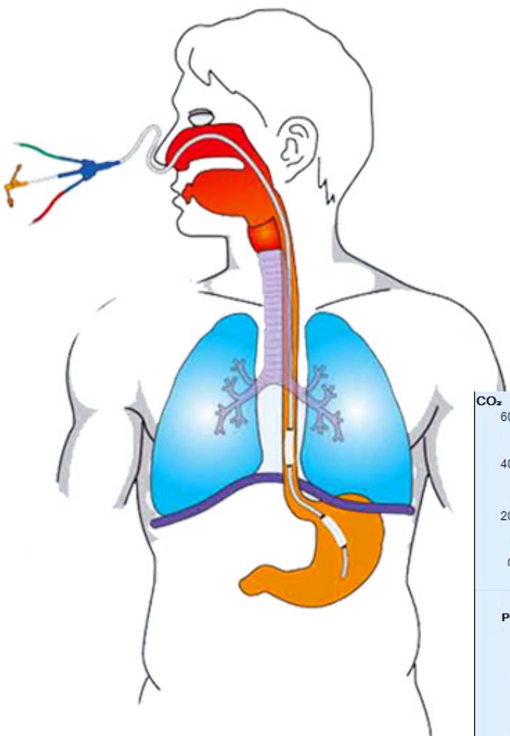


Targeting Dynamic Compliance and driving pressure:
Recruitment Trends



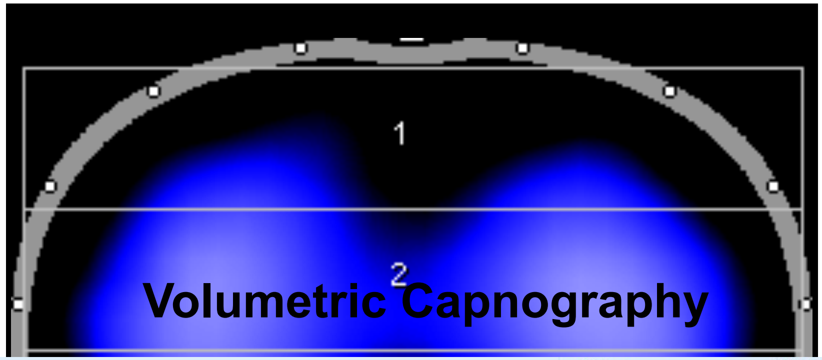
Promising technologies

Transpulmonary Pressure

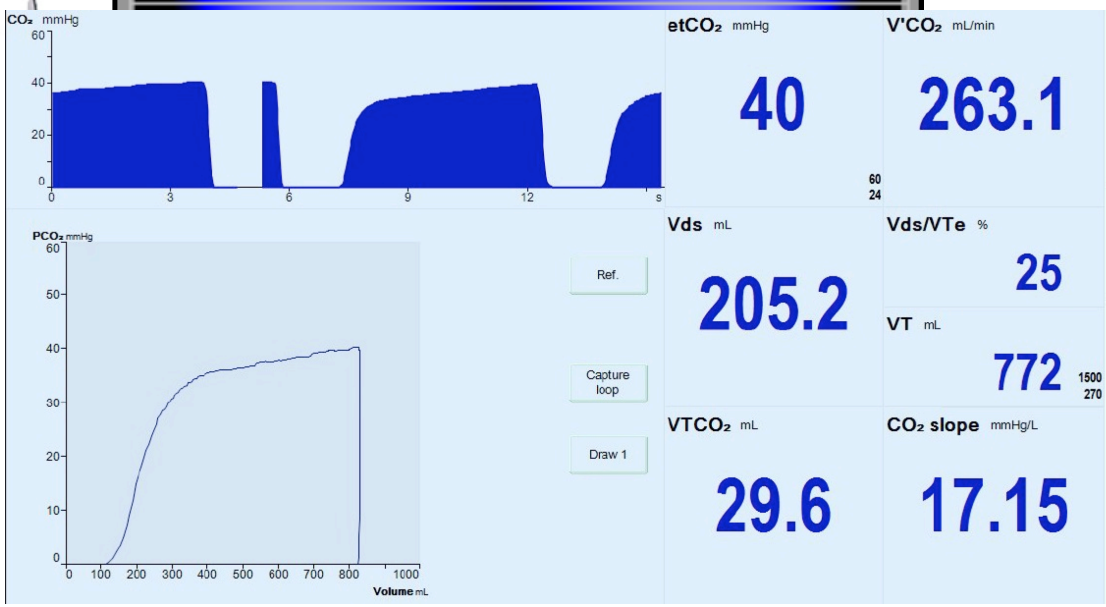


- EPVent 2 Trial?

Electrical Impedance Tomography



Volumetric Capnography



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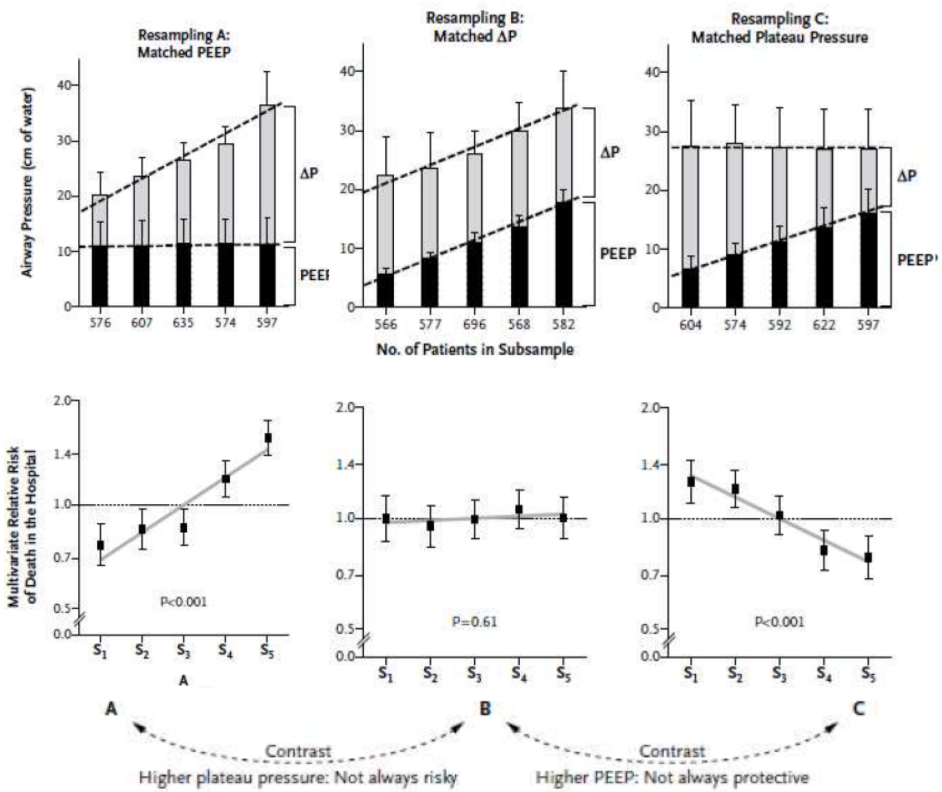
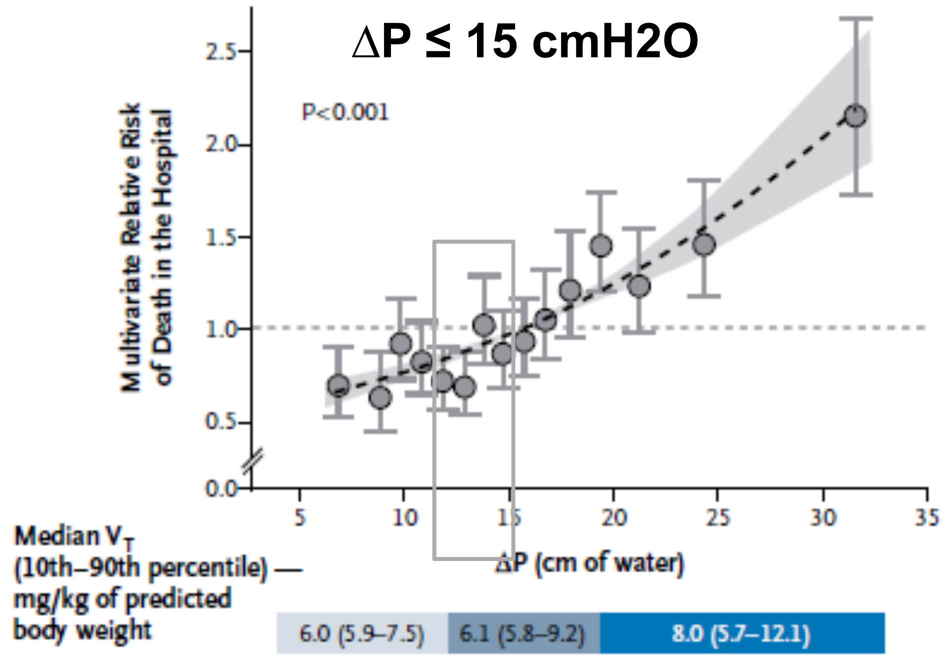
Lung Protective Ventilation:

Is it just low VT and Pplateau < 30 that decreases mortality???????



N = 3652, from 9 previous studies



Amato et al. N Engl J Med. (2015)372;8:747-755

Lung Protective Ventilation Large Trial

Trial's acronym or intervention tested	Experimental group			Control group			Relative risk (95% CI)
	N patients	Definition	Mortality rate	N patients	Definition	Mortality rate	
ARMA [6]	432	Lower VT	31.0	429	Higher VT	39.8	0.68 (0.51–0.90)
FACTT [30]	503	Restrictive fluid strategy	25.5	497	Liberal fluid strategy	28.4	0.90 (0.69–1.10)
ALVEOLI [31]	273	Higher PEEP	27.5	276	Lower PEEP	25.0	0.88 (0.60–1.29)
EXPRESS [32]	382	Recruitment augmented	39.0	385	Minimal distension	35.3	0.85 (0.64–1.15)
LOVS [33]	508	Higher PEEP	40.4	475	Lower PEEP	36.4	0.85 (0.65–1.10)
ACURASYS [27]	178	Neuromuscular blockade	31.6	162	Placebo	40.7	0.68 (0.48–0.98)
Aerosolized albuterol [34]	152	Inhaled β_2 agonist	23.0	130	Placebo	17.7	1.30 (0.83–1.77)
BALTI-2 [35]	162	I.V. β_2 agonist	34.0	164	Placebo	23.0	1.47 (1.03–2.08)
OSCILLATE [36■■]	275	HFOV	40.0	273	Conventional ventilation	29.0	1.41 (1.12–1.61)
OSCAR [37■■]	398	HFOV	41.7	397	Conventional ventilation	41.1	1.03 (0.75–1.40)
PROSEVA [19■■]	237	Prone position	16.0	229	Supine position	32.8	0.39 (0.25–0.63)

Curr opin crit care. 2014, 20;92-97

What is lung protective ventilation?

- General Agreement that lower VT’s are better than higher VT’s
- General Agreement on lower Pplateau safer than higher Pplateau
- Recruit or to not recruit?
- What is the best PEEP and how do you know?

What is Lung Protective Ventilation??????????

- Likely a multi prong approach
- Maintain a fully inflated homogeneously ventilated lung
  - Recruit collapse lungs
- Mitigate or prevent Volutrauma and Barotrauma (Dynamic strain and stress)
- Mitigate or prevent Atelectrauma (Shearing injury)
- Prevent alveolar collapse on exhalation
  - Low/High FiO_2/PEEP tables, Individualized PEEP
- Minimize strain at the alveolar level
  - 4 – 8ml/kg with lowest ΔP

Thank you for your attention.