

Setting PEEP and Tidal Volume in ARDS

New York State Thoracic Society
Annual Assembly

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Roy Brower
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Disclosures

- No conflicts of interest
- No off-label

Case Presentation

- 27 year old M with alcoholic hepatitis and pneumonia
- Height 193 cm (6'4"). Predicted Body Wt = 87 kg
- $6 \text{ ml/kg} = 520 \text{ mL}$ PEEP = 10.
 $P_{plat} = 34 \text{ cm H}_2\text{O}$
Driving Pressure ($P_{plat} - \text{PEEP}, \Delta P$) = 24

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- Chest volumes not large

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 - $P_{plat} = 34$. Driving Pressure (ΔP) = 24
- Chest volumes not large
- Tidal volume decreased to $5, 4 \text{ mL/kg PBW}$
 - $P_{plat} = 28$, Driving Pressure (ΔP) = 18

ACUTE RESPIRATORY DISTRESS IN ADULTS

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FELLOW IN PULMONARY DISEASE*

Lancet 1967

Continuous positive-pressure breathing (CPPB) in adult respiratory distress syndrome

D. G. Ashbaugh, M.D. (by invitation), T. L. Petty, M.D.** (by invitation),
D. B. Bigelow, M.D.*** (by invitation), and T. M. Harris, M.D.**** (by
invitation), Denver, Colo.*

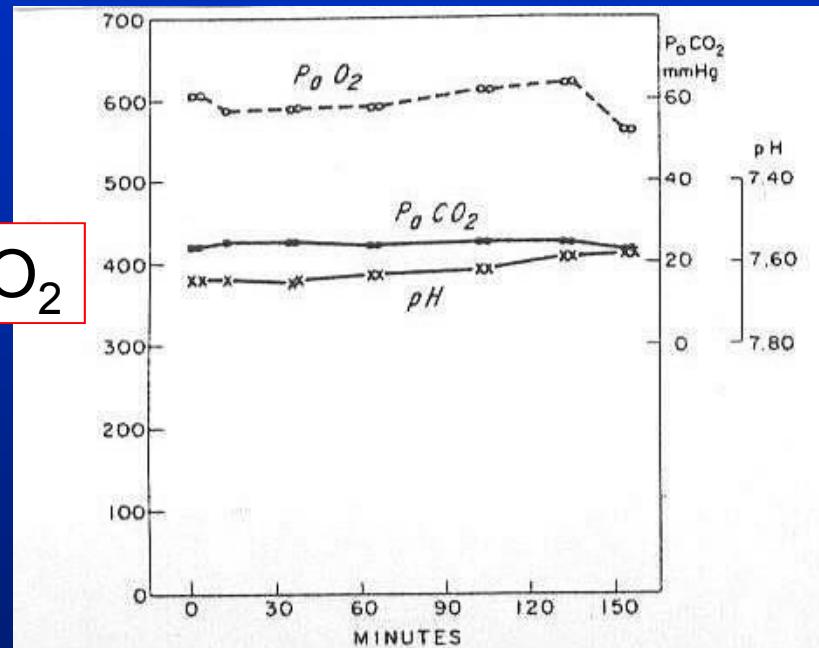
Sponsored by W. R. Waddell, M.D., Denver, Colo.

J Thor CV Surg 1969

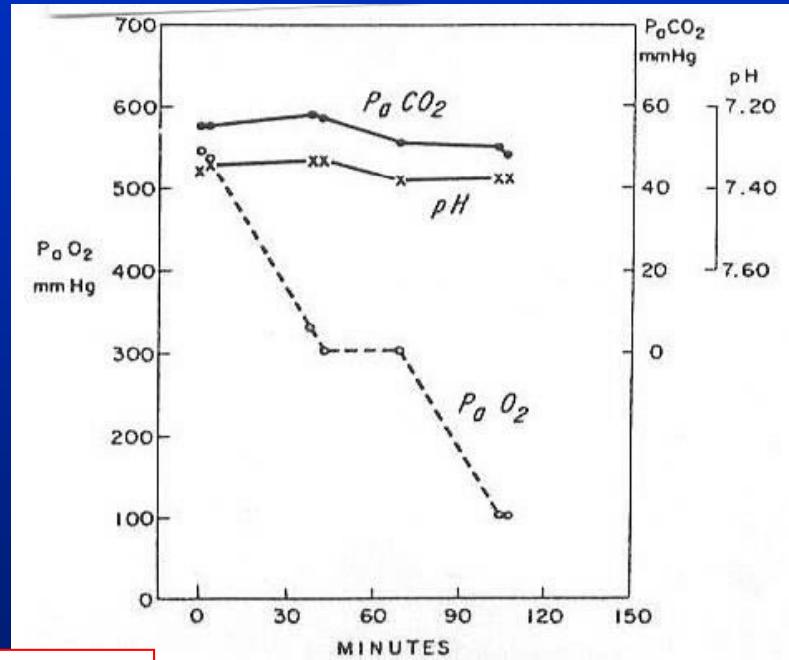
“The lungs become very stiff and require 40 to 60 cm. of water to achieve adequate tidal volumes.”

Impaired Oxygenation During Anesthesia with Controlled Ventilation

PaO_2



Minutes



Bendixen et al. N Eng J Med 1963

MEDICAL PROGRESS

ACUTE RESPIRATORY FAILURE IN THE ADULT (Third of Three Parts)

H. PONTOPPIDAN, M.D., B. GEFFIN, M.D., AND E. LOWENSTEIN, M.D.

New Eng J Med 1972

“Extensive clinical experience ... indicates that volumes of 7 ml per kilogram ... [are] poorly tolerated.... Larger tidal volumes (10-15 ml per kilogram) are preferable, having been used in several thousand ventilated patients with no evidence of development of pulmonary damage.

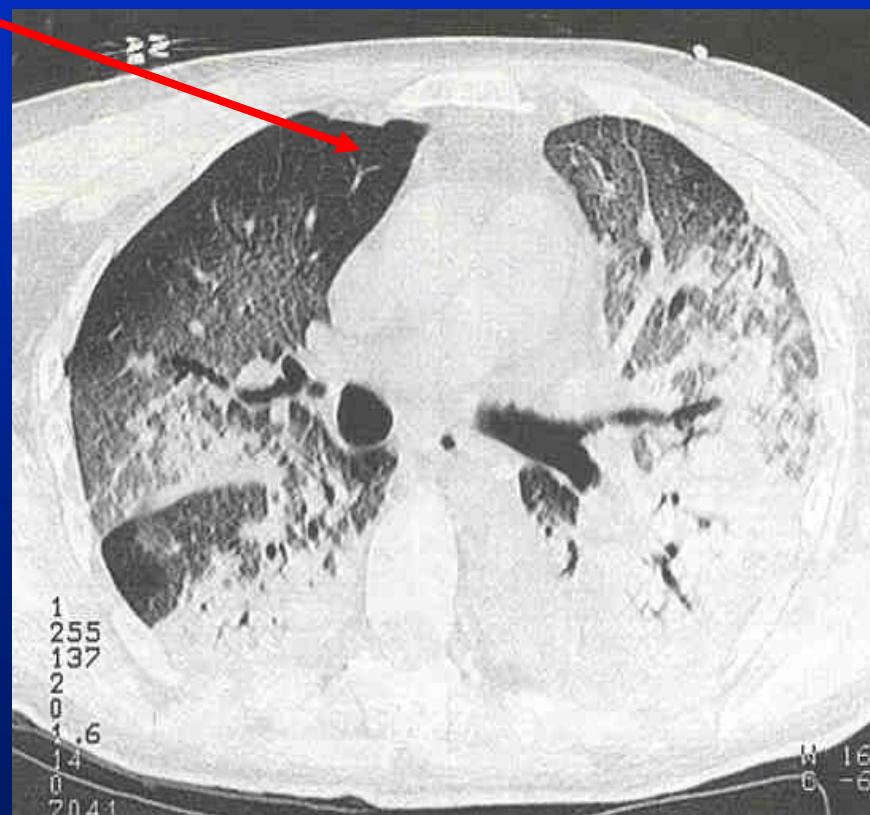
Tidal Volumes 1965-1983

Year	Authors	Journal	Tidal Volume (mL/kg)
1965	Sykes et al. (12)	<i>Br J Anaesth</i>	10–15
1969	McIntyre et al. (13)	<i>Can Anaesth Soc J</i>	8–14
1970	Kumar et al. (14)	<i>N Engl J Med</i>	11–13
1972	Pontoppidan et al. (15)	<i>N Engl J Med</i>	10–15
1972	Falke et al. (16)	<i>J Clin Invest</i>	9–24
1972	Lutch and Murray (17)	<i>Ann Intern Med</i>	10–16
1973	Kumar et al. (18)	<i>Crit Care Med</i>	12–18
1974	Steier et al. (19)	<i>J Thorac Cardiovasc Surg</i>	14–21
1975	Suter et al. (20)	<i>N Engl J Med</i>	15
1979	Hemmer and Suter (21)	<i>Anesthesiology</i>	15
1981	Jardin et al. (22)	<i>N Engl J Med</i>	12–20
1983	Mathru et al. (23)	<i>Crit Care Med</i>	12–15

Brochard and Lemaire
Crit Care Med 1999

Ventilator-Induced Lung Injury

High Volume
High Pressure
VILI



The New England Journal of Medicine

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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*

V_T Recommendation

V_T Goal = 6 mL/kg Predicted Body Weight

PBW based on gender, height



V_T Recommendation

V_T Goal = 6 mL/kg Predicted Body Weight

PBW based on gender, height

Intended as a guide to lung size

V_T Recommendation ARDS Network

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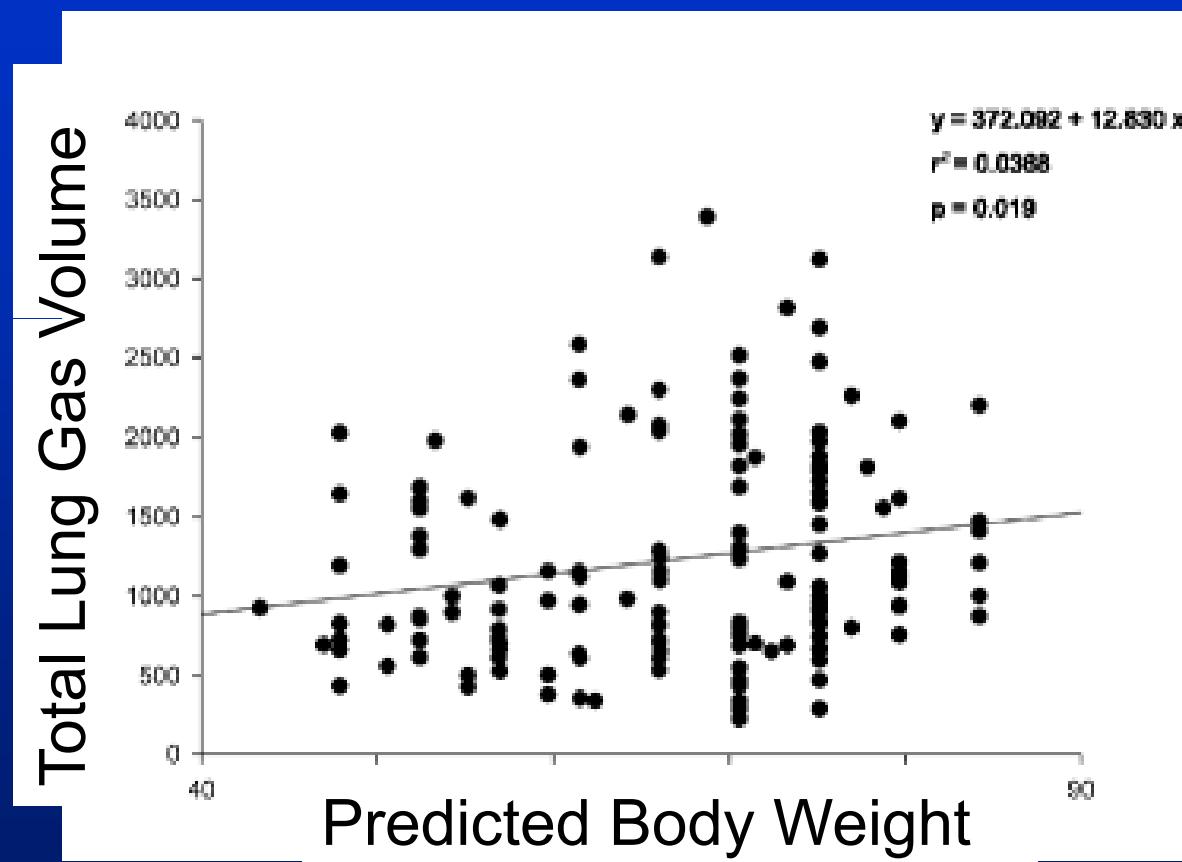
Intended as a guide to lung size

Male, 180 cm

Predicted FRC = 3.8 L

Measured FRC SD = 0.99 L

Predicted Body Weight and Aerated Lung Volume in ARDS Patients



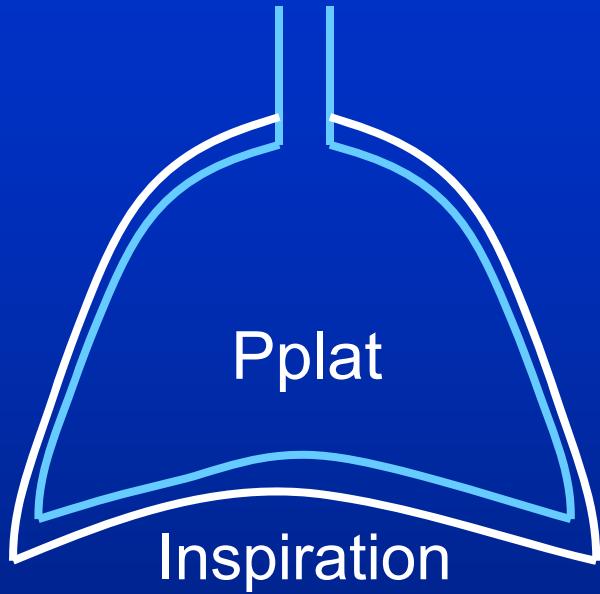
Chiumello et al. Crit Care 2016

Clinical Recommendation

V_T Goal = 6 mL/kg PBW

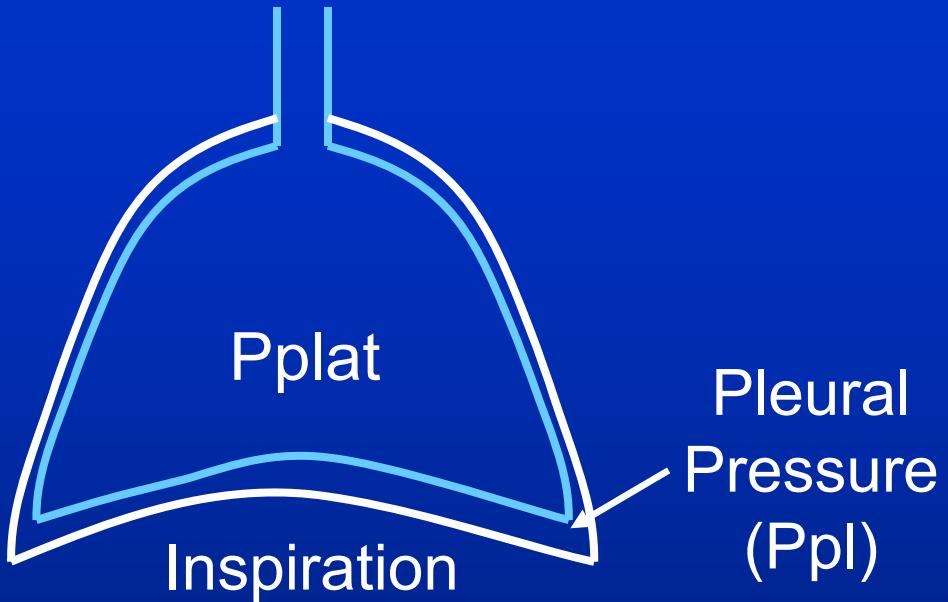
If $P_{plat} > 30$ cm H_2O , decrease V_T to 5 or 4 mL/kg PBW.

Pplat to Guide Tidal Volume?



Pplat = *Mean distending pressure of respiratory system*
(lungs and chest wall)

Pplat to Guide Tidal Volume?



Pplat = Distending pressure of the respiratory system

$P_{TP} = Pplat - Ppl =$ Distending pressure of the lung



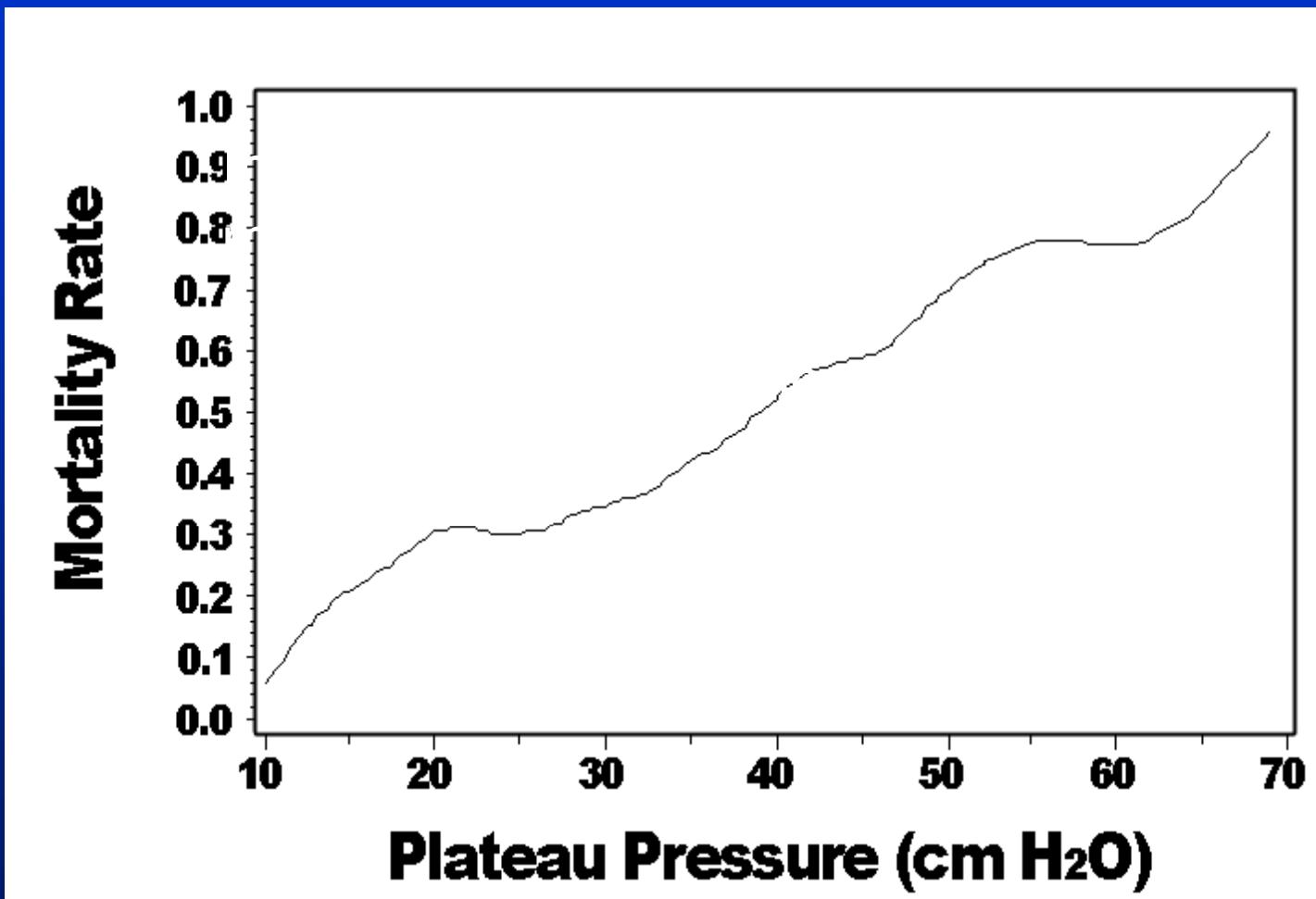
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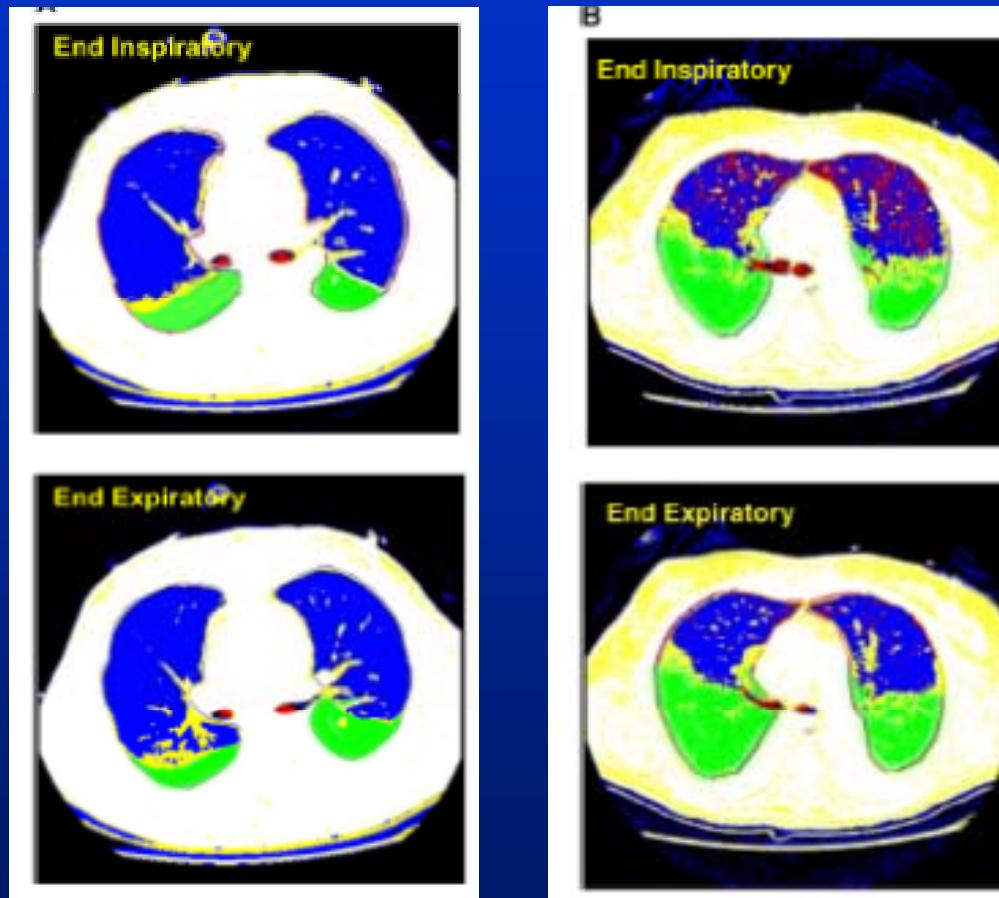
Are $P_{plats} < 30 \text{ cm H}_2\text{O}$ safe?

Safe Plateau Pressure?



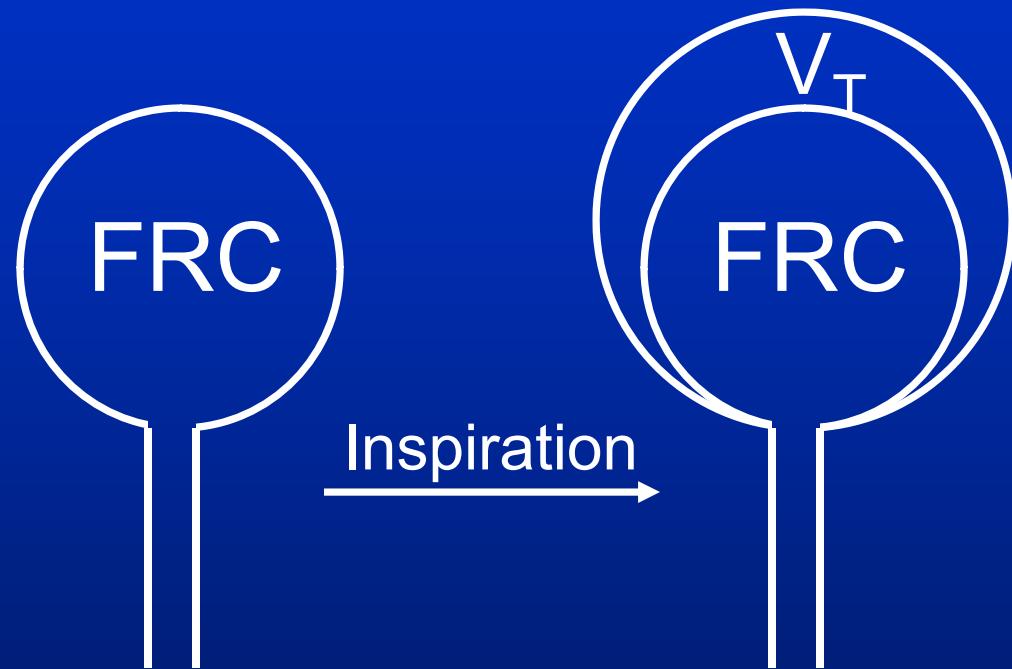
Hager et al, AJRCCM 2005

Variable Consolidation, Edema, and Atelectasis



Terragni et al.
Am J Resp Crit Care Med 2007

Strain



$$\text{Strain} = V_T / \text{FRC}$$

Strain Approach

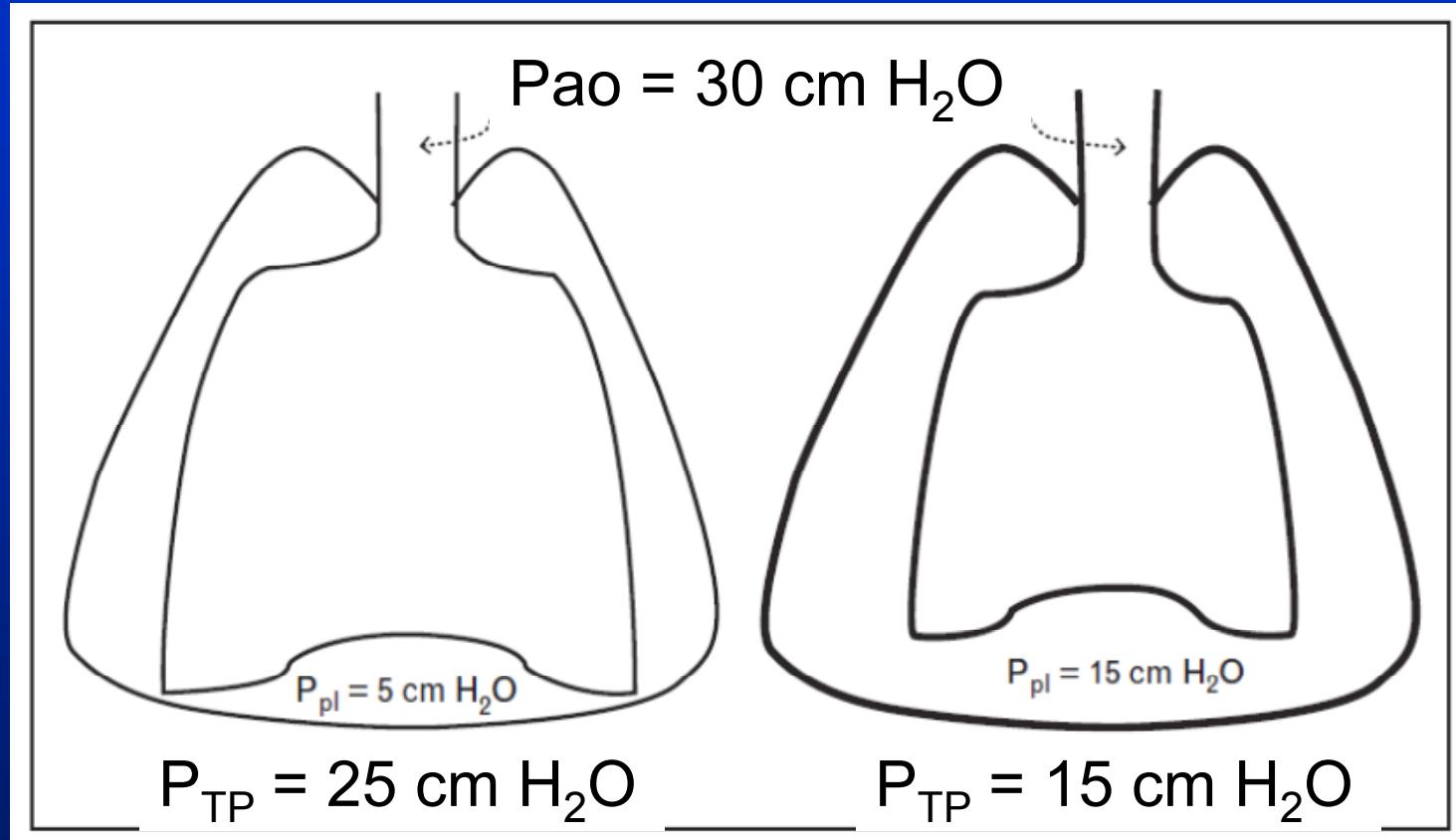
- Measure FRC
 - Computerized Tomography
 - Helium Dilution
 - Nitrogen Wash-in-Wash-out
- Set V_T to keep strain below a safe level
 - What is a safe level?

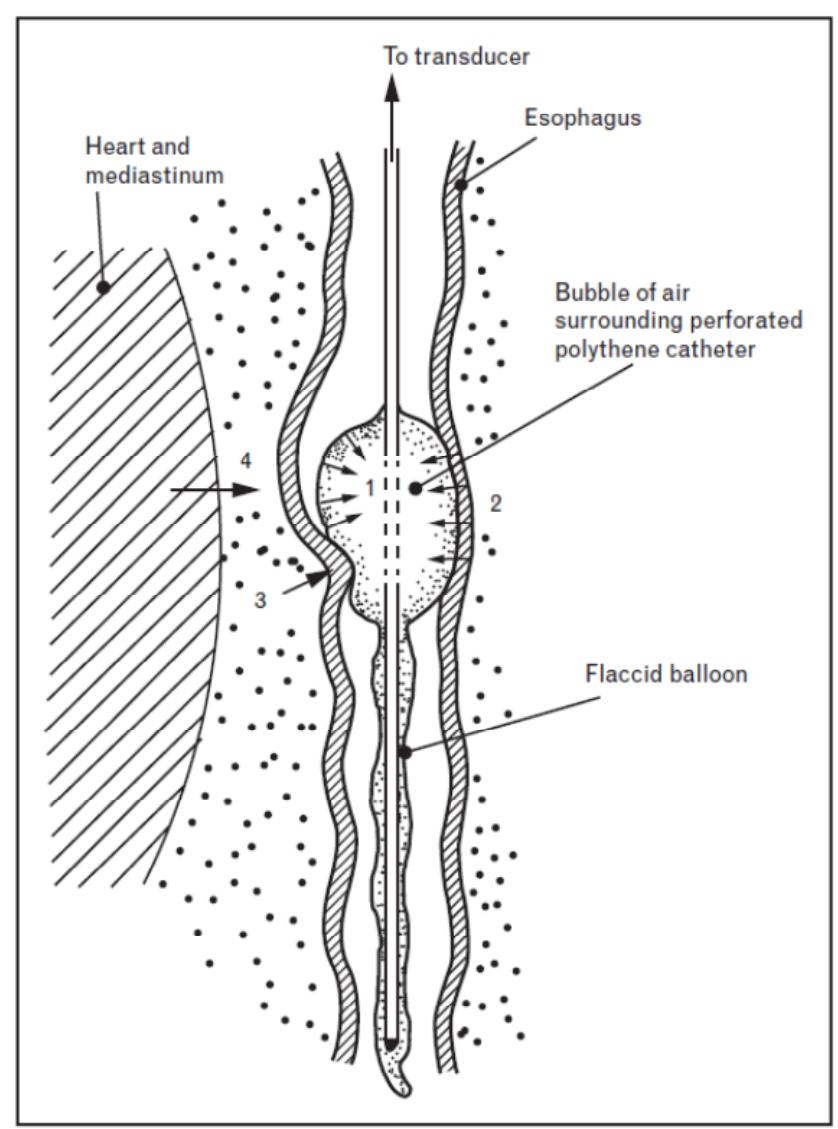
Stress



Stress = Force/Area

Airway, Pleural, and Transpulmonary Pressures

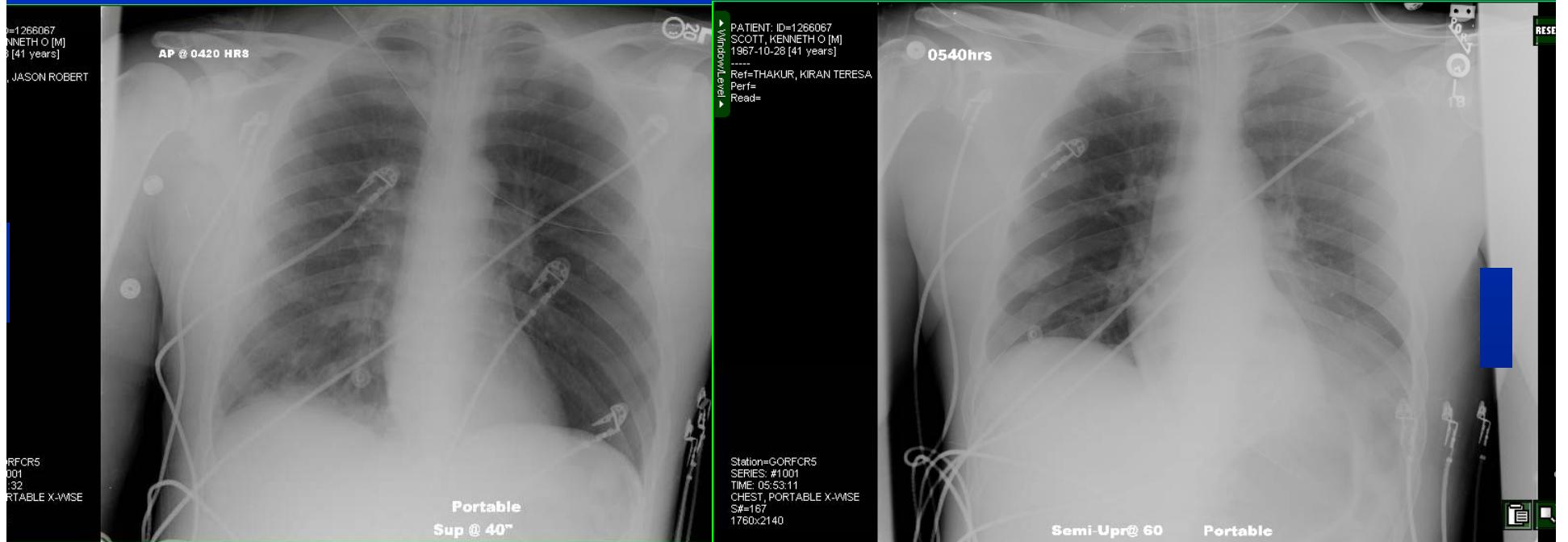




Potential sources of error in estimating pleural pressure by esophageal manometry

Gibson and Pride. Br J Dis Chest 1976

Pleural Pressures Vary by Region



January 4

January 5

Problems with P_{TP} Approach

- Requires esophageal catheter
- Pleural pressures not uniform in chest
 - Esophageal pressure not a good average
- P_{TP} goal for setting Tidal Volume = ???

The NEW ENGLAND JOURNAL of MEDICINE

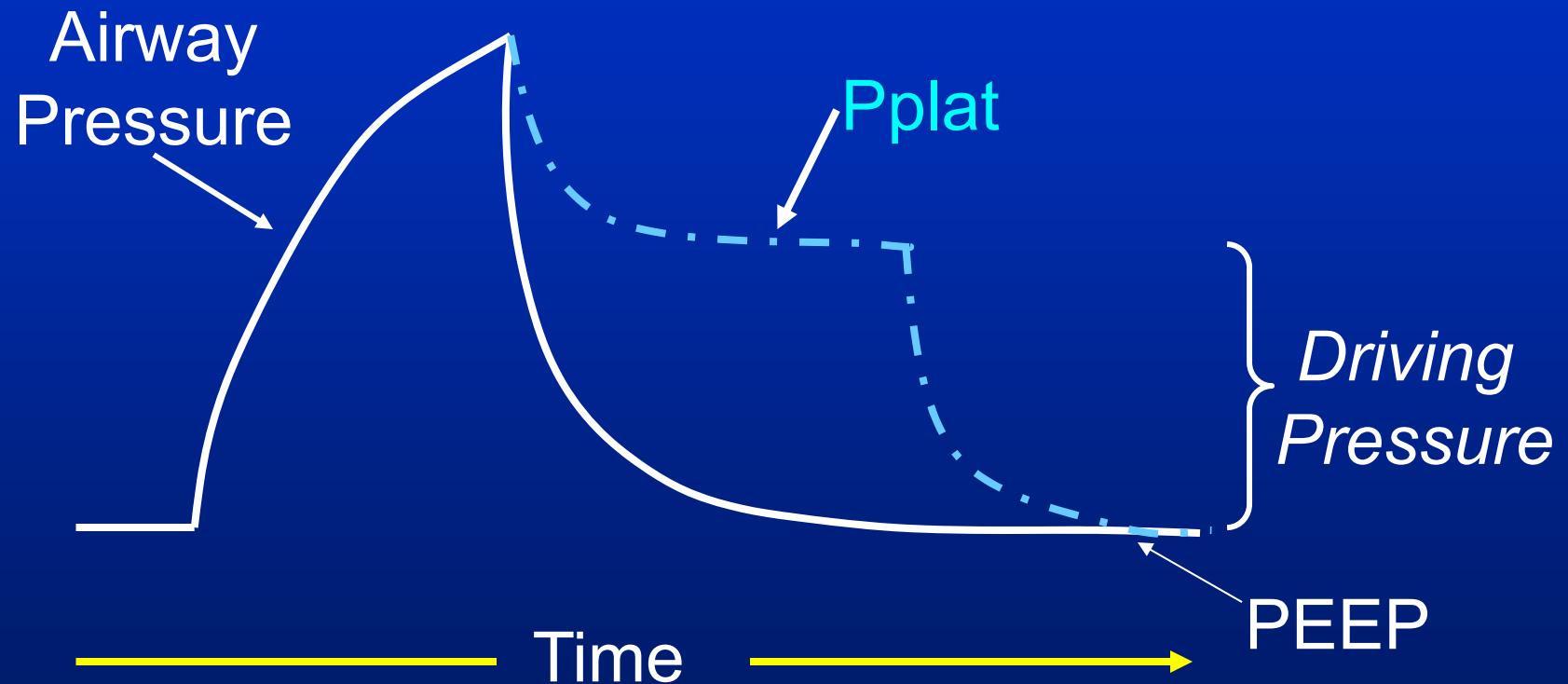
SPECIAL ARTICLE

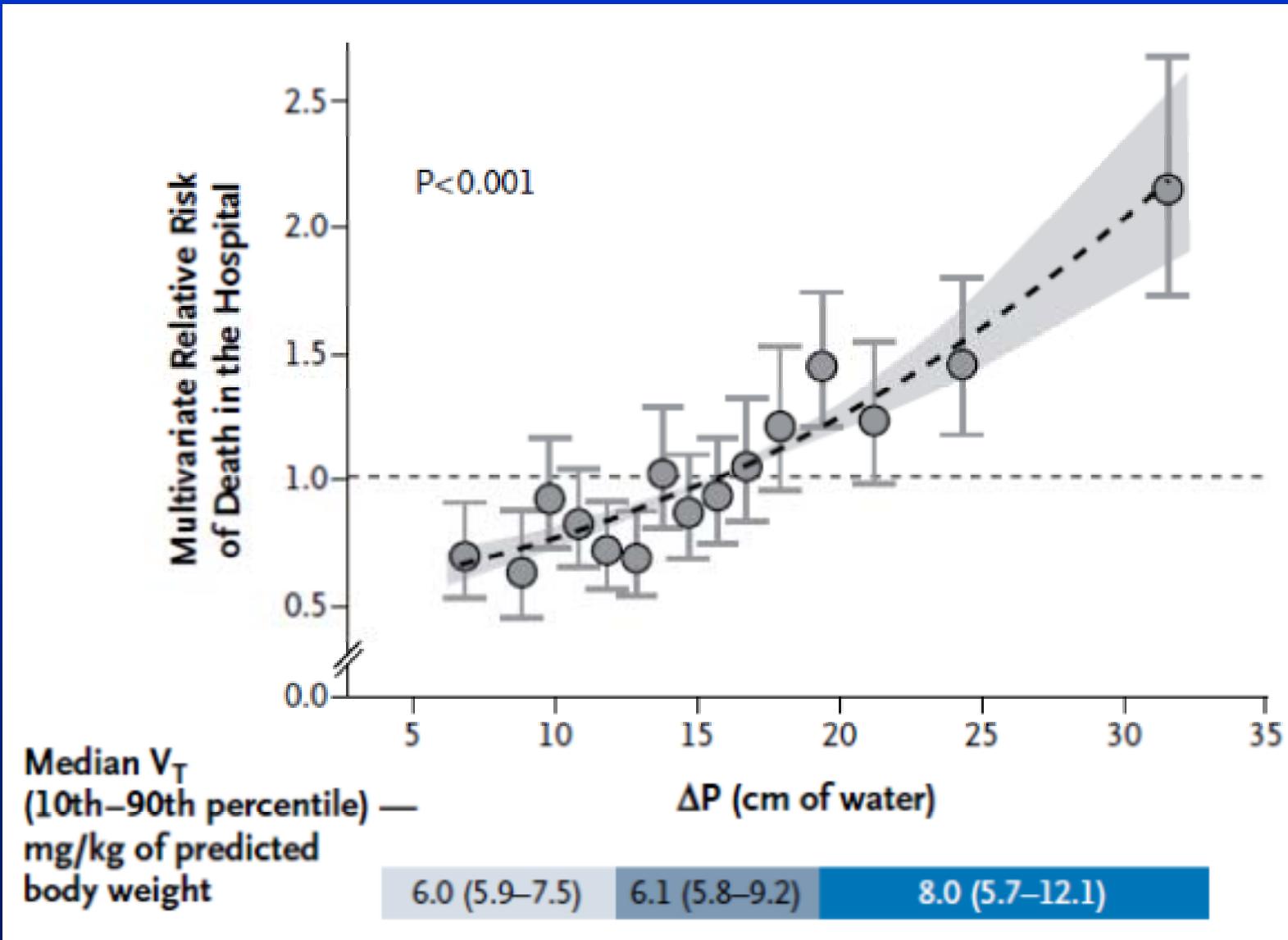
Driving Pressure and Survival in the Acute Respiratory Distress Syndrome

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.

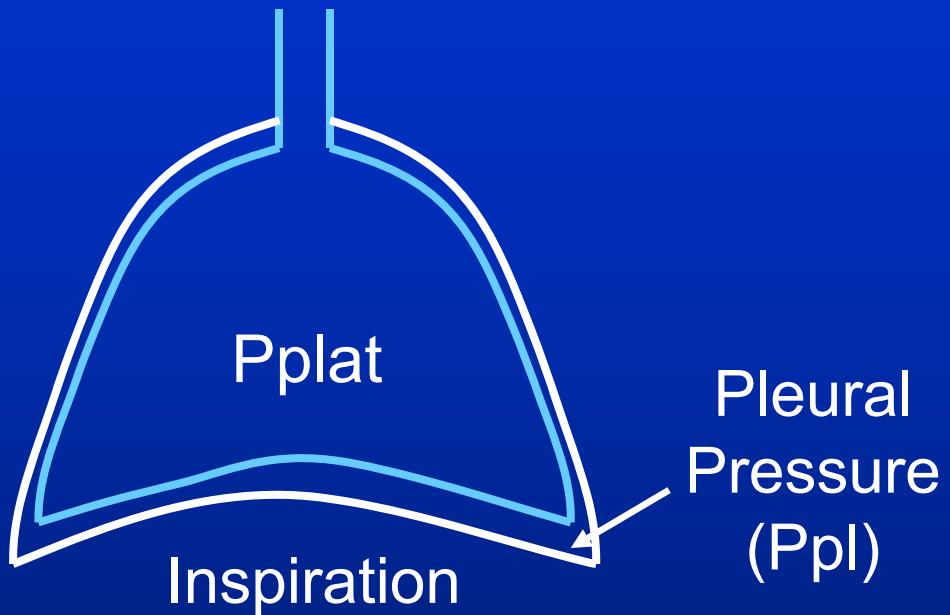
New Eng J Med 2015

Driving Pressure





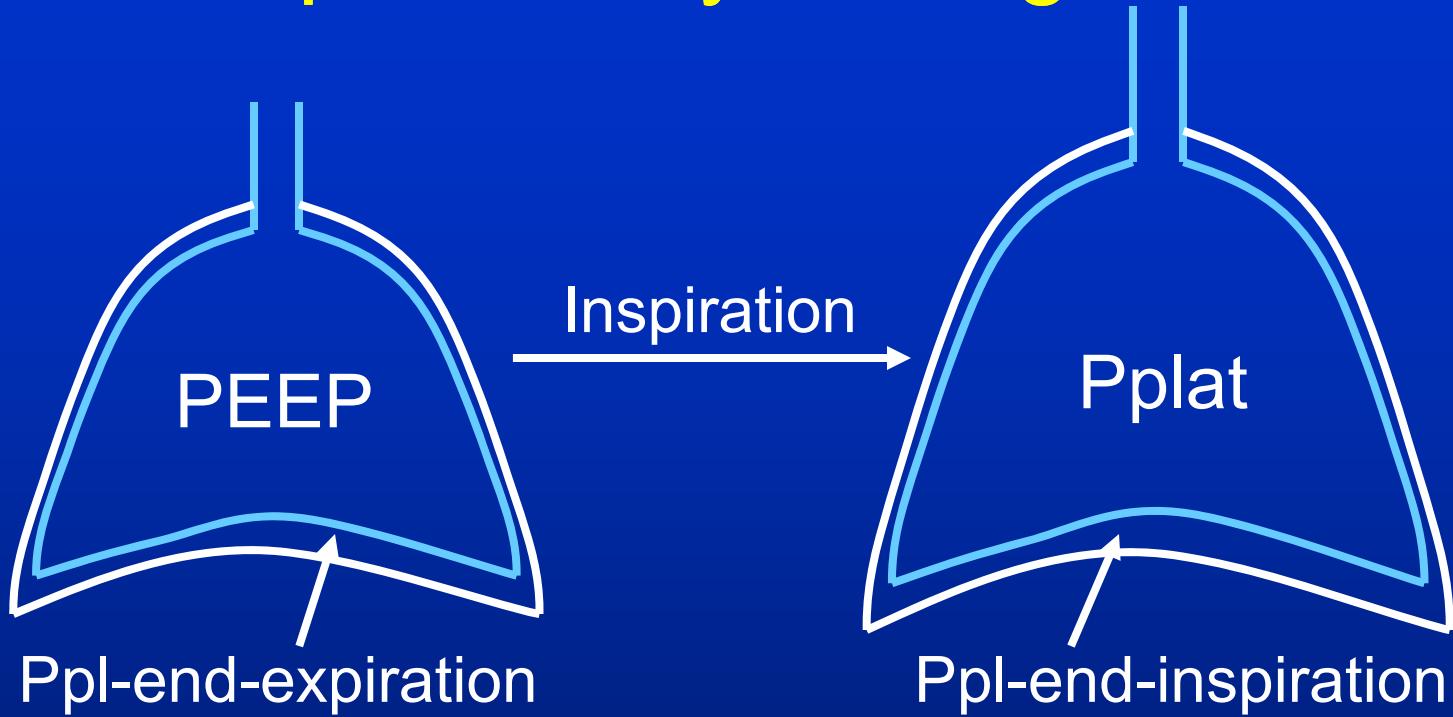
Problems with Driving Pressure Approach



P_{plat} = Distending pressure of the respir system

$P_{TP} = P_{plat} - P_{pl}$ = Distending pressure of the lung

Transpulmonary Driving Pressure



Transpulmonary Driving Pressure (ΔP_{TP})

$$P_{TP}ei - P_{TP}ee$$

$$\Delta P_{TP} = V_T/C_L$$

Problems with ΔP_{TP} Approach

- Requires esophageal catheter
 - Many assumptions
- Safe upper limit?
 - Normal: $C_L = 200$, $V_T = 400$, then
$$\Delta P_{TP} = 400/200 = 2 \text{ cm H}_2\text{O}$$
 - ARDS: $C_L = 20 - 50$, $V_T = 400$
$$\Delta P_{TP} = 8 - 20 \text{ cm H}_2\text{O}$$

How to Set V_T in ARDS

- Method must be acceptable to most clinicians
- Initial $V_T = 6 \text{ mL/kg PBW}$ (easiest)
- Reduce V_T in decrements of $\sim 0.5 \text{ ml/kg PBW}$ over several hours until signs of intolerance.

PBW vs Strain vs Stress vs Driving Pressure vs Transpulmonary Driving Pressure?

Decrease V_T until *signs of intolerance*:

- Tachycardia
- Hypertension or hypotension
- Agitation
- Tachypnea, dyssynchrony
- Acidosis
- Hypoxemia despite high FiO_2

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- $PaCO_2 = 55$, pH = 7.28
- Tidal volume decreased to 2.8 mL/kg PBW. RR 40.
- $P_{plat} = 24$, $\Delta P = 14$

Living on the Edge of the Evidence





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Lancet 1967; 2:319-323

Setting PEEP

Traditional Approach

Adjust PEEP to allow acceptable arterial oxygenation on $\text{FiO}_2 \leq .70$

$$\text{PEEP} = 5 - 12 \text{ cm H}_2\text{O}$$

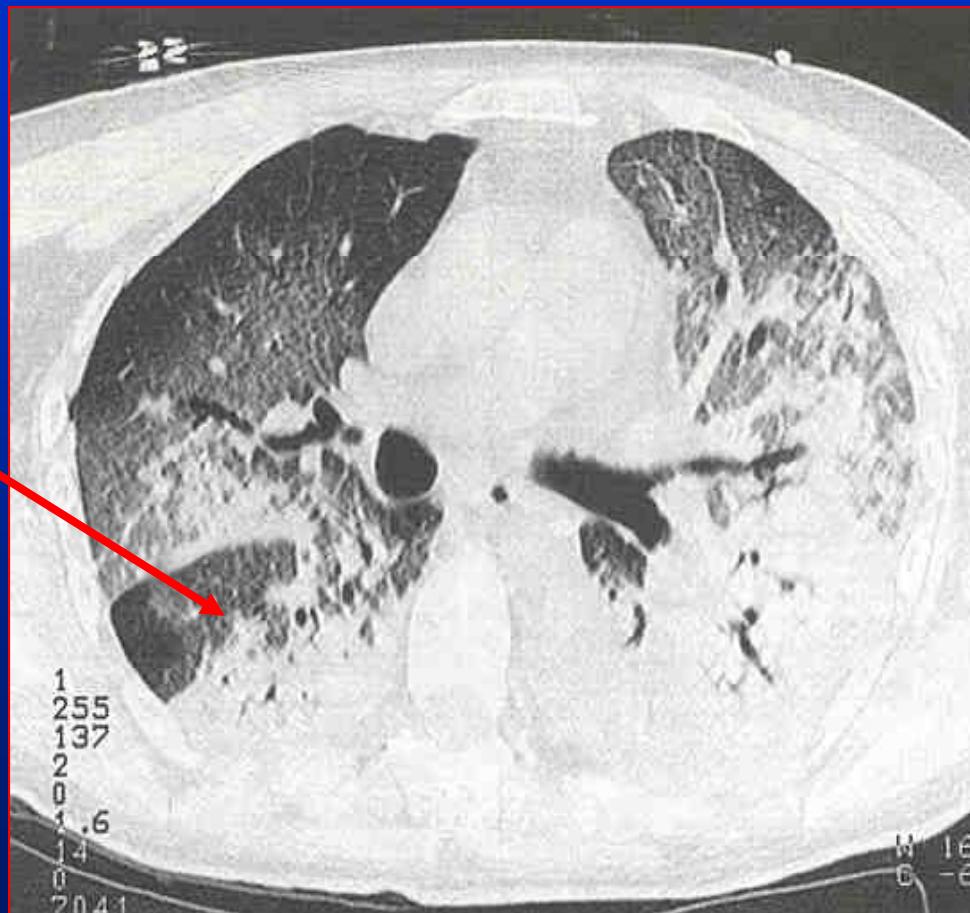
How to Set PEEP

Table of fixed combinations of PEEP and FiO₂

FiO ₂	.3	.4	.4	.5	.5	.6	.7	.7	.7	.8	.9	.9	.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	18-24

Ventilator-Induced Lung Injury

Low Volume
Low Pressure
VILI



How to Set PEEP

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PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	18-24

Higher PEEP/Lower FiO₂

FiO ₂	.3	.3	.4	.4	.5	.5	.5-.8	.8	.9	1.0
PEEP	12	14	14	16	16	18	20	22	22	22-24

4 Higher PEEP Trials

	% Mortality	
	<u>Higher PEEP</u>	<u>Lower PEEP</u>
ARDSNet (549)	27.5	24.9
Canadian (983)	36.4	40.4
French (767)	35.4	39.4
<u>ART (1010)</u>	<u>55.3*</u>	<u>49.3</u>
Combined (3309)	40.4	40.2

ARDSnet NEJM 2004 Meade JAMA 2008
Mercat JAMA 2008 Cavalcanti JAMA 2017

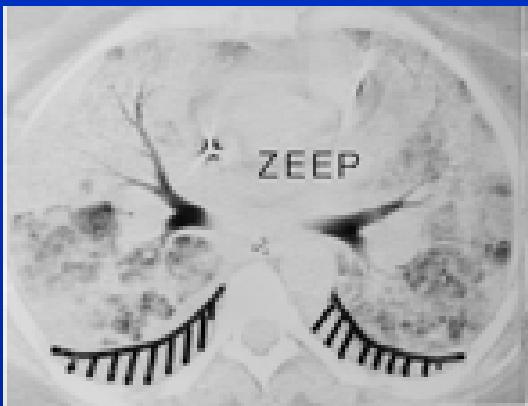
Why Mortality Not Lower with Higher PEEP?

Effects of Higher PEEP in each patient

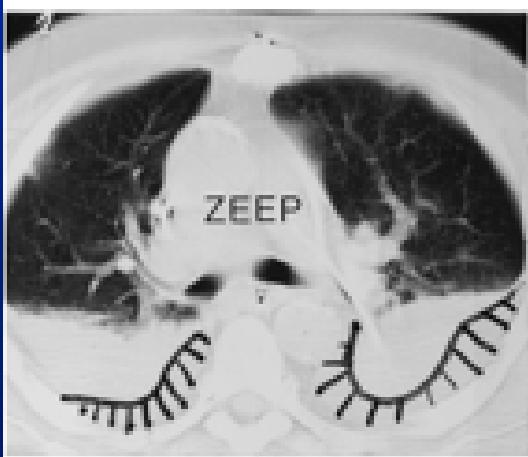
- Reduce VILI from Low volume/Low pressure
- Increase VILI from Overdistention

Effects of PEEP are Variable Among Patients

Diffuse



Recruitment



Overdistention

Recruitment

Overdistention

Lobar

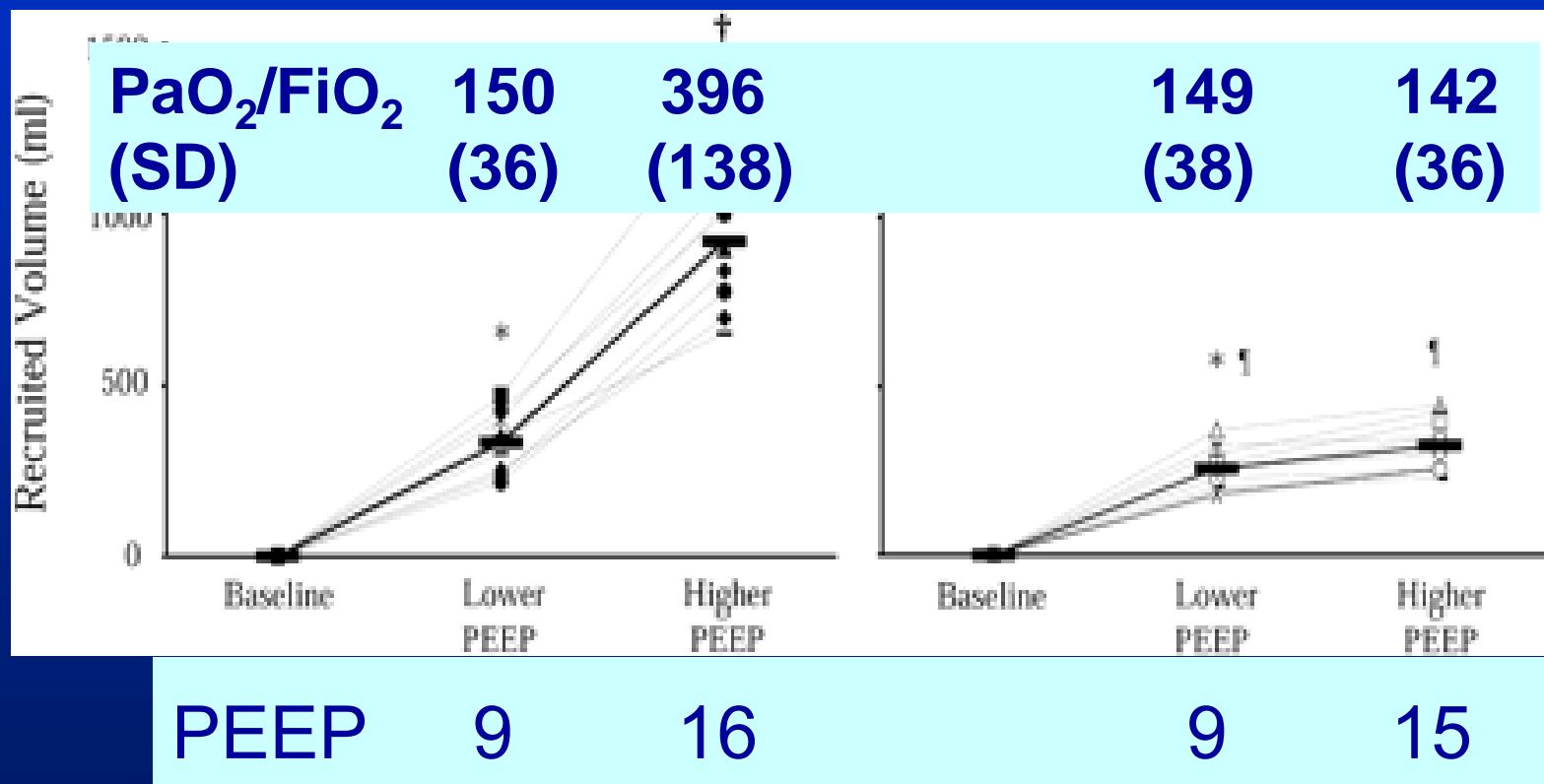


- Who are the PEEP responders?
- How much PEEP in responders?
- When to decrease PEEP in responders?
- How much PEEP in nonresponders?

Effects of PEEP

Responders

Nonresponders



Grasso et al. Am J Resp Crit Care Med 2005; 171: 1002-1008

Lower PEEP → Higher PEEP Tables

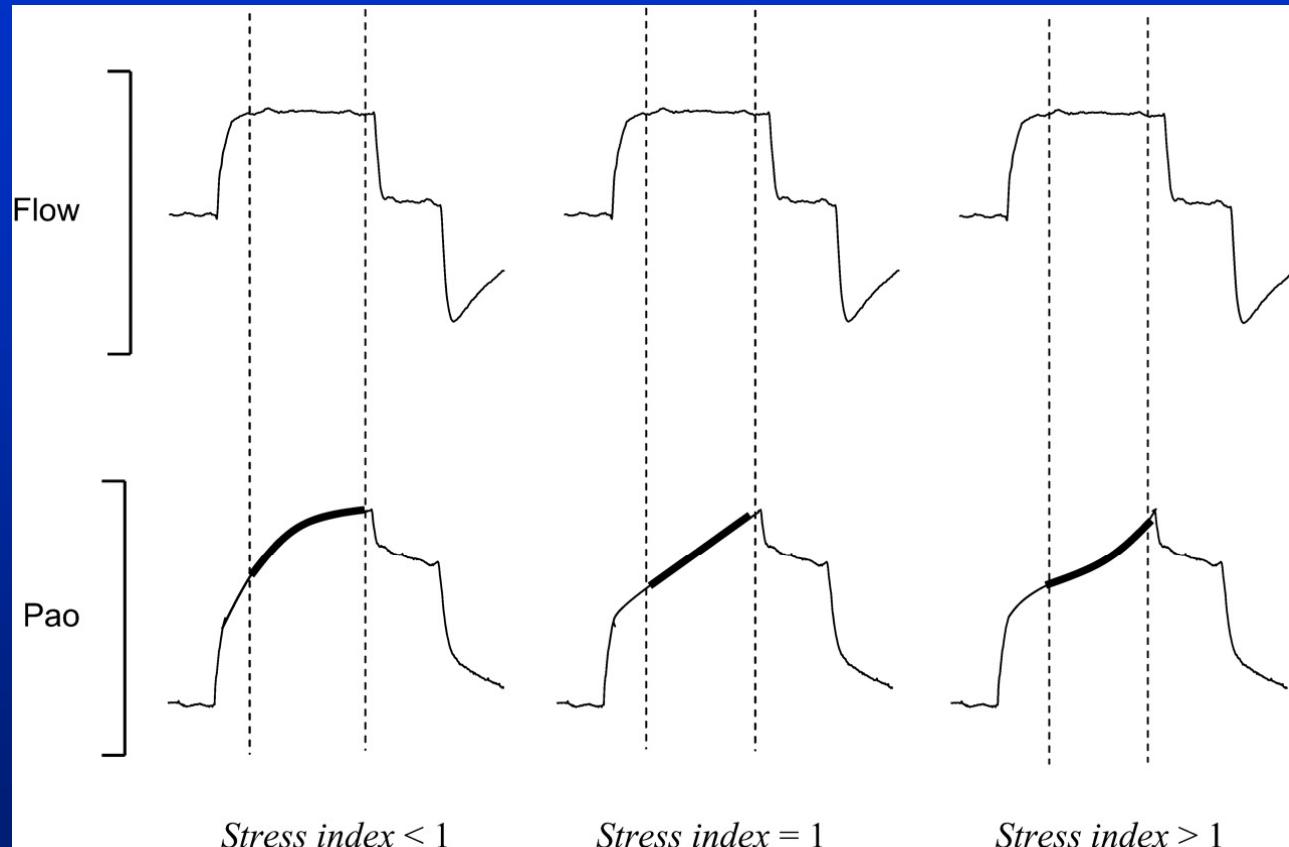
- Easy to identify PEEP responders
- No special equipment
- Optimal PEEP?
- Some patients may need lower PEEP than they receive on the lower PEEP table

EXPRESS PEEP

- Raise PEEP until inspiratory Pplat approaches 30 cm H₂O
 - Greater Ventilator-free days
 - Mortality NS but favorable trend

Mercat et al
JAMA 2008

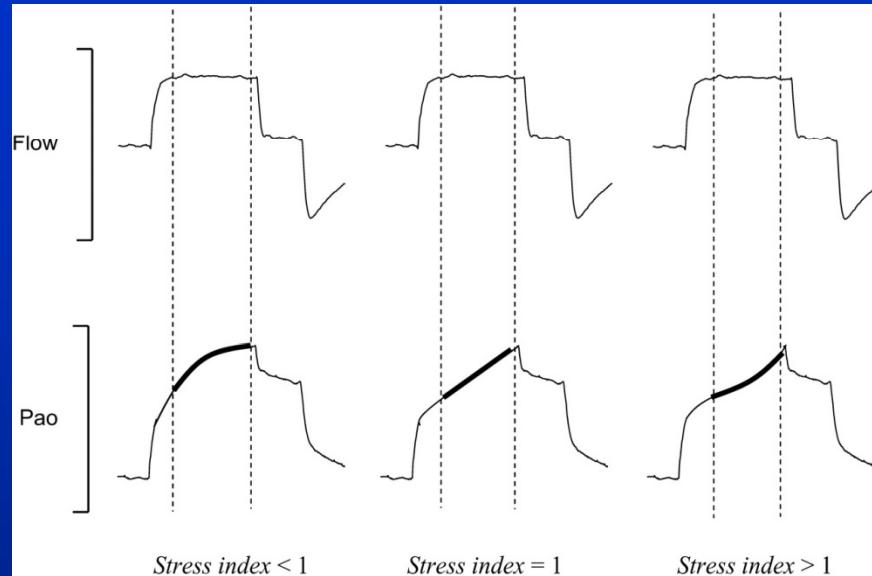
Stress Index



$$Pao = a \cdot \text{inspiratory time}^b + c$$

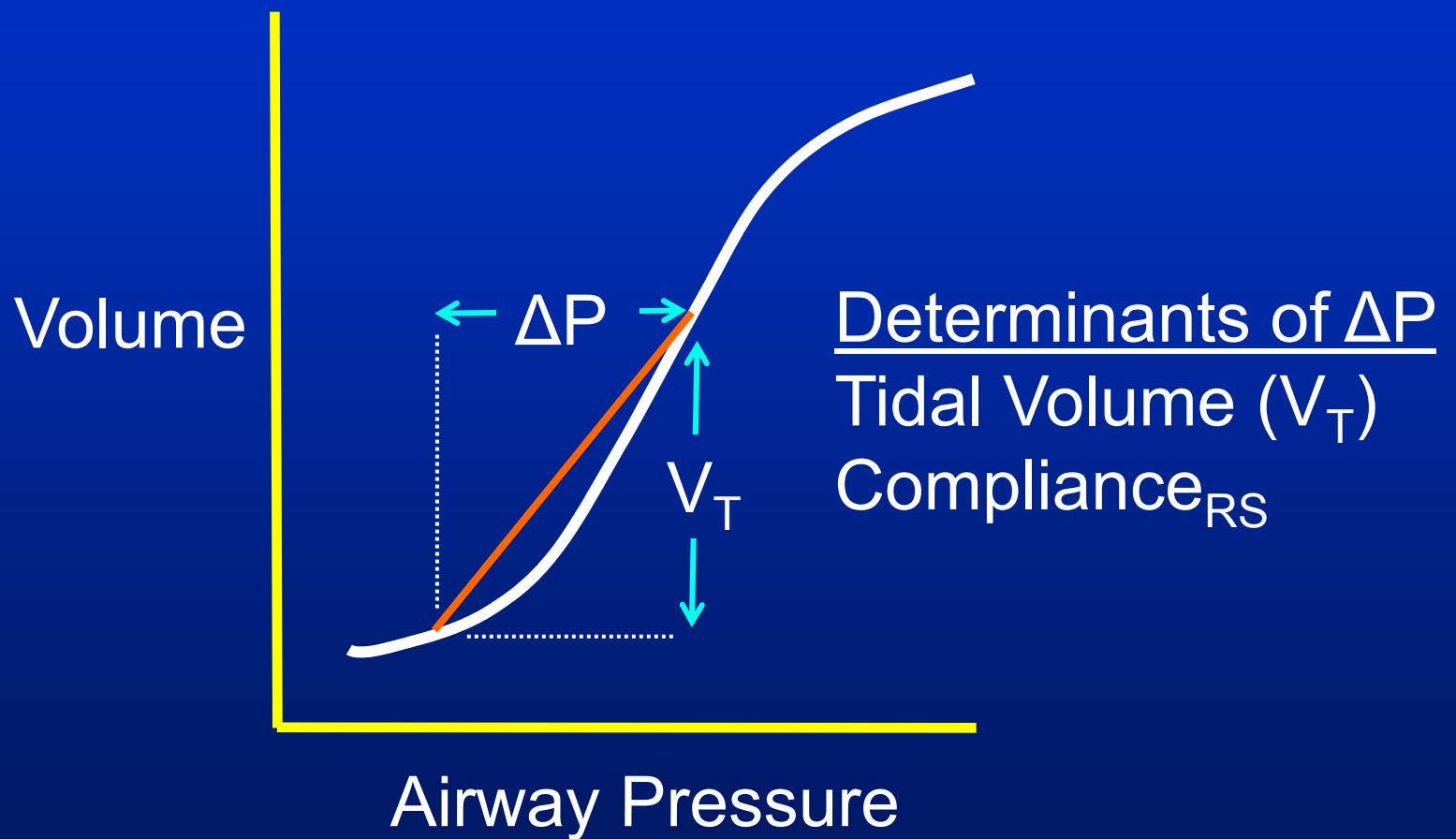
Grasso S et al. Am J Resp Crit Care Med 2007;176:761-767

Stress Index



- Special monitoring equipment needed
- Must be relaxed during inspiration

Driving Pressure (ΔP)



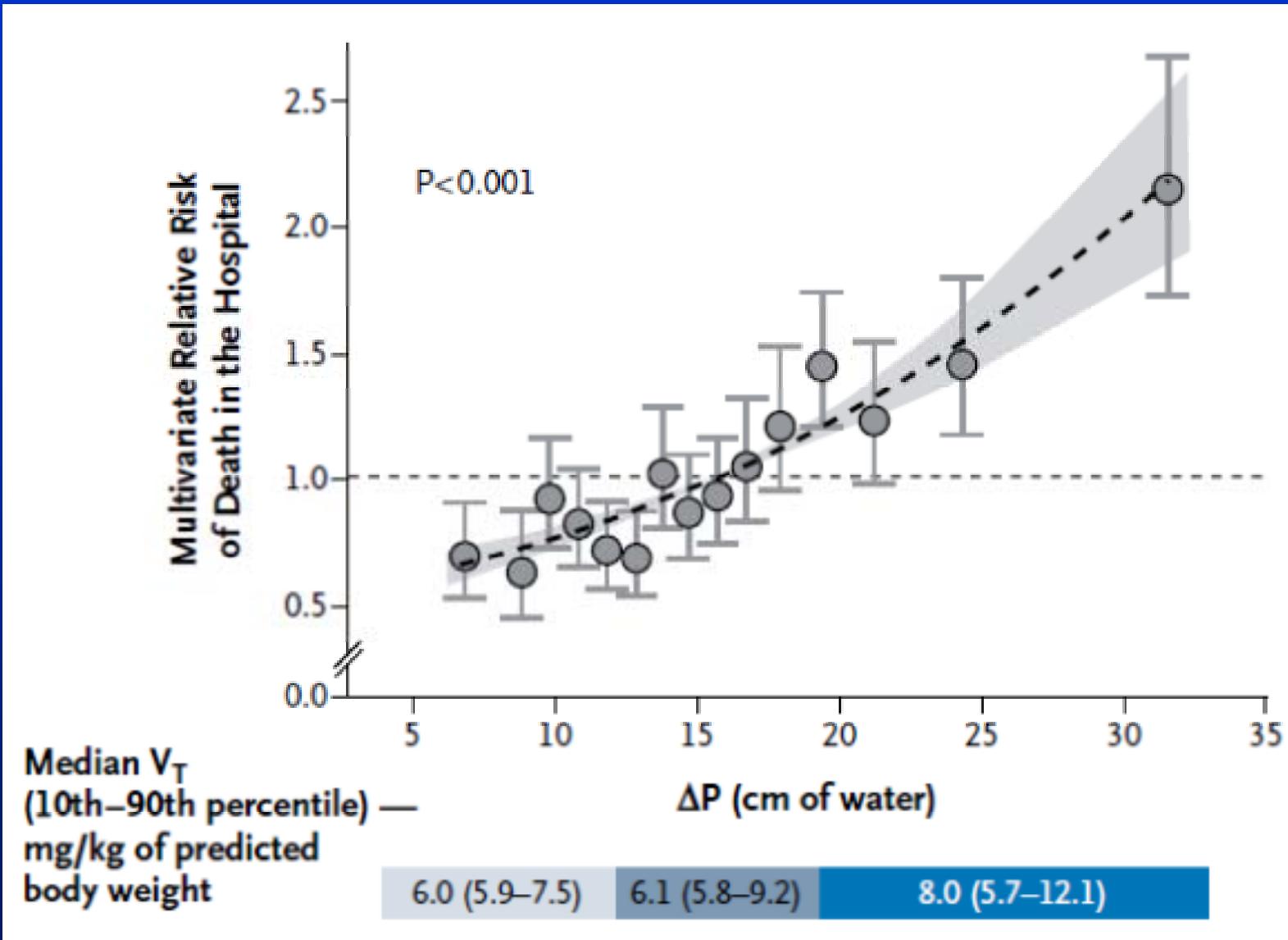
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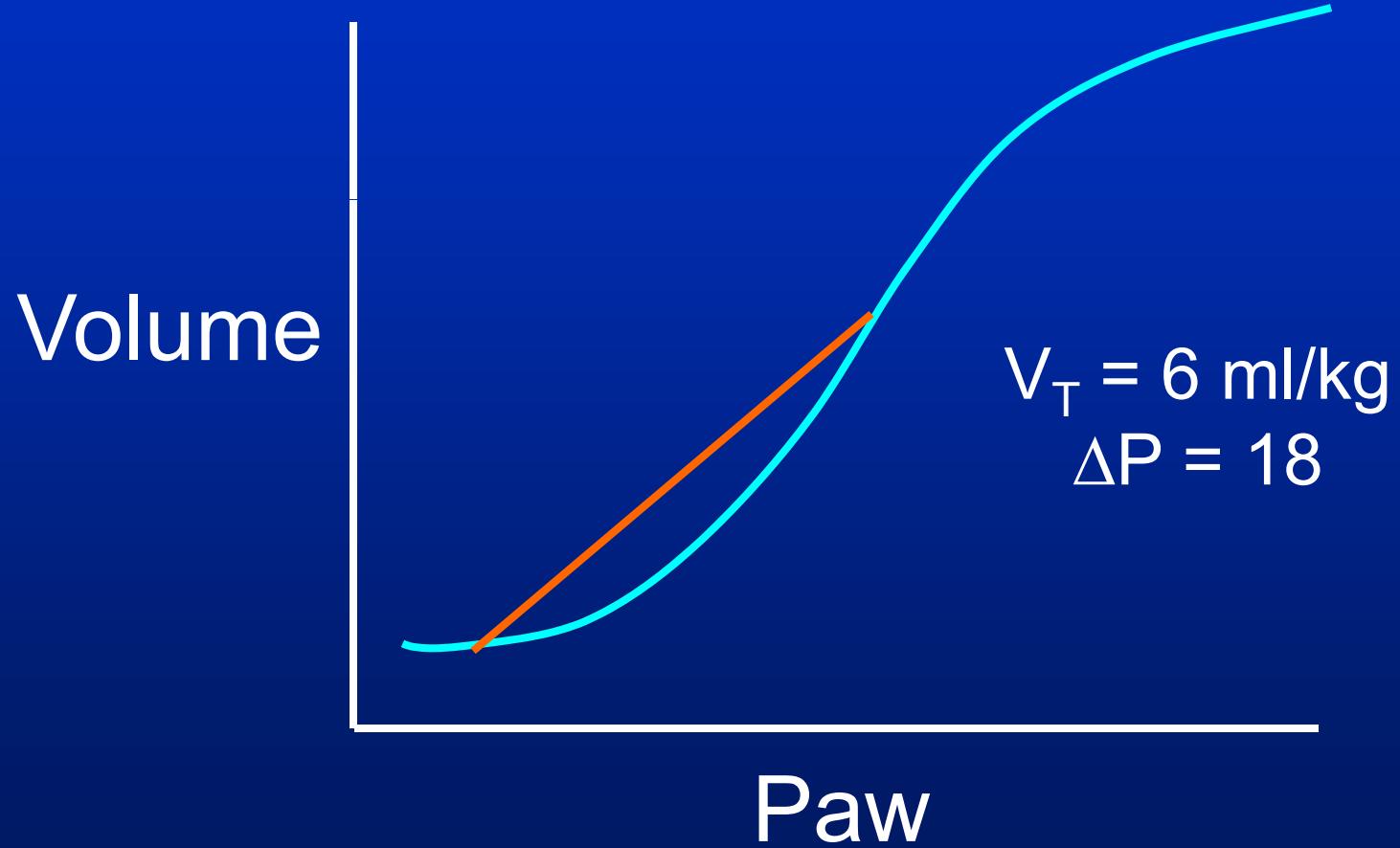
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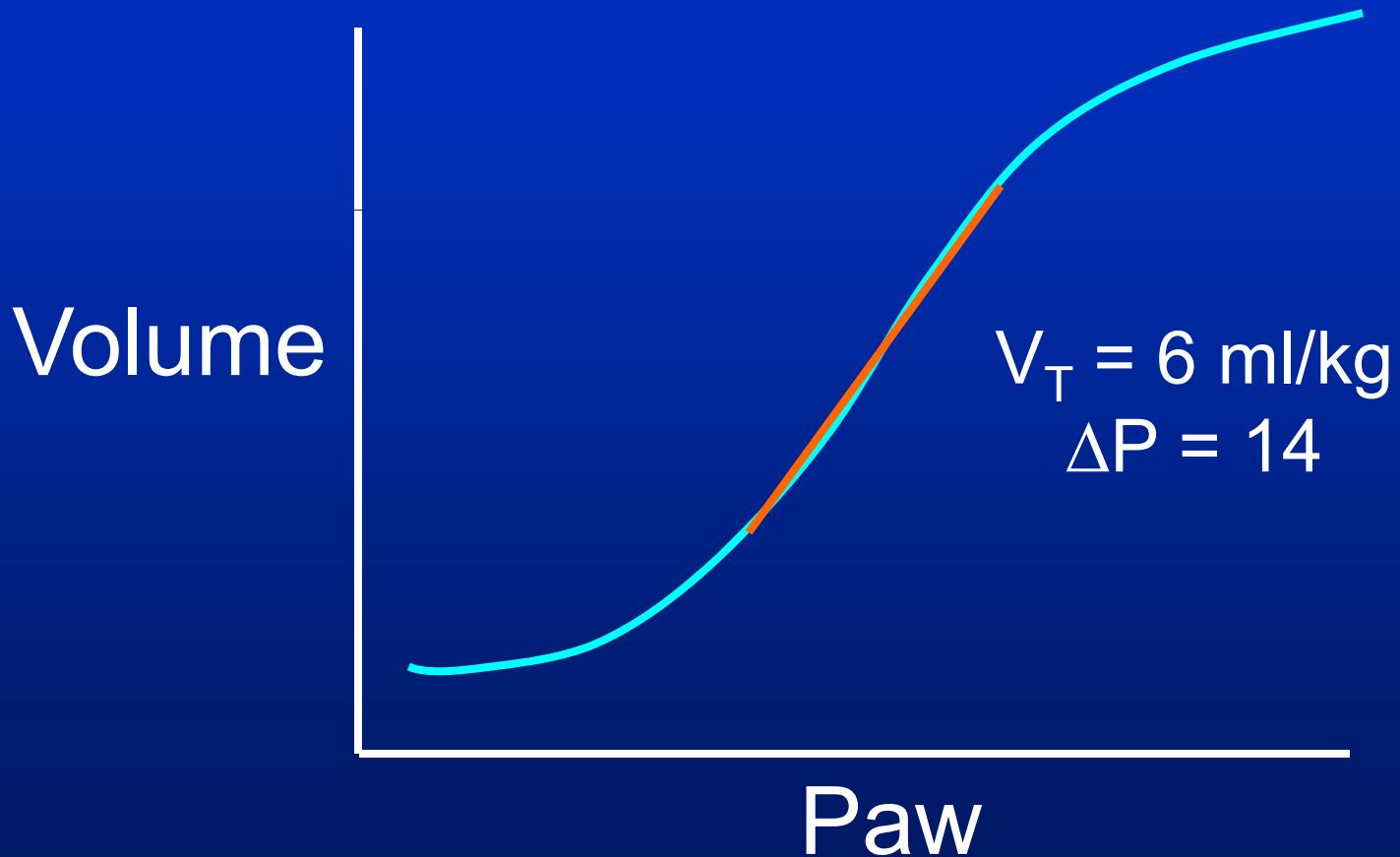
New Eng J Med 2015



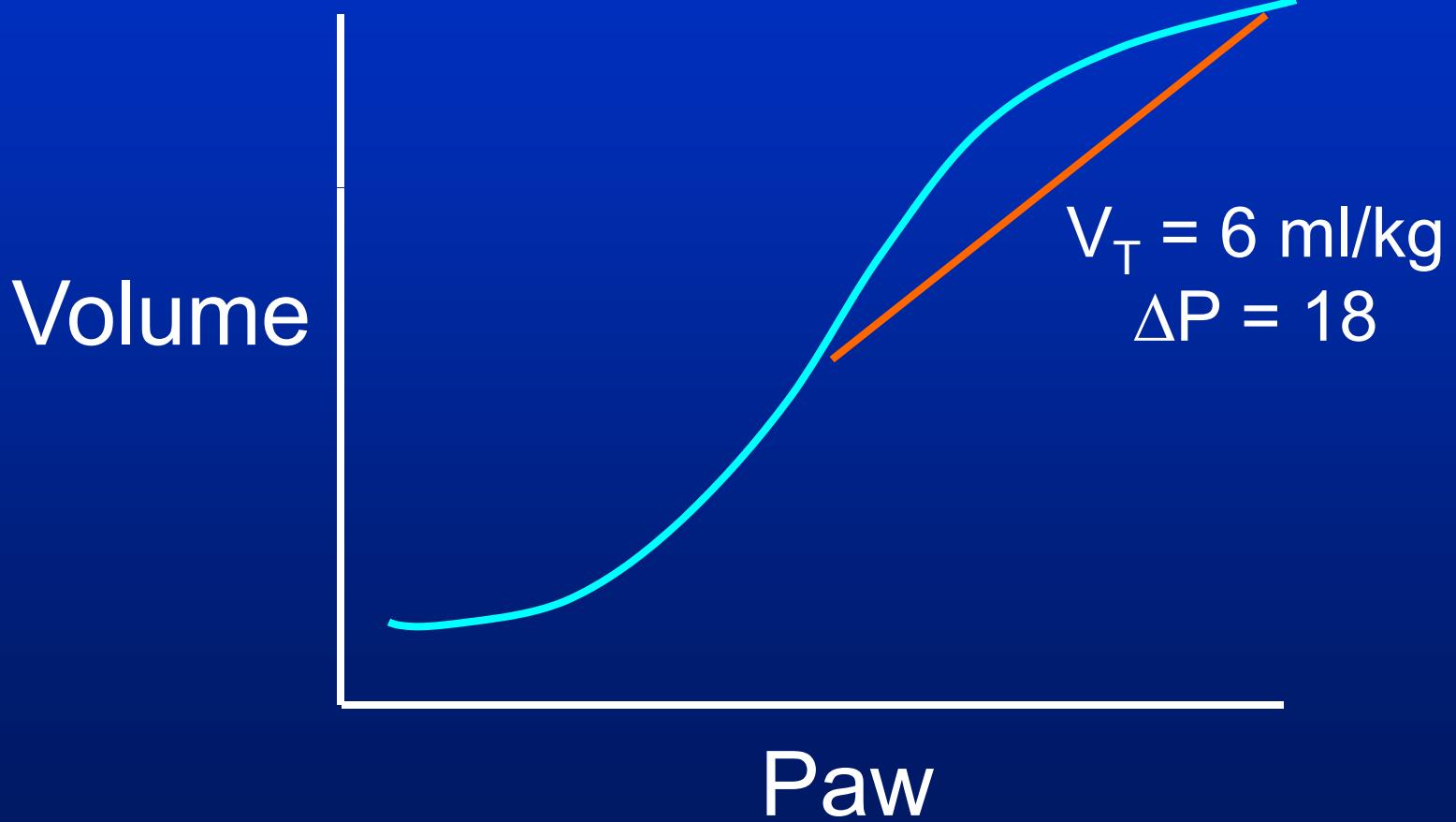
ΔP -Guided PEEP



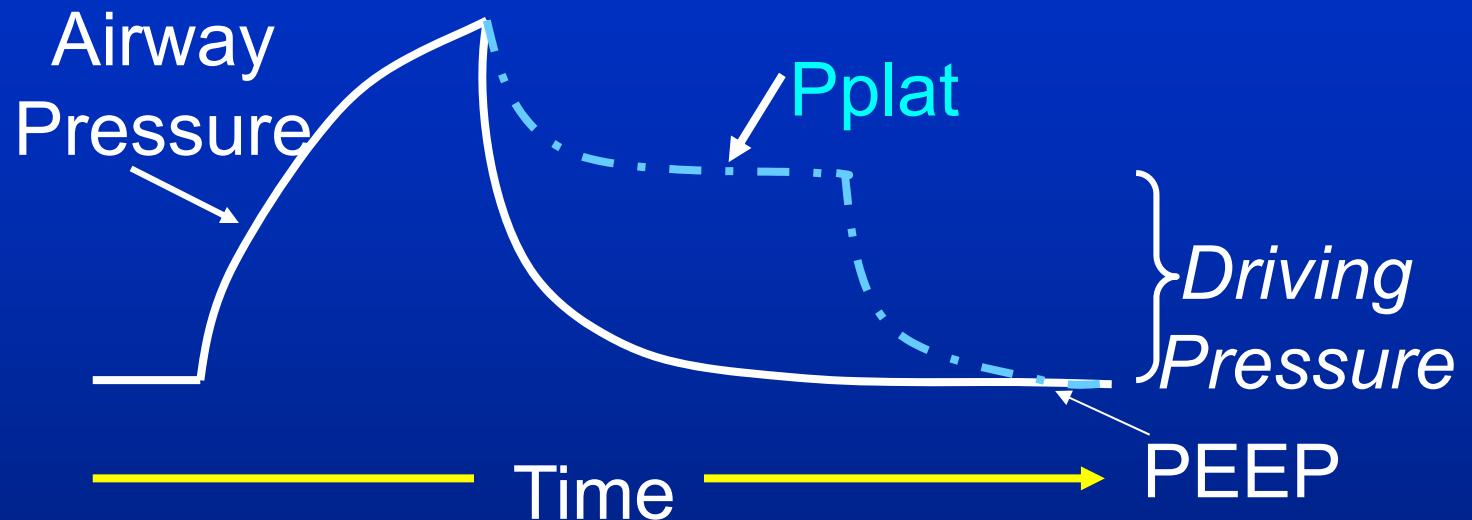
ΔP -Guided PEEP



ΔP -Guided PEEP



Driving Pressure



- Special monitoring equipment not needed
- Inspiratory efforts OK
- Patient must be relaxed during exhalation

Higher PEEP to More Recruitable Lung and Lower PEEP to Less Recruitable Lung

- Table of fixed combinations of PEEP and FiO_2 YES
- Raise PEEP until P_{plat} approaches 30 cm H_2O No
- Raise PEEP until transpulmonary pressure > 0 No
- Adjust PEEP to Stress Index = 1.0 No
- Adjust PEEP to minimize Driving Pressure ?

Chiumello D
Crit Care Med 2014

How to Set PEEP

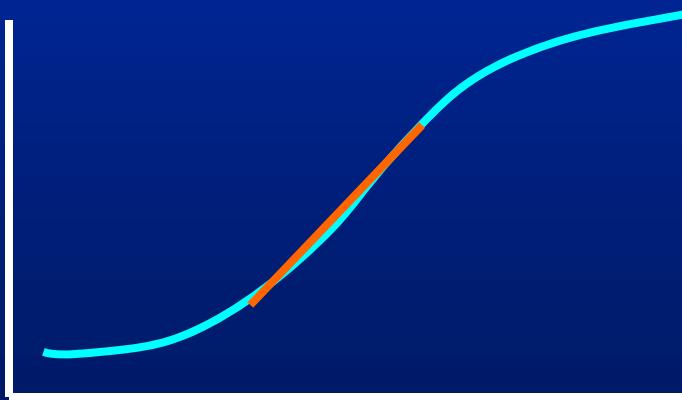
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PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	18-24



Thank You





Thank You



Trials of Lung-protective Mechanical Ventilation

Clinical Trials (3562 Patients)

1. Amato NEJM 1998 – Lower V_T + Higher PEEP
2. Stewart NEJM 1998 – Lower V_T
3. Brochard AJRCCM 1998 – Lower V_T
4. Brower CCM 1999 – Lower V_T
5. ARDS Network NEJM 2000 - Lower V_T
6. ARDS Network NEJM 2004 – Higher PEEP
7. Mercat JAMA 2008 – Higher PEEP
8. Meade JAMA 2008 – Higher PEEP
9. Talmor NEJM 2008 – Pes guided higher PEEP

Model Variables

Patient variables

Days on mech vent

Age

APACHE III (1.31)

Organ failures

Arterial pH (0.64)

PaCO₂

PaO₂/FIO₂

Tidal-compliance

Mech Vent Variables

Tidal volume

Plateau pressure

PEEP

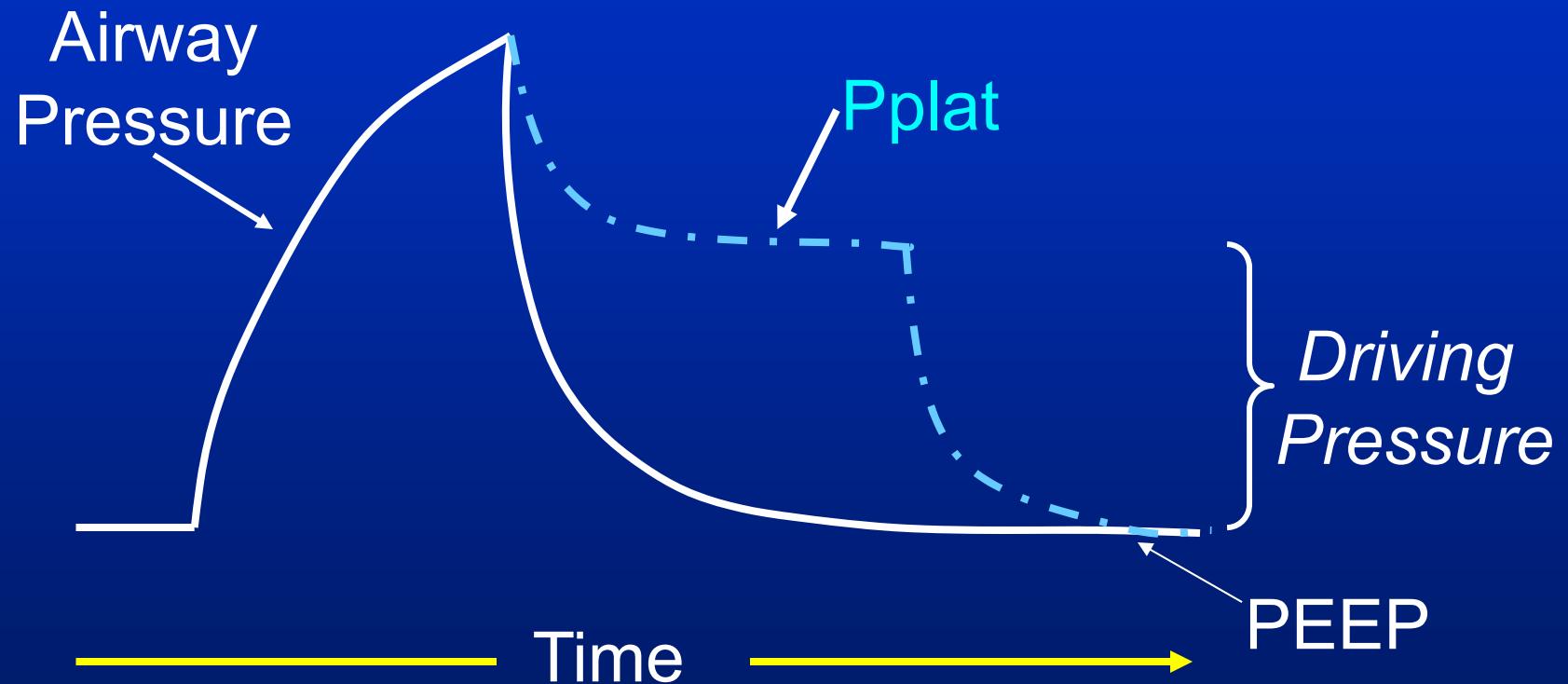
FiO₂ (1.32)

Respiratory rate

Mean airway pressure

ΔP (Pplat – PEEP) (1.47)

Driving Pressure



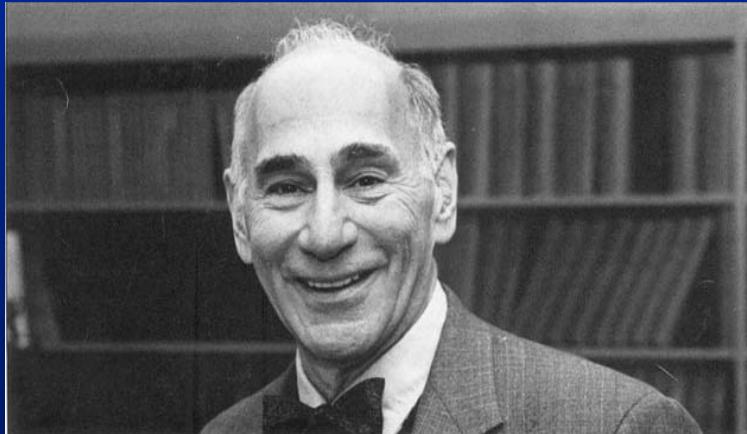
Reprinted from JOURNAL OF APPLIED PHYSIOLOGY
Vol. 21, No. 5, September, 1966
Printed in U.S.A.

Effect of ventilation on surface forces in excised dogs' lungs^{1,2}

EDMUND E. FARIDY,³ SOLBERT PERMUTT,
AND RICHARD L. RILEY

*Department of Environmental Medicine, Johns Hopkins University,
Baltimore, Maryland*

22
to Roy —
Important, if true!!!
Sol

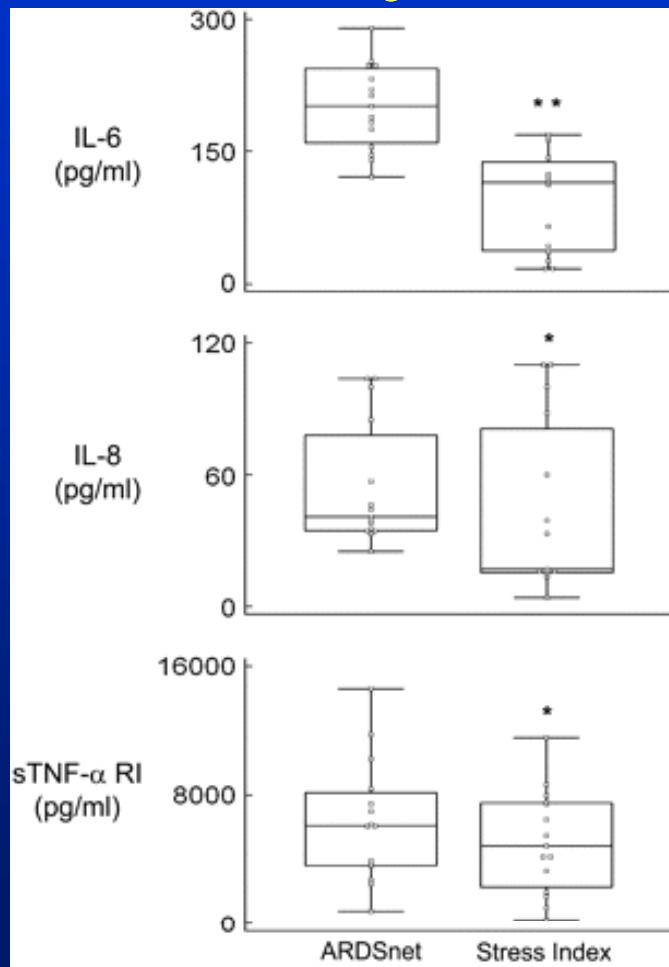


Sol Permutt

Mechanical Ventilation and ARDS

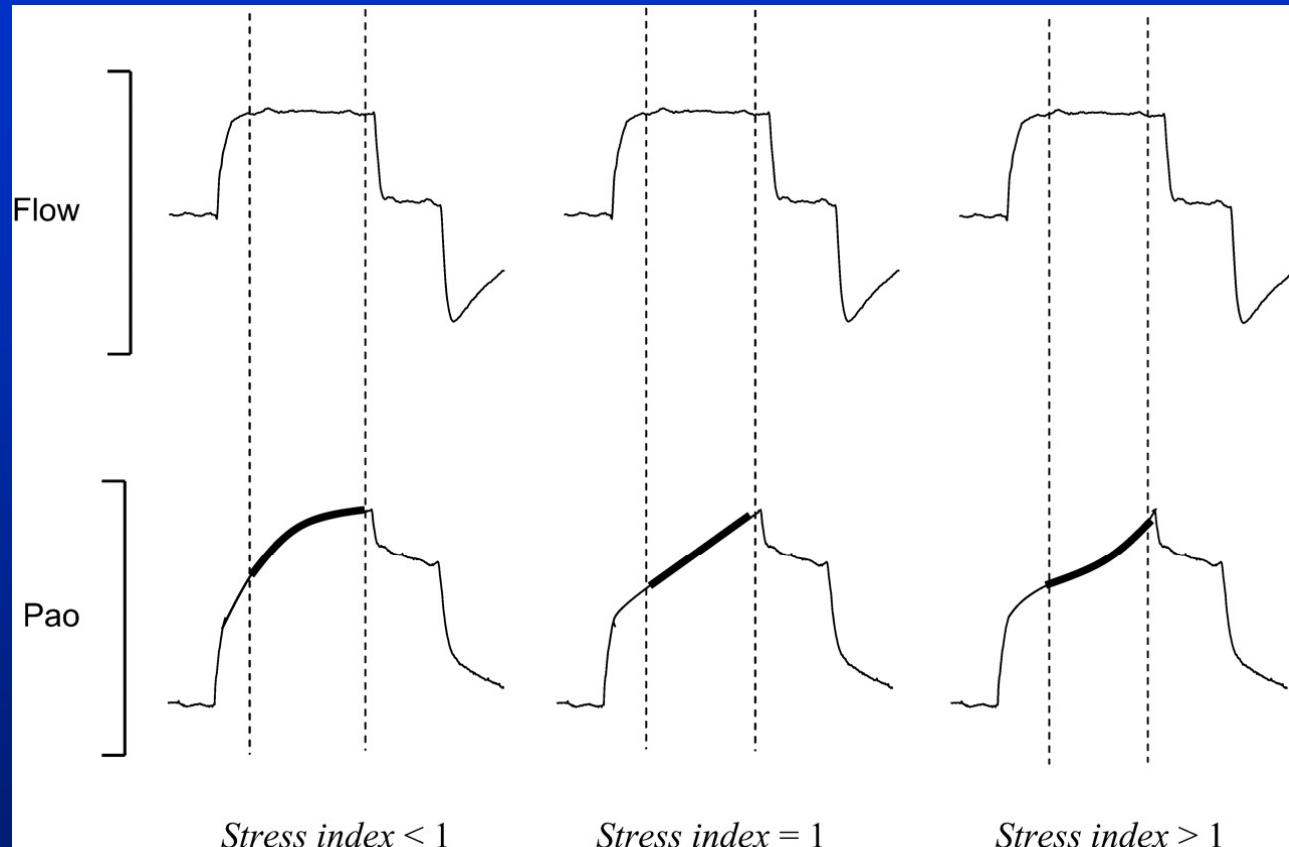
- Critical for survival
 - ensure gas exchange
 - buy time ...
- Can cause lung injury
 - may prevent recovery

Effects of Lower-lower PEEP on Inflammatory Mediators



Grasso S et al.
Am J Resp Crit Care
Med 2007;
176:761-767

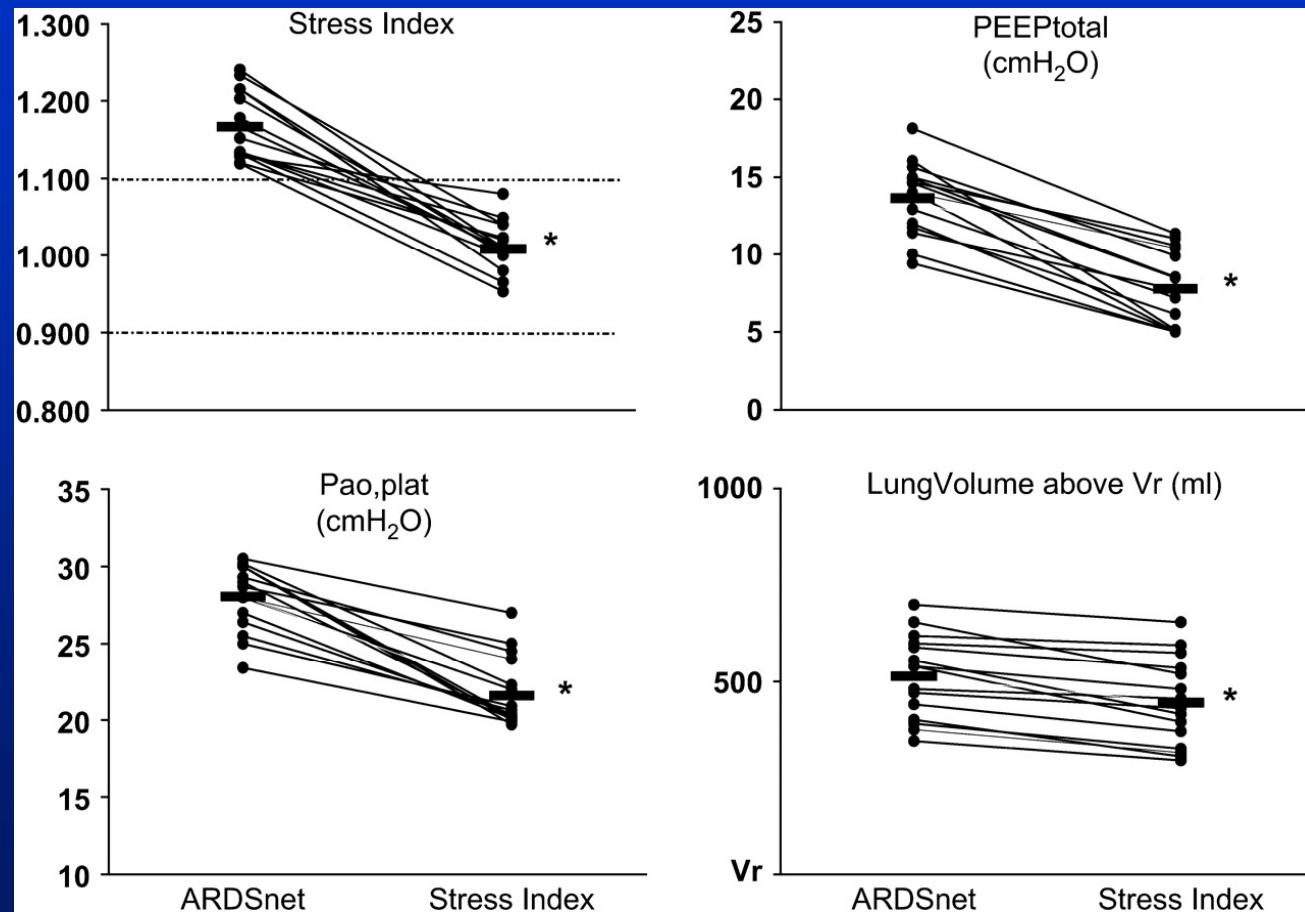
Stress Index



$$Pao = a \cdot \text{inspiratory time}^b + c$$

Grasso S et al. Am J Resp Crit Care Med 2007;176:761-767

Stress Index in “Lobar” ARDS PEEP, Pplat, and Lung Volume



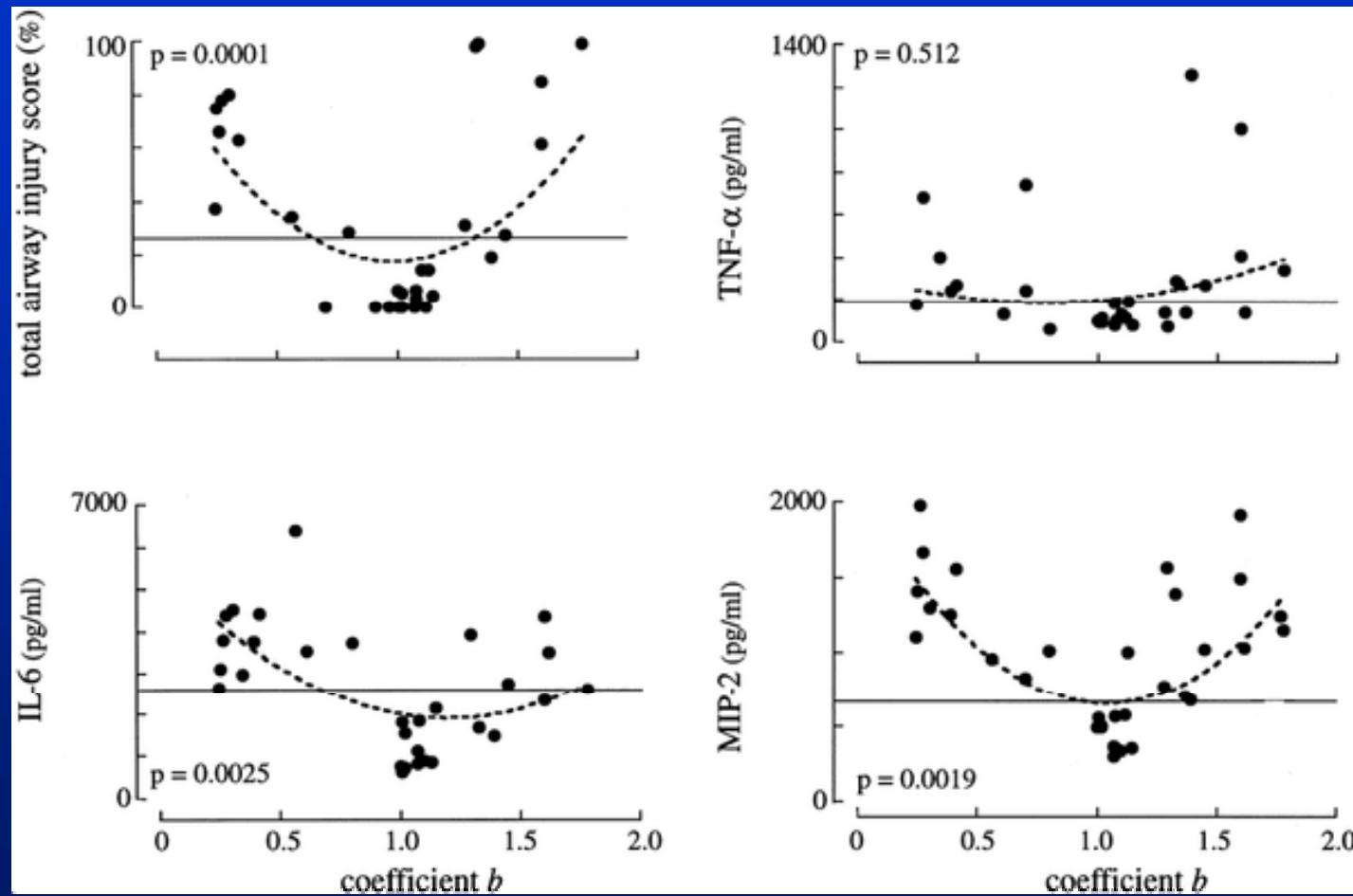
Grasso S et al. Am J Resp Crit Care Med 2007;176:761-767

Effects of Lowering PEEP on Gas Exchange in Lobar ARDS

	<u>ARDSNet Table</u>	<u>Stress Index</u>
PaO ₂ /FiO ₂	122 ± 44	110 ± 32 (NS)
PaCO ₂ (mm Hg)	46 ± 6	42 ± 6 (<0.01)

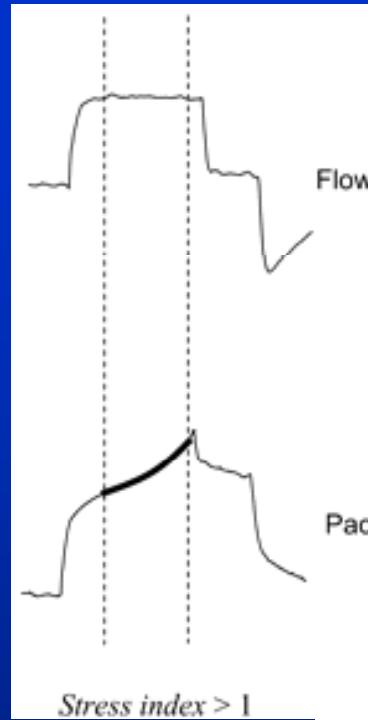
Grasso S et al. Am J Resp Crit Care Med 2007;176:761-767

Stress Index Predicts Lung Injury



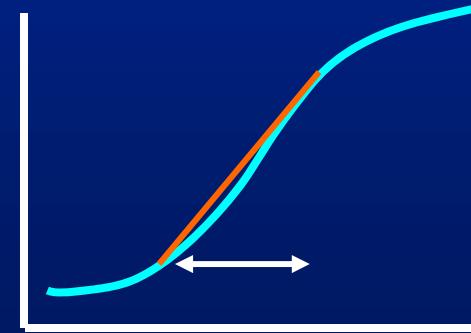
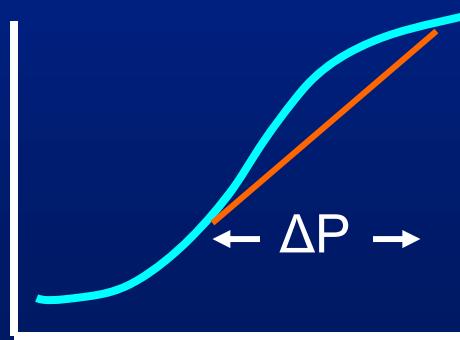
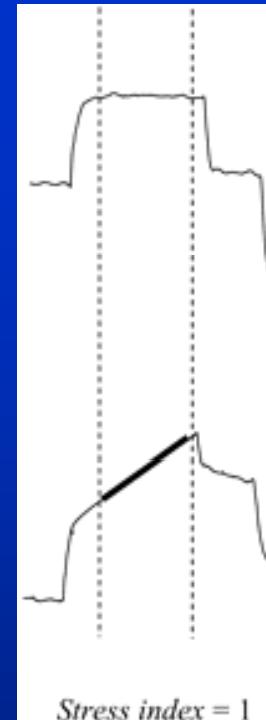
Ranieri et al. Anesthesiology. 2000 Nov;93(5):1320-8.

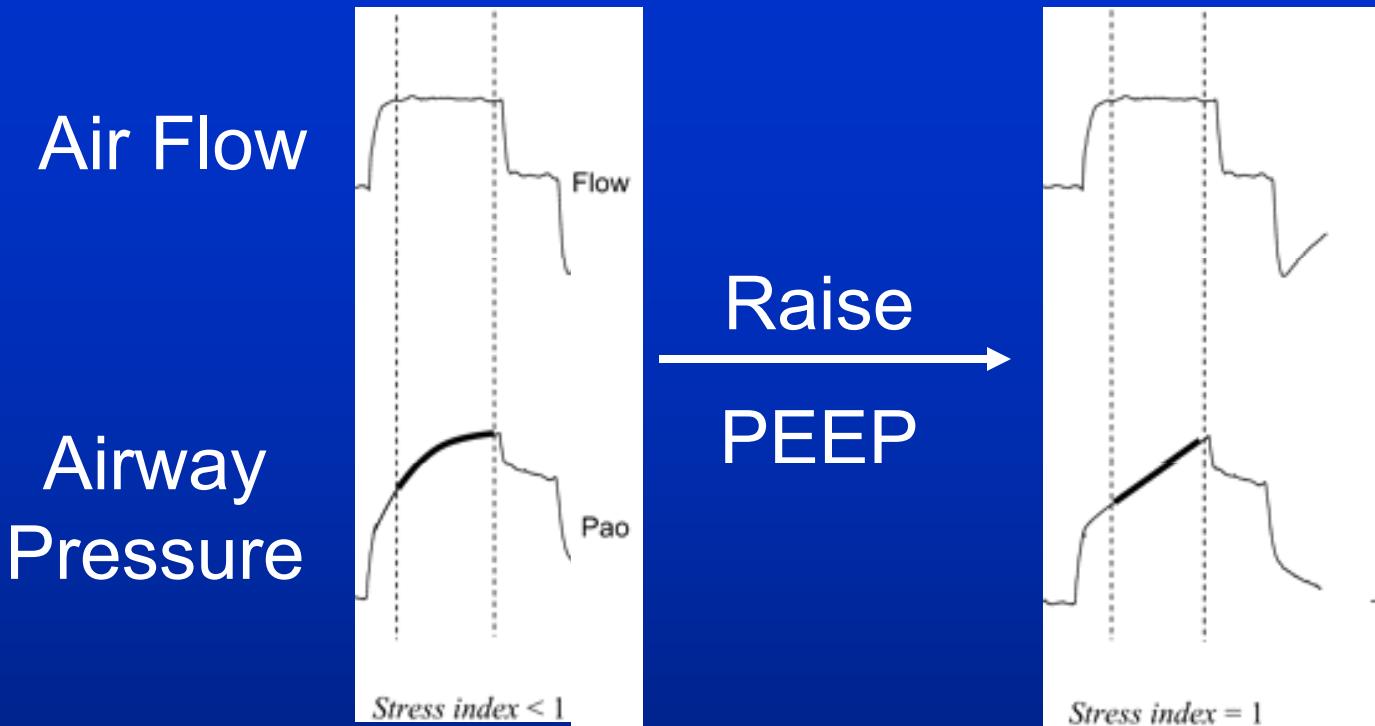
Air Flow



Airway Pressure

Decrease
PEEP





Grasso S et
al. Am J
Resp Crit
Care Med
2007;176:76
1-767



Driving Pressures in Higher PEEP Trials

	<u>Pplat</u>	<u>PEEP</u>	<u>ΔP</u>	<u>Δ-ΔP</u>
ARDSnet				
Lower	24.0	8.9	15.1	
Higher	27.0	14.7	12.3	-2.8
Canadian				
Lower	24.9	10.1	14.8	
Higher	30.2	15.6	14.6	-0.2
French				
Lower	21.1	8.4	12.7	
Higher	27.5	14.6	12.9	+0.2

Model Variables

Patient variables

Days on mech vent

Age

APACHE III

Organ failures

Arterial pH

PaCO₂

PaO₂/FIO₂

Tidal-compliance

Mech Vent Variables

Tidal volume

Plateau pressure

PEEP

FiO₂

Respiratory rate

Mean airway pressure

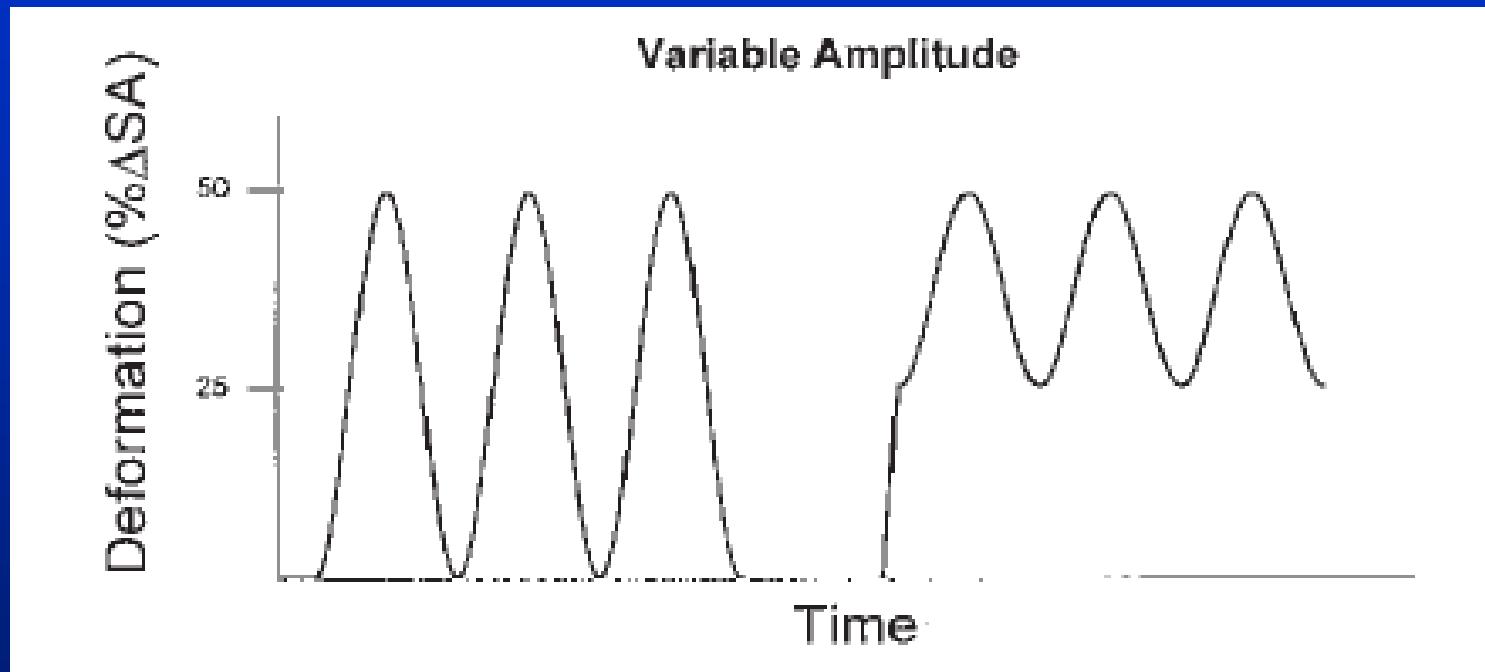
ΔP (Pplat – PEEP)

Driving Pressure ($P_{plat} - P_{PEEP}$) = V_T/C_{RS}

E.g., $V_T = 600$, $C_{RS} = 25 \text{ ml/cm H}_2\text{O}$

Driving Pressure = $600/25 = 24 \text{ cm H}_2\text{O}$

Alveolar Type II Epithelial Cells



Tschumperlin et al. Am J Respir Crit Care Med 2000

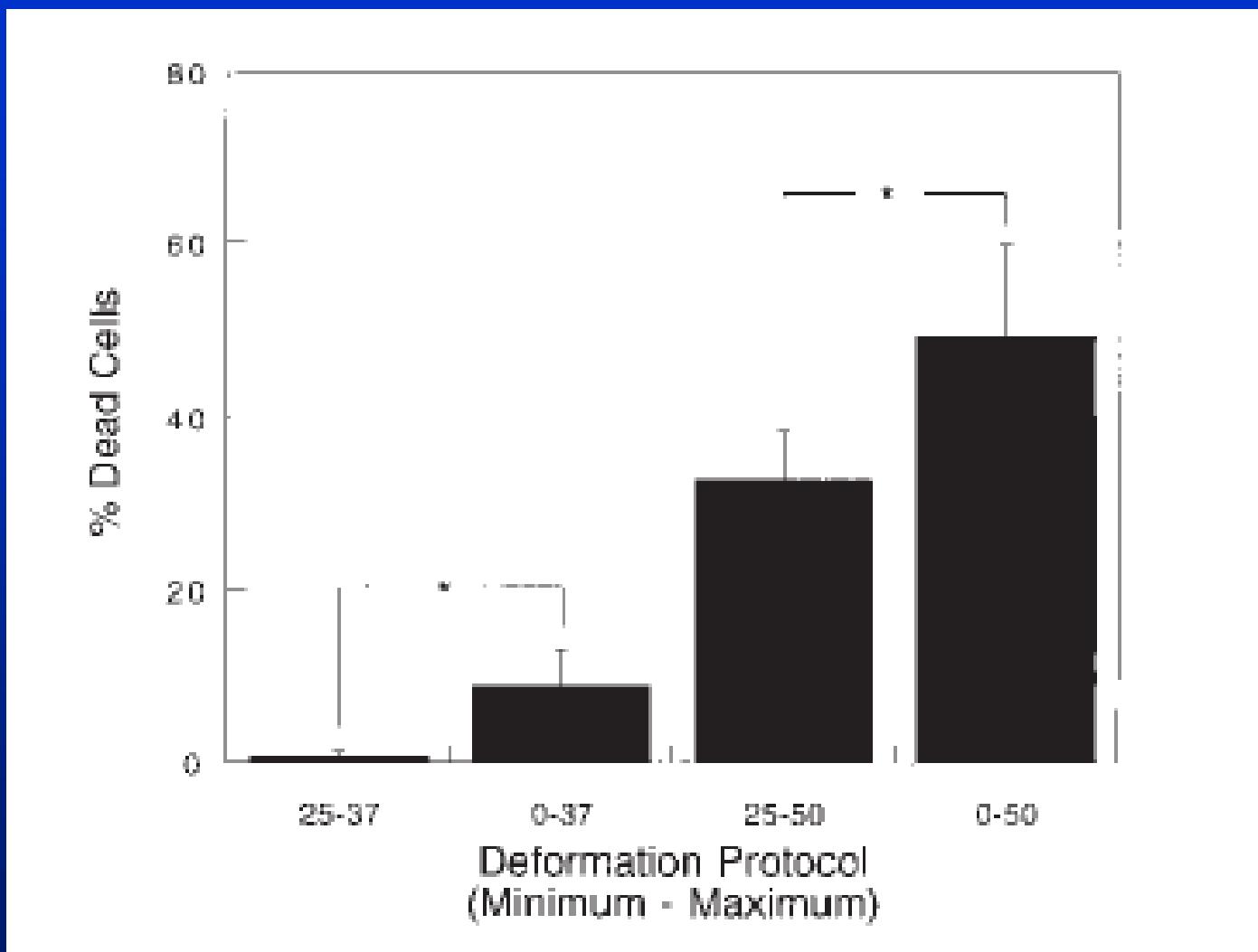
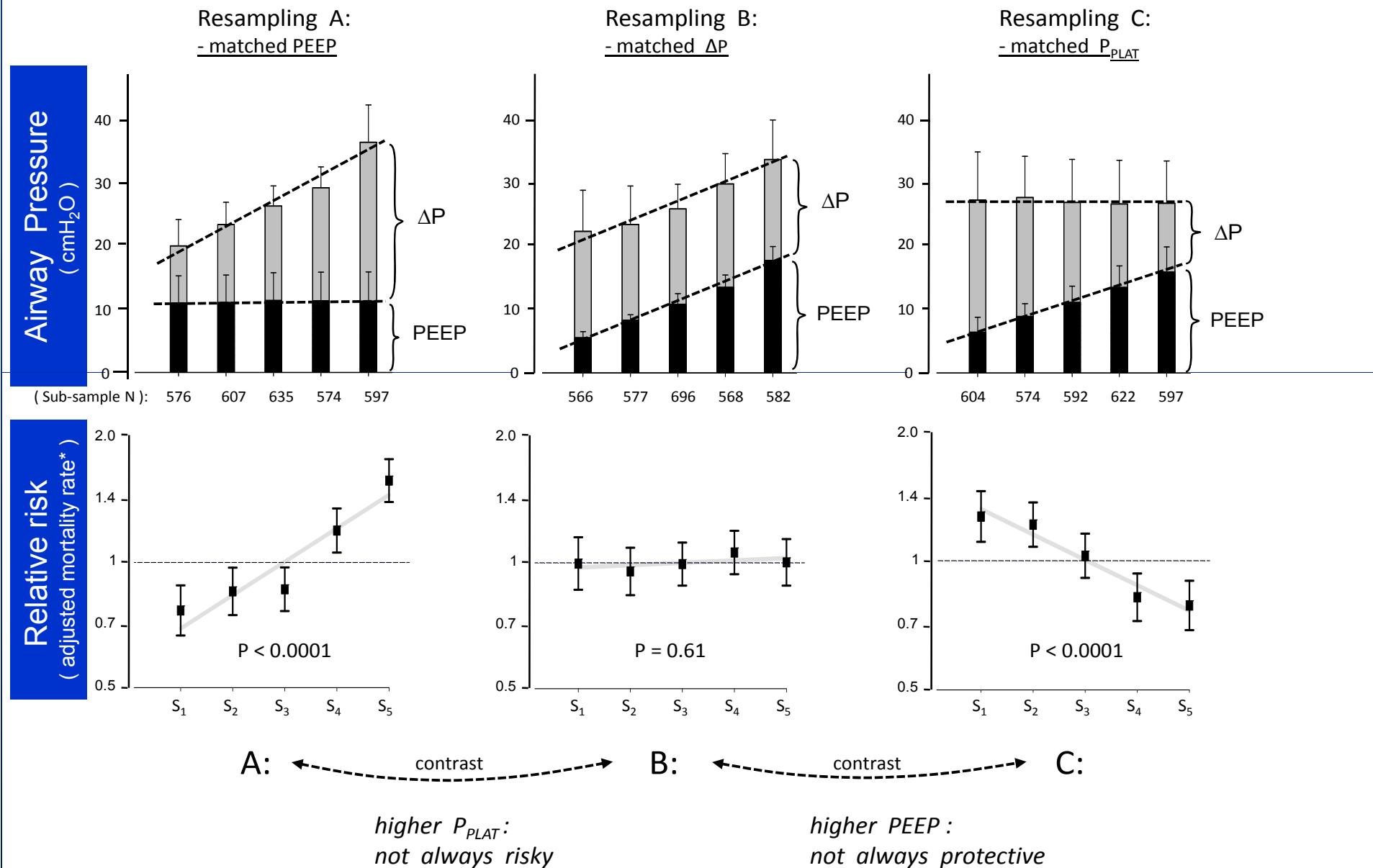


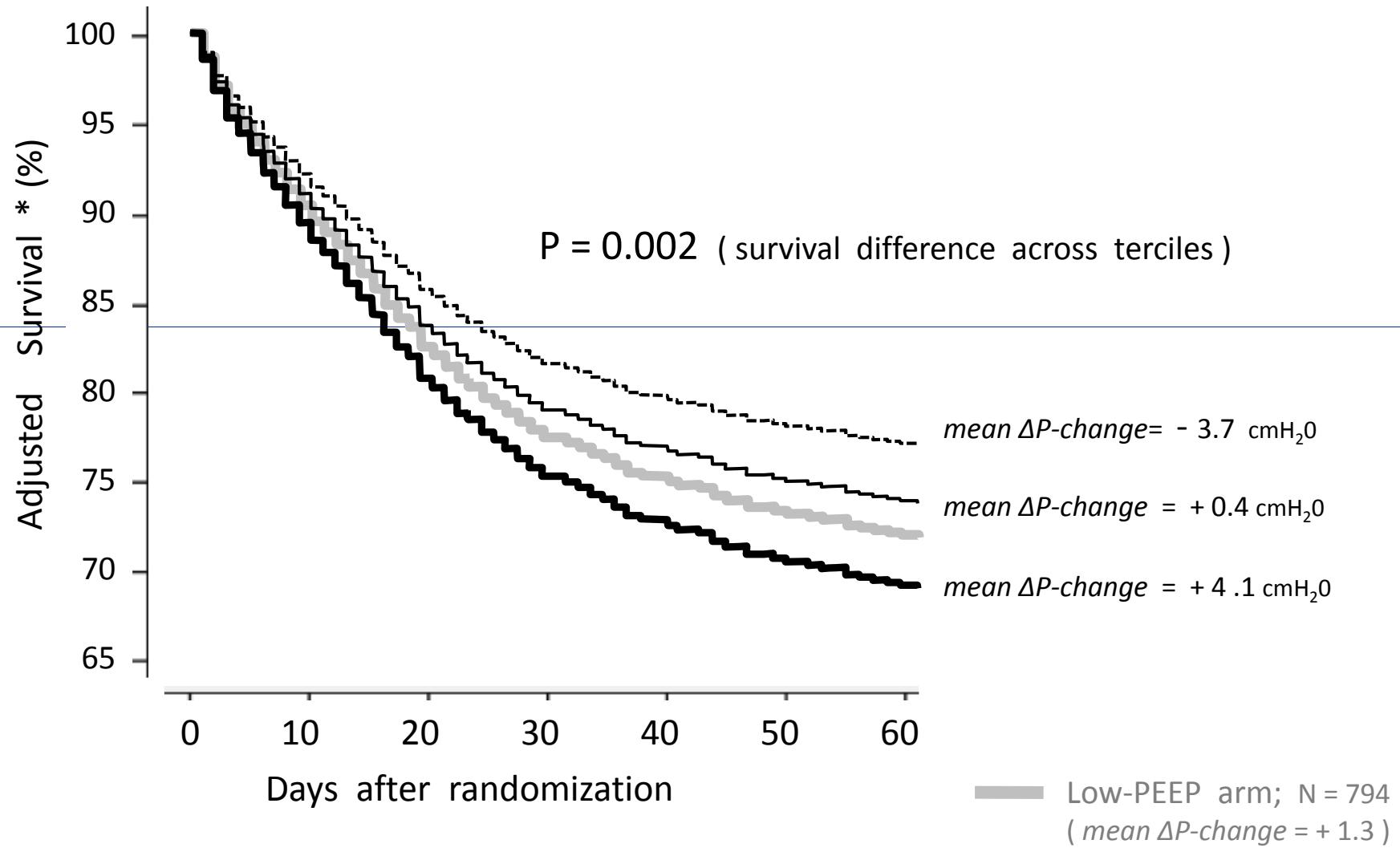
Figure 1:



*: adjusted for age, APACHE/SAPS risk, arterial-pH, P/F ratio, and study-trial

Figure 4 :

ΔP -changes driven by randomization mediate survival in the higher-PEEP arms



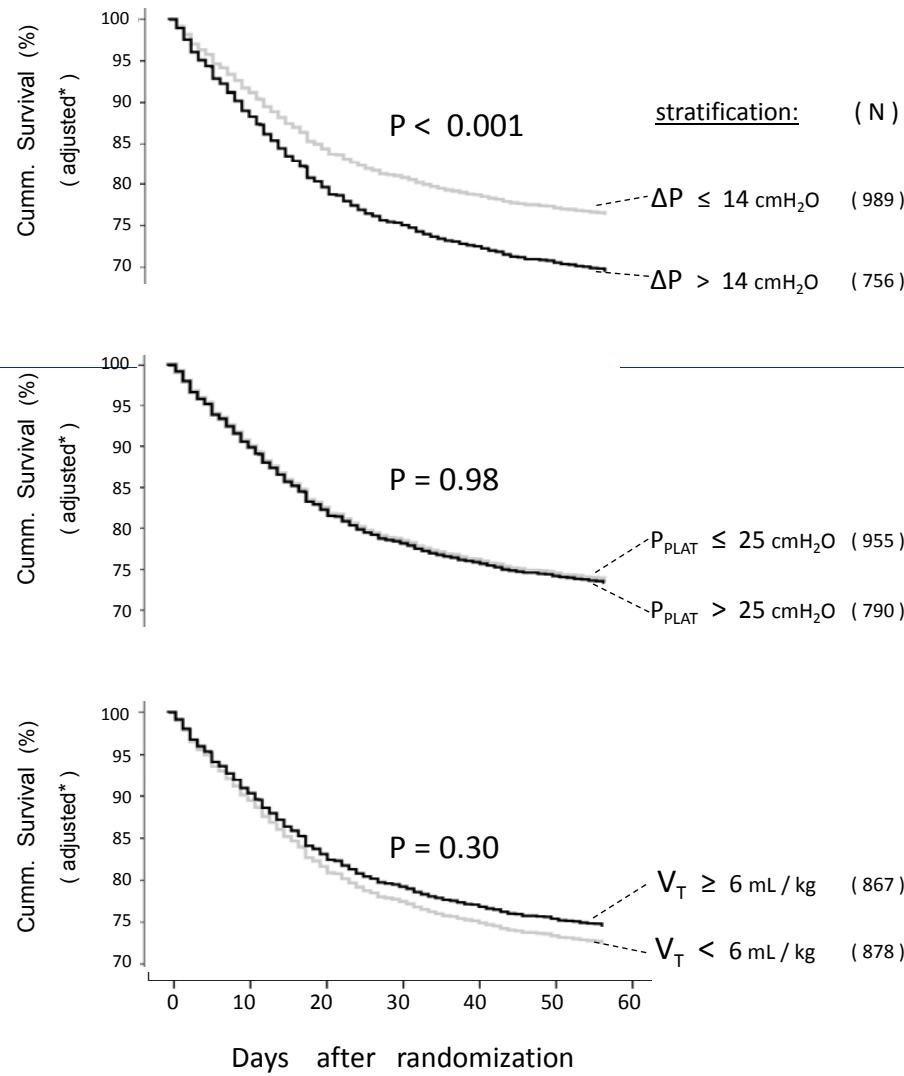
*: Adjusted for: age, APACHE/SAPS risk, arterial-pH, P/F ratio, study-trial, and Disease- ΔP

Figure 2a :

Subsample of patients under “protective settings”

(N = 1745)

All with Plateau-pressure $\leq 30 \text{ cmH}_2\text{O}$ & $V_T \leq 7 \text{ mL / ibw}$



*: adjusted for age, APACHE/SAPS risk, arterial-pH, P/F ratio, and study-trial



they are compressed. Thus we have

$$\epsilon = \frac{\Delta L}{L} = \frac{L - L_0}{L_0}$$

Strain

Ratio of total deformation to the initial dimension of the material body in which the forces are being applied.

L

they are compressed. Thus we have

$$\epsilon = \frac{\Delta L}{L} = \frac{L - L_0}{L_0}$$

Strain

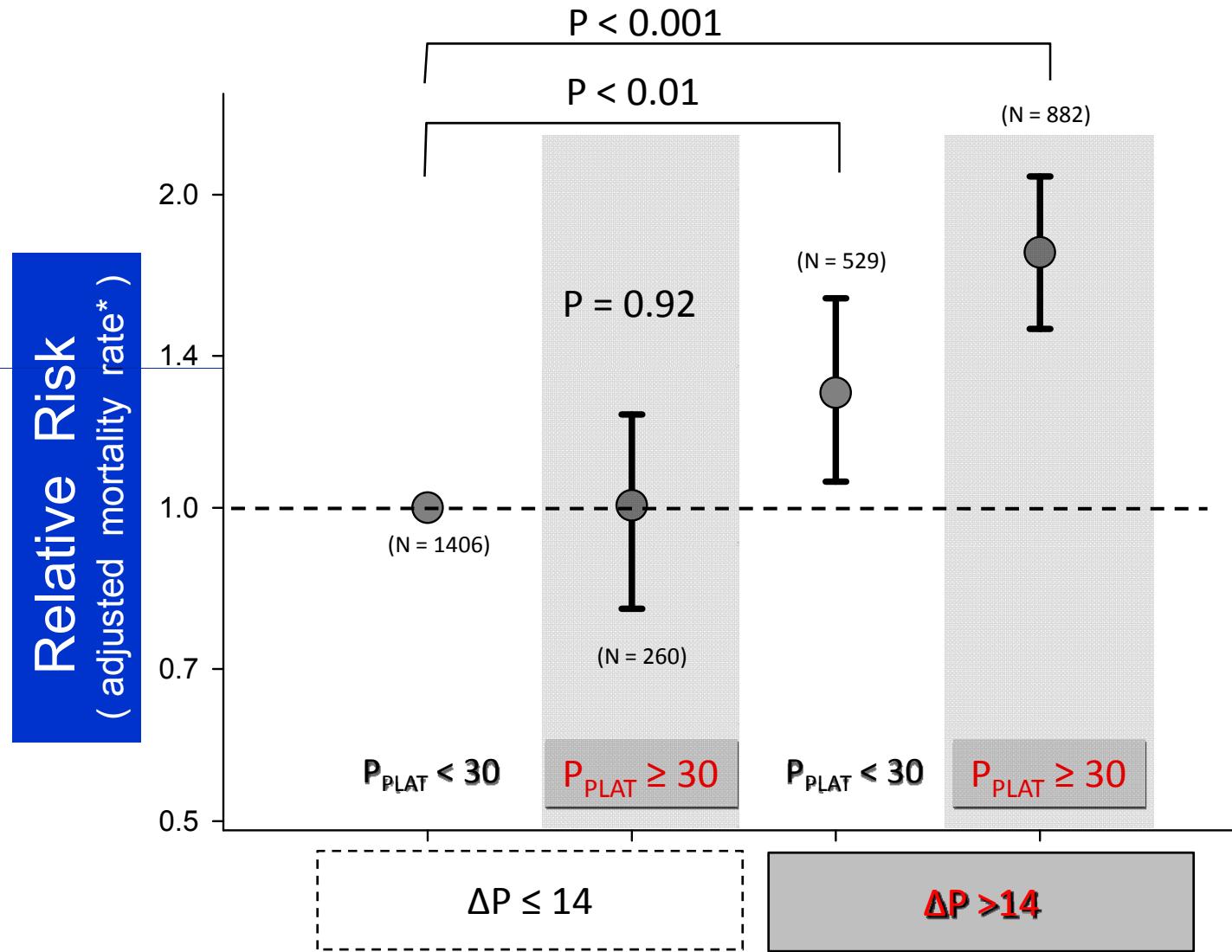
Ratio of total deformation to the initial dimension of the material body in which the forces are being applied.



$$\text{Strain} = \Delta L/L$$

Figure 2b :

Combined population of ARDS (N = 3080)

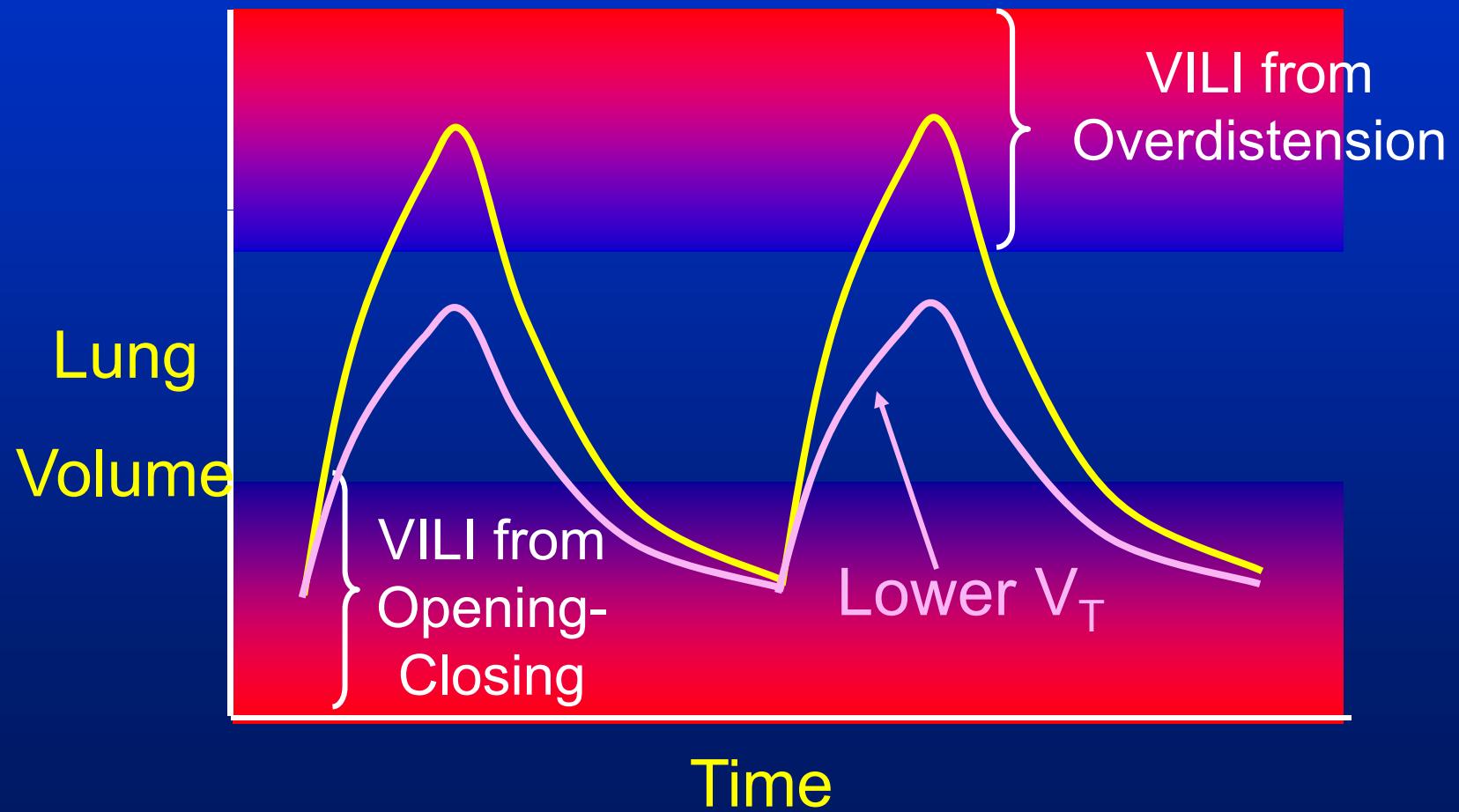


*: adjusted for age, APACHE/SAPS risk, arterial-pH, P/F ratio , and study-trial

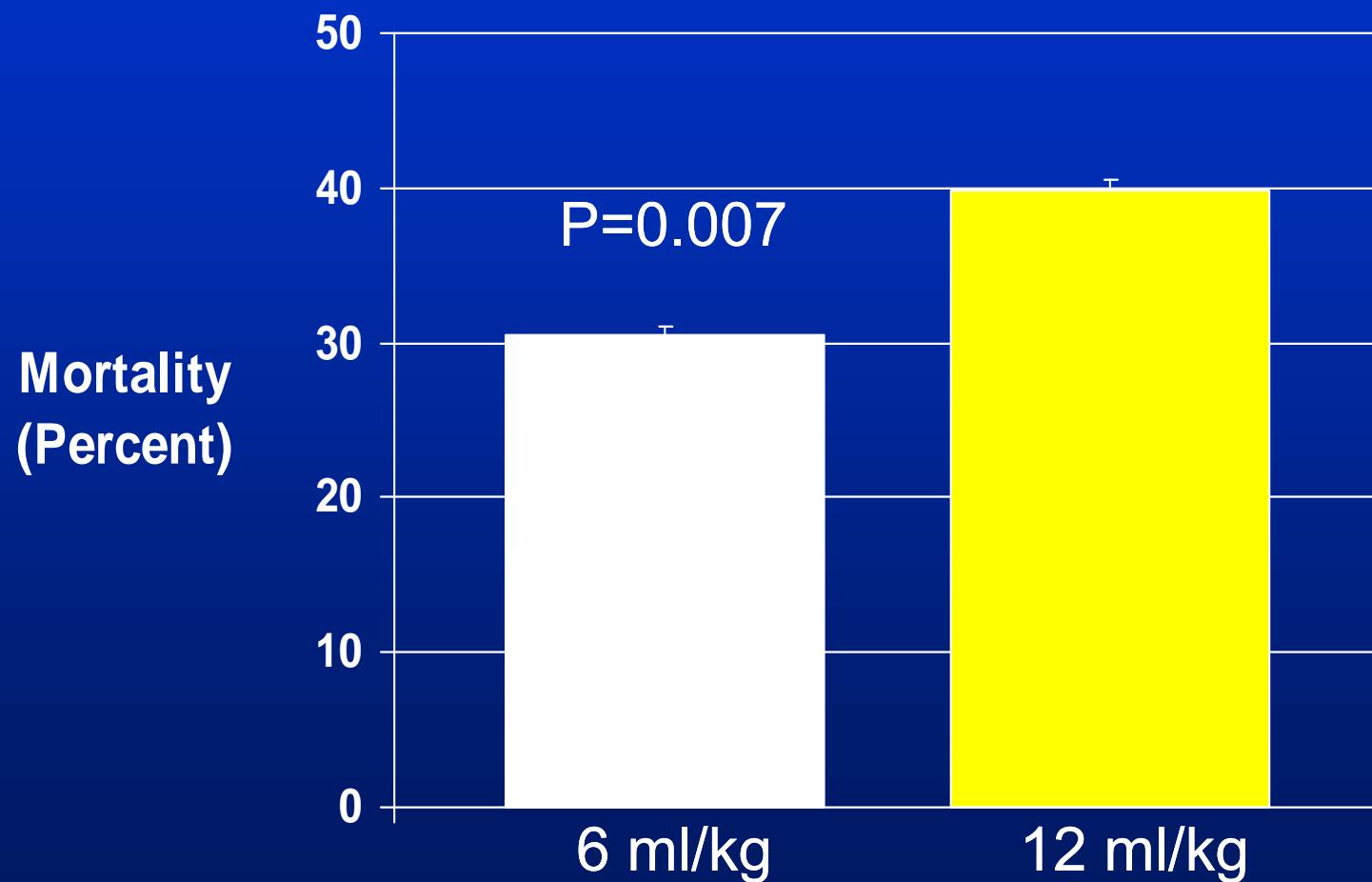
Driving Pressures in Higher PEEP Trials

	<u>Pplat</u>	<u>PEEP</u>	<u>ΔP</u>	<u>Δ-ΔP</u>
ARDSnet				
Lower	24.0	8.9	15.1	
Higher	27.0	14.7	12.3	-2.8
Canadian				
Lower	24.9	10.1	14.8	
Higher	30.2	15.6	14.6	-0.2
French				
Lower	21.1	8.4	12.7	
Higher	27.5	14.6	12.9	+0.2
ARDSnet Tidal Volume				
Lower	25	9.4	15.6	-8.8
Higher	33	8.6	24.4	

Lower V_T /Pressure Ventilation



ARDS Network Tidal Volume Trial Mortality Before Hospital Discharge



ARDSnet. NEJM 2000

ARDS Network Tidal Volume Trial

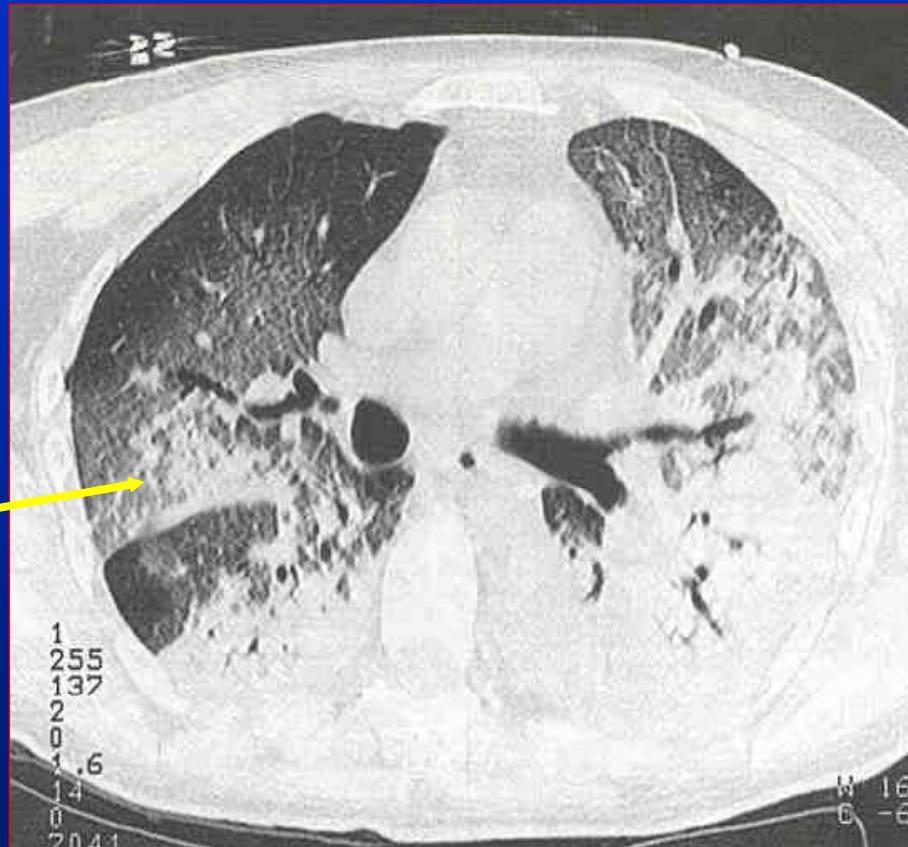
Tidal Volume goal = 6 ml/kg PBW

Plateau Pressure limit = 30 cm H₂O

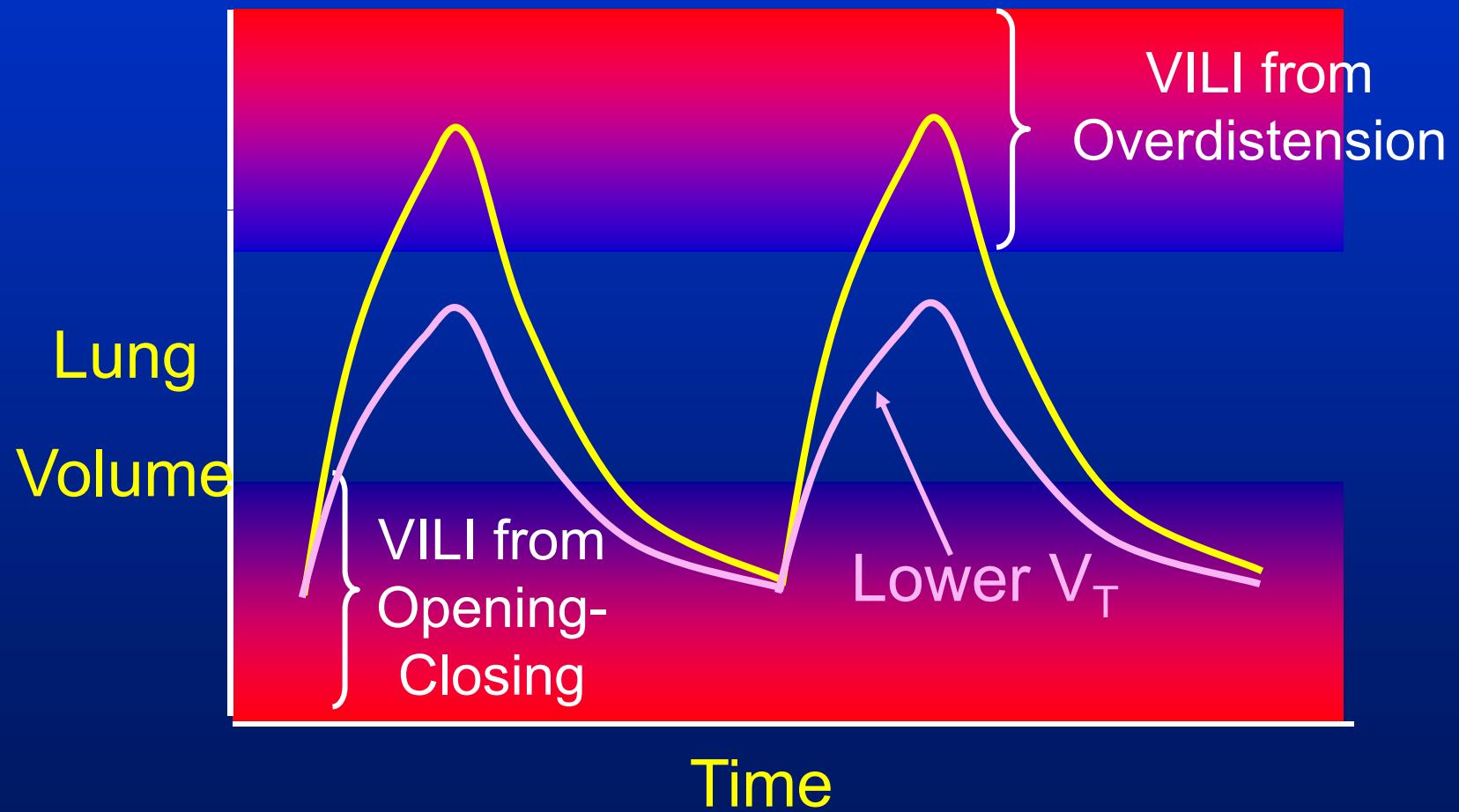
Mechanical Ventilation Traditional Approach

PEEP 0-12 cm H₂O

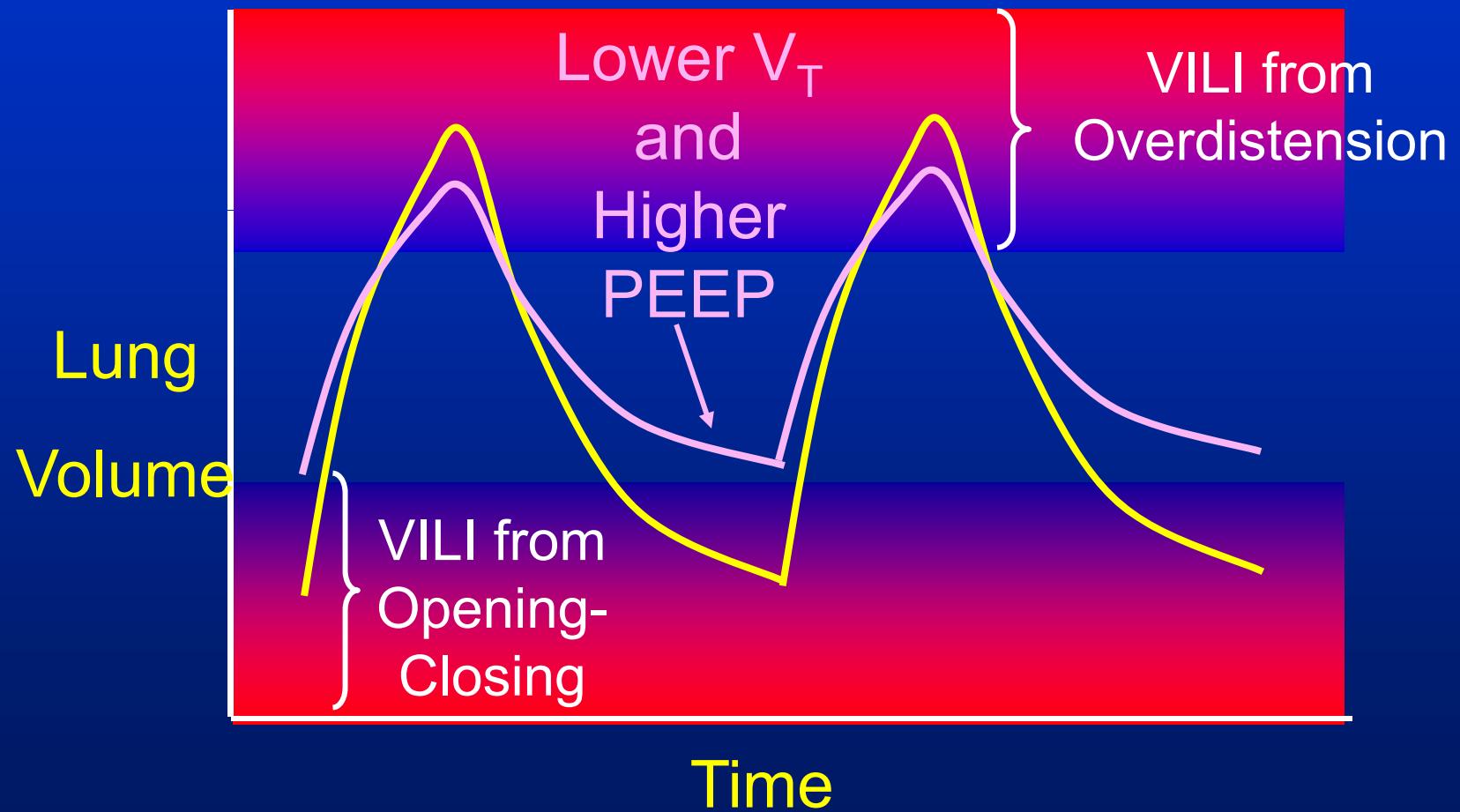
Low Volume/Low
Pressure at End-
expiration



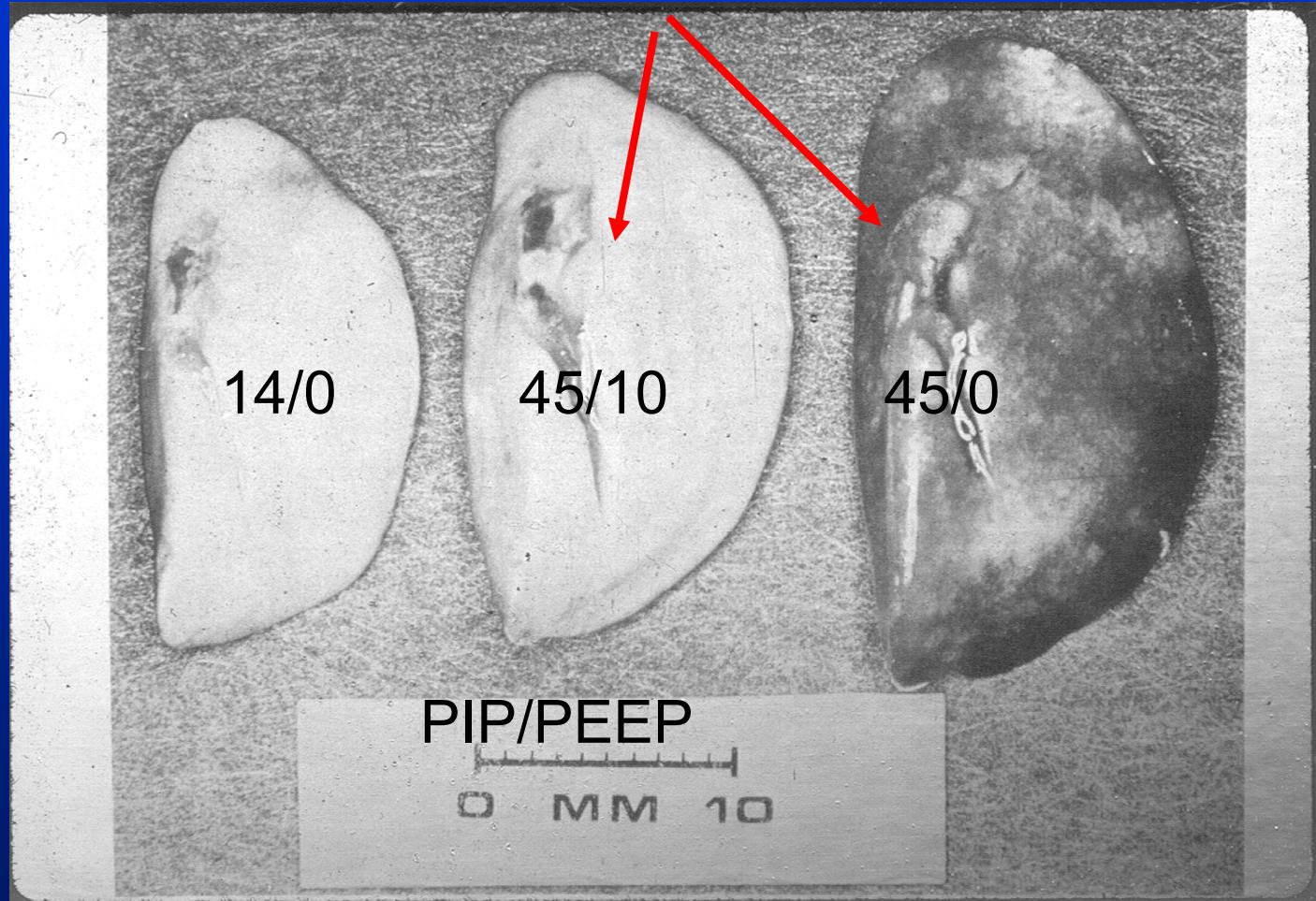
Lower V_T /Pressure Ventilation



Lower V_T and Higher PEEP



Ventilator-Induced Lung Injury



Webb and Tierney
Am Rev Resp Dis
110:556-565, 1974

3 Higher PEEP Trials

	Mortality (%)	
	<u>Higher PEEP</u>	<u>Lower PEEP</u>
ARDSnet (549) ¹	27.5	24.9
Canadian (983) ²	36.4	40.4
<u>French (767)³</u>	<u>35.4</u>	<u>39.4</u>
Combined (2299)	33.9	36.2

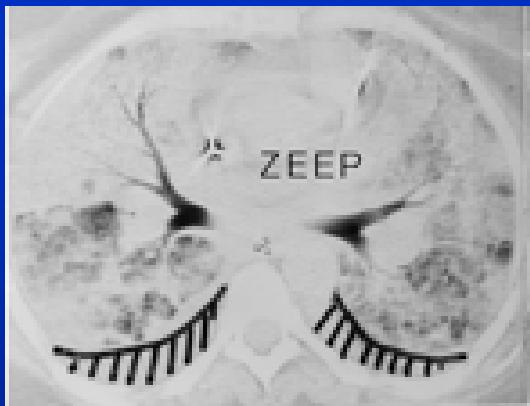
1 ARDSnet NEJM 2004

2 Meade JAMA 2008

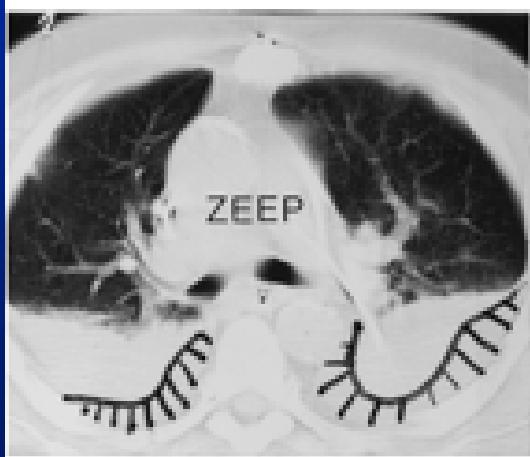
3 Mercat JAMA 2008

Effects of PEEP are Variable

Diffuse



Recruitment



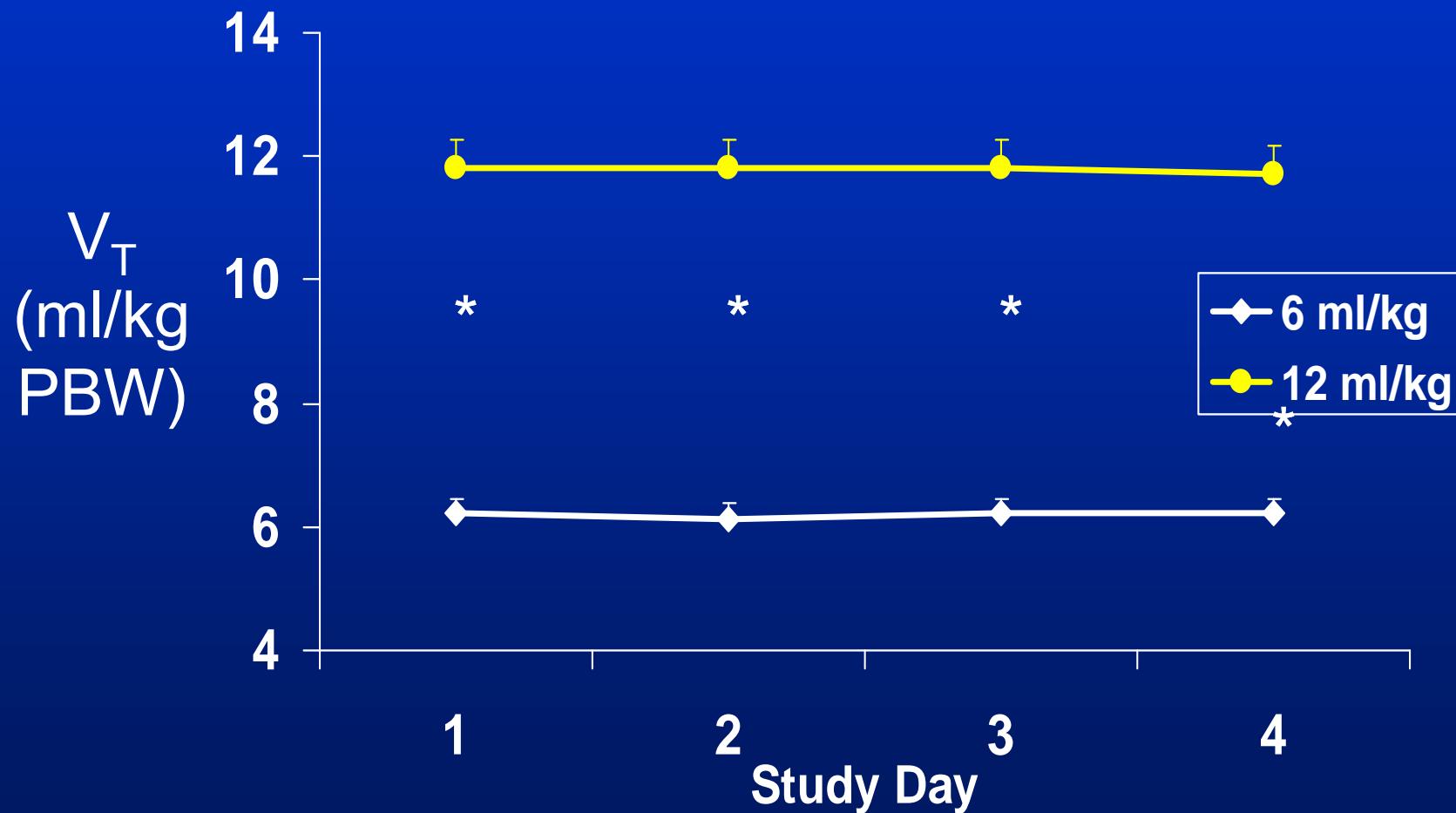
Overdistention

Recruitment

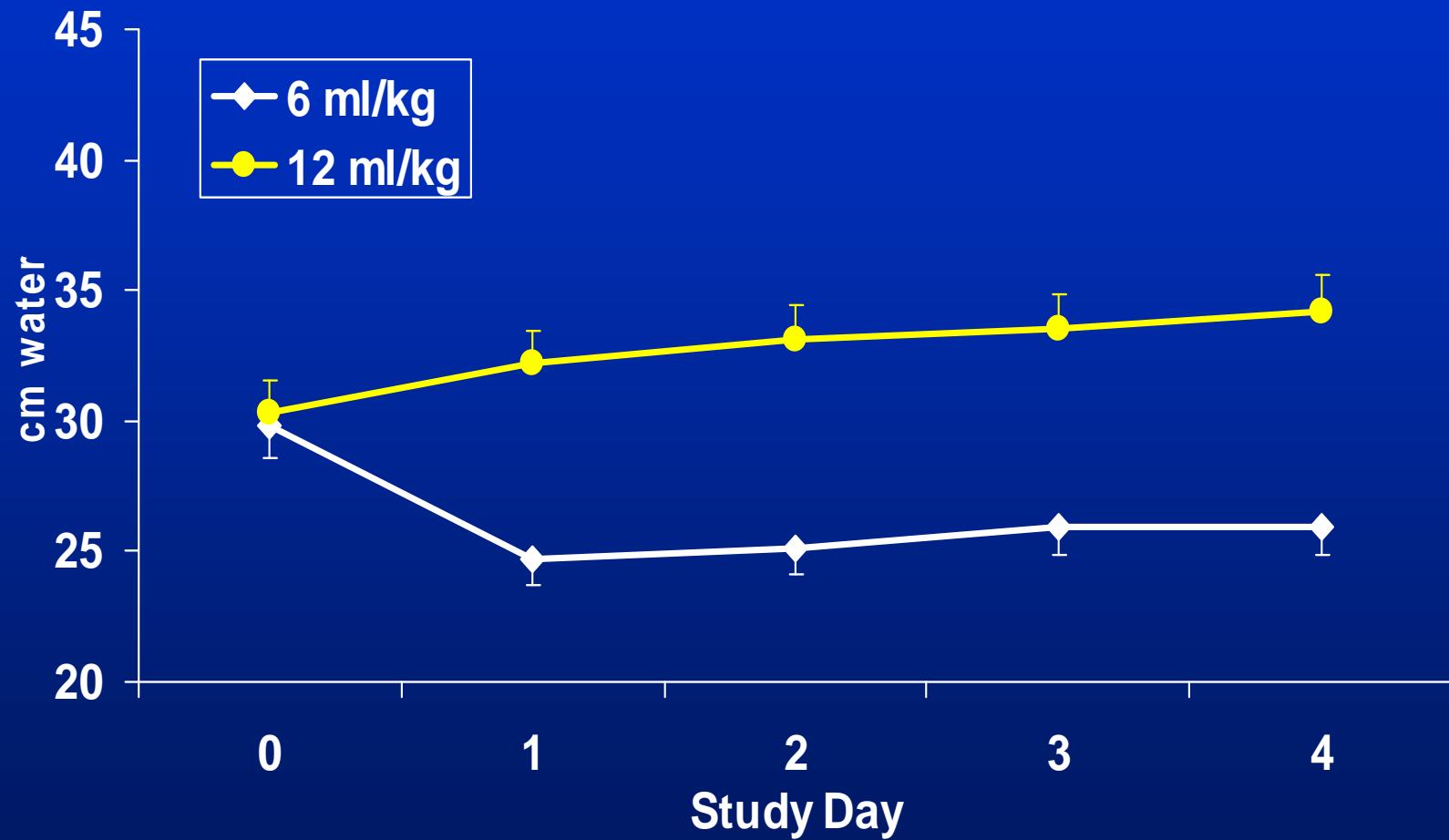
Overdistention

Lobar

ARDS Network Trial – Tidal Volumes



ARDS Network Trial - Plateau Pressures

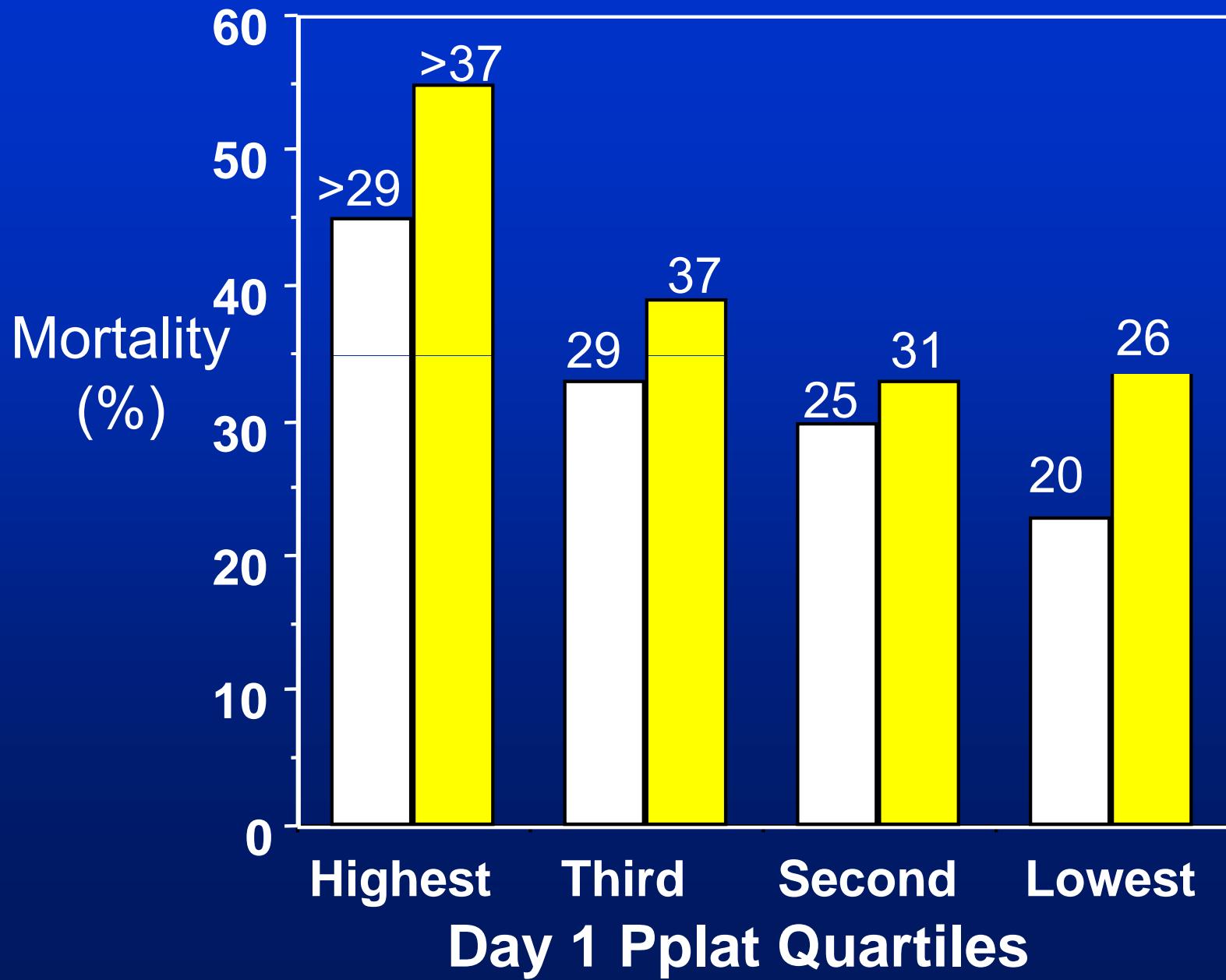


ARDS Network Trial of Lower Tidal Volume Ventilation in ALI/ARDS

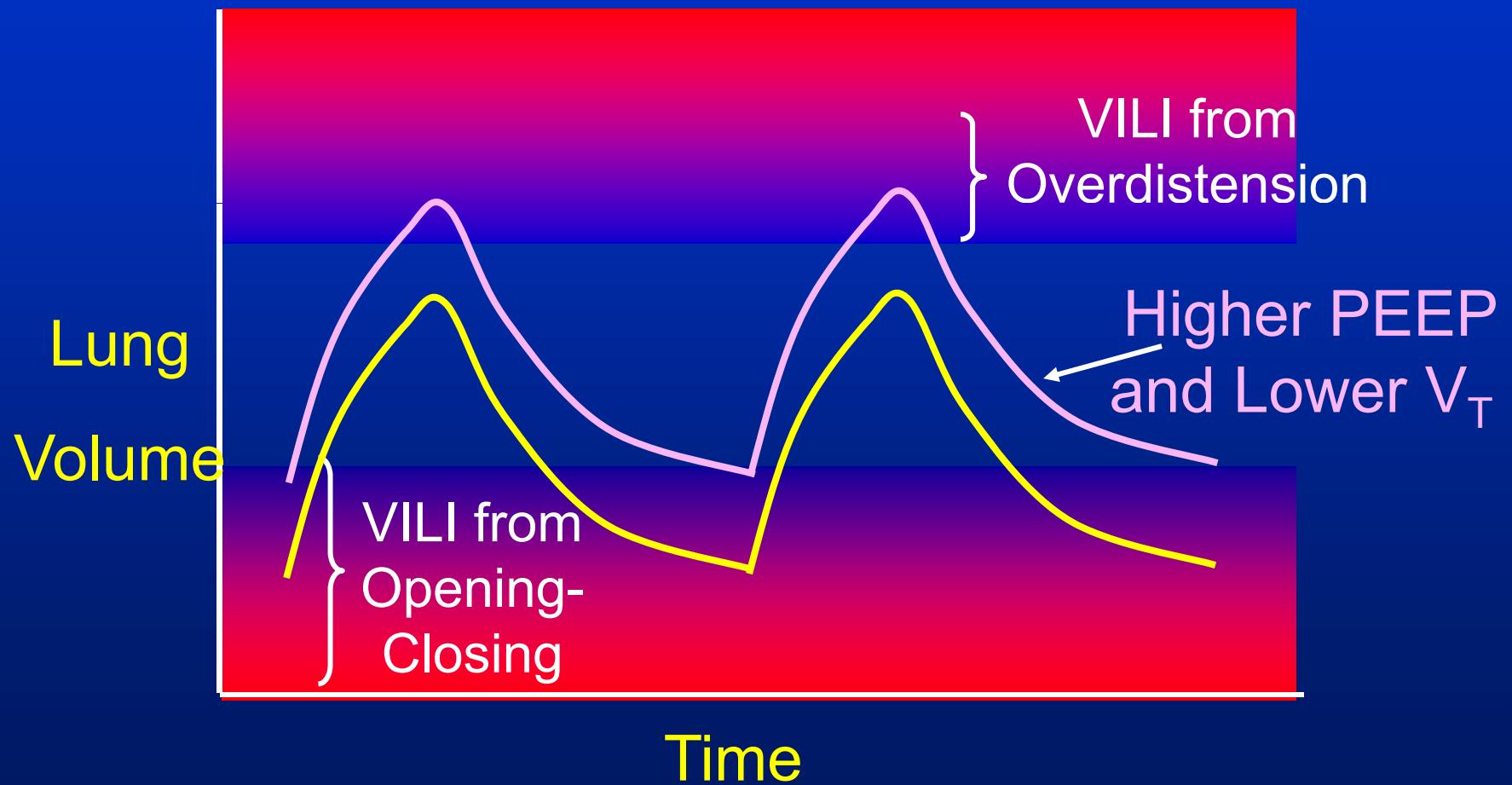
Subset analysis

No “safe” level of P_{plat} identified

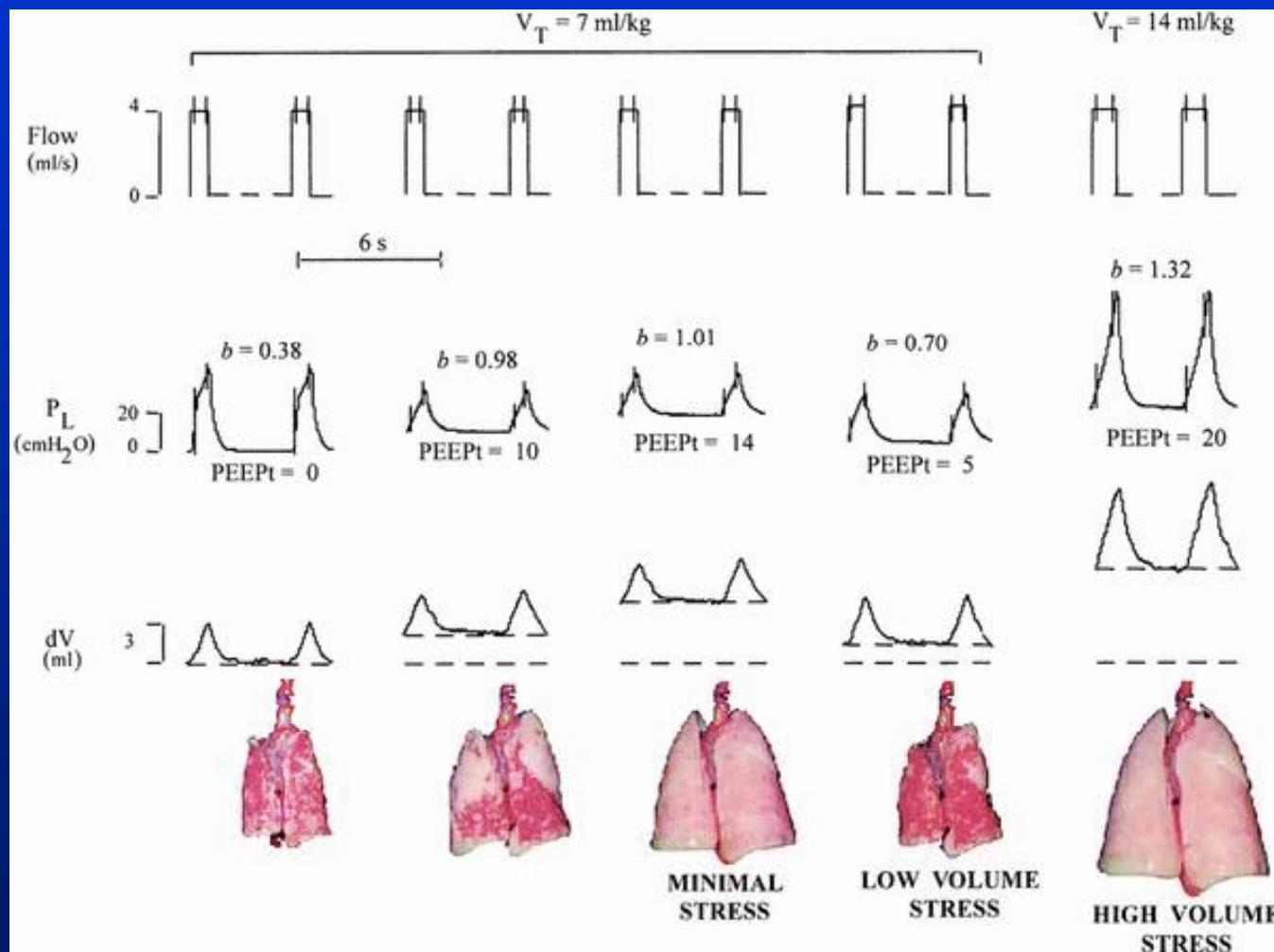
Mortality by Day 1 Pplat Quartiles (n=822)



Lower V_T /Pressure Ventilation and Higher PEEP



Stress Index



Ranieri et al. Anesthesiology. 2000 Nov;93(5):1320-8.

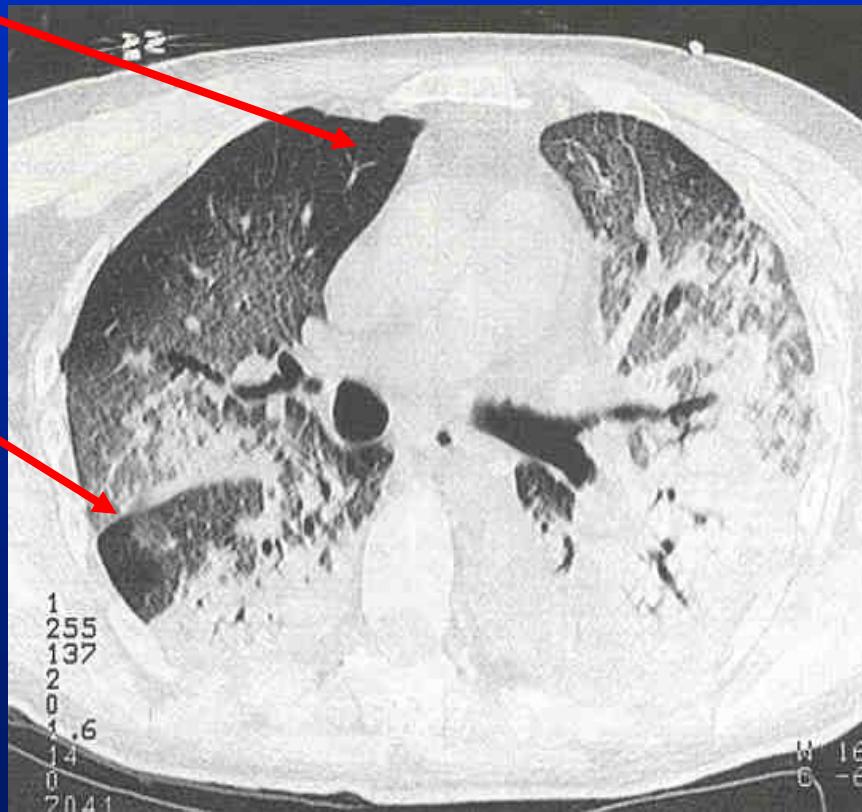
Lung-protective Mechanical Ventilation in ALI and ARDS PEEP Questions

- Who are the responders?
- How much PEEP in responders?
- How much PEEP in nonresponders?
- When to decrease PEEP in responders?

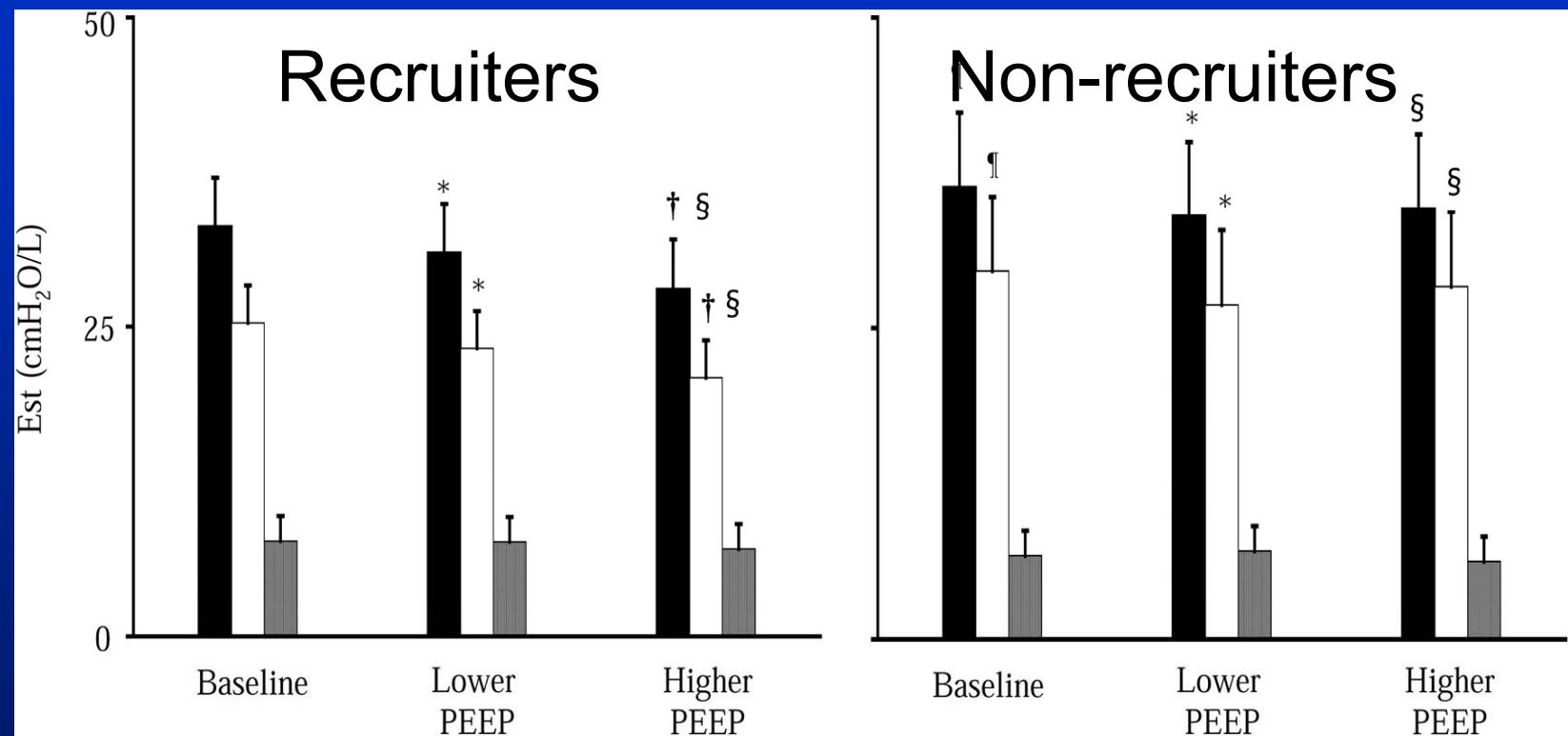
Ventilator-Induced Lung Injury

High Volume
High Pressure
VILI

Low Volume
Low Pressure
VILI

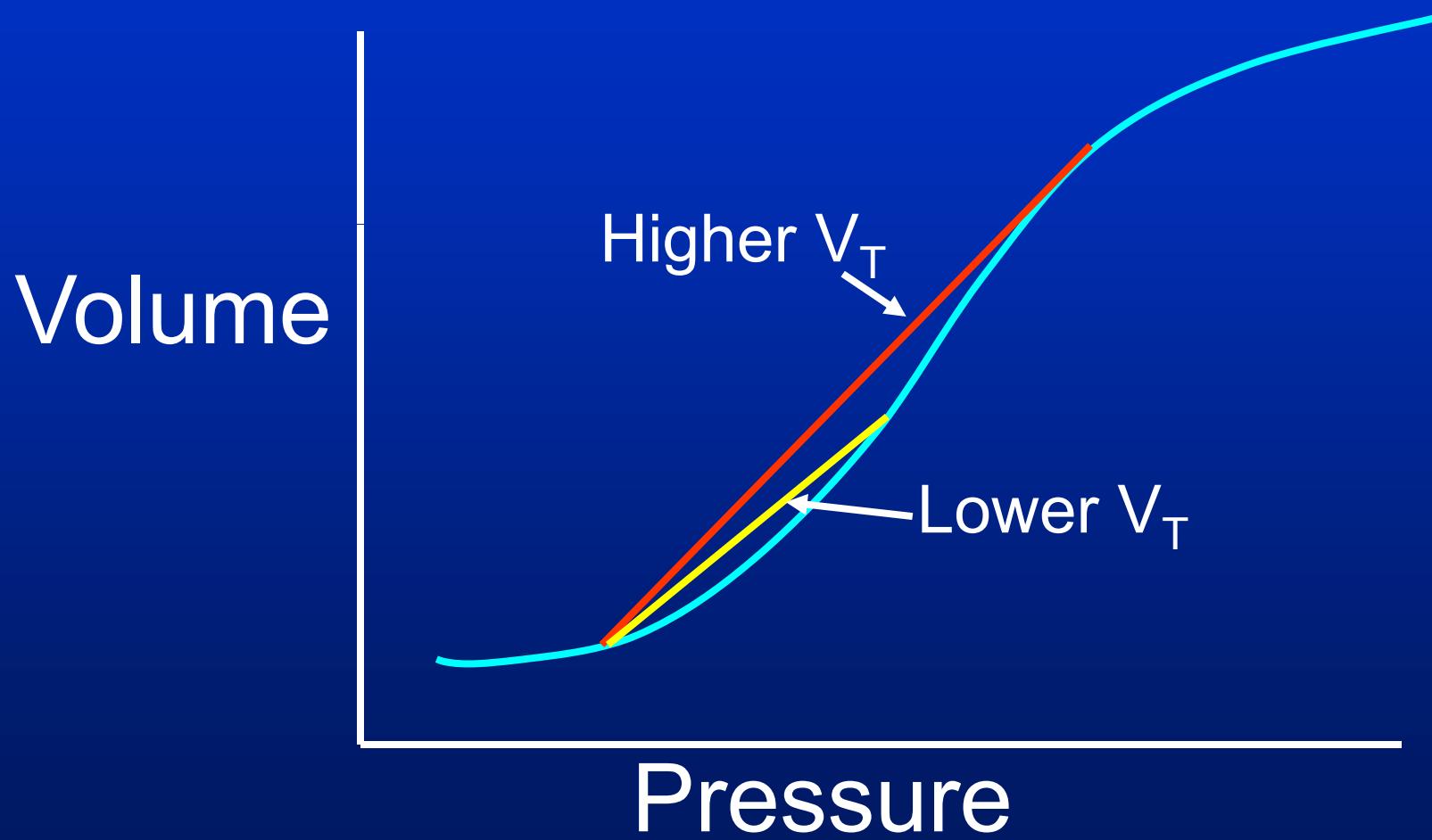


Effects of PEEP on Elastance Recruiters and Nonrecruiters

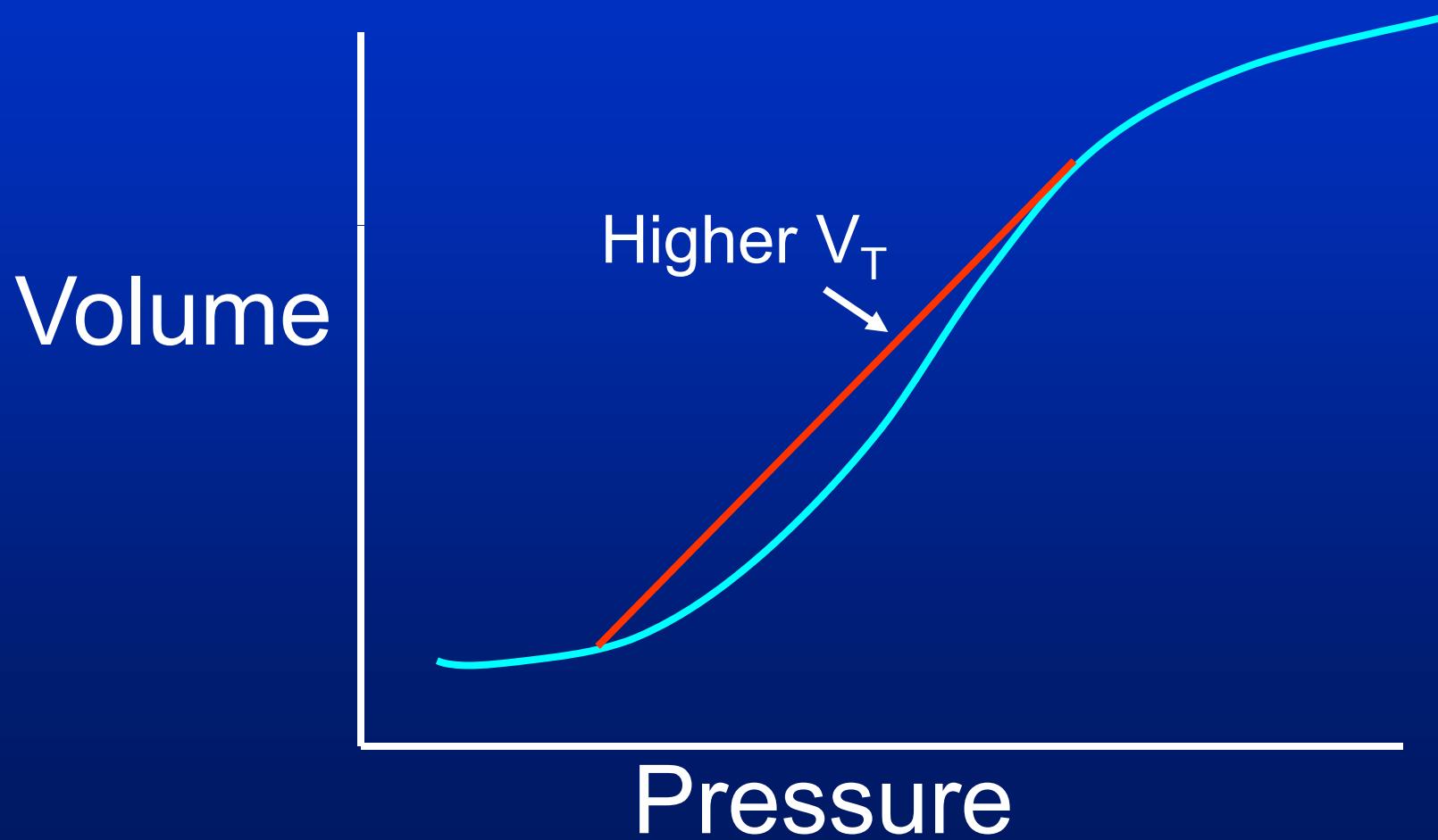


Grasso et al. Am J Resp Crit Care Med 2005; 171: 1002-1008

Lower V_T and Inspiratory Pressure
Reduced Overdistention AND Opening-Closing



Higher V_T and Inspiratory Pressure



Ventilator-induced Lung Injury

*Effect of Positive Pressure Ventilation on Surface
Tension Properties of Lung Extracts*

Lazar J. Greenfield, M.D., Paul A. Ebert, M.D., Donald W. Benson, M.D., Ph.D.

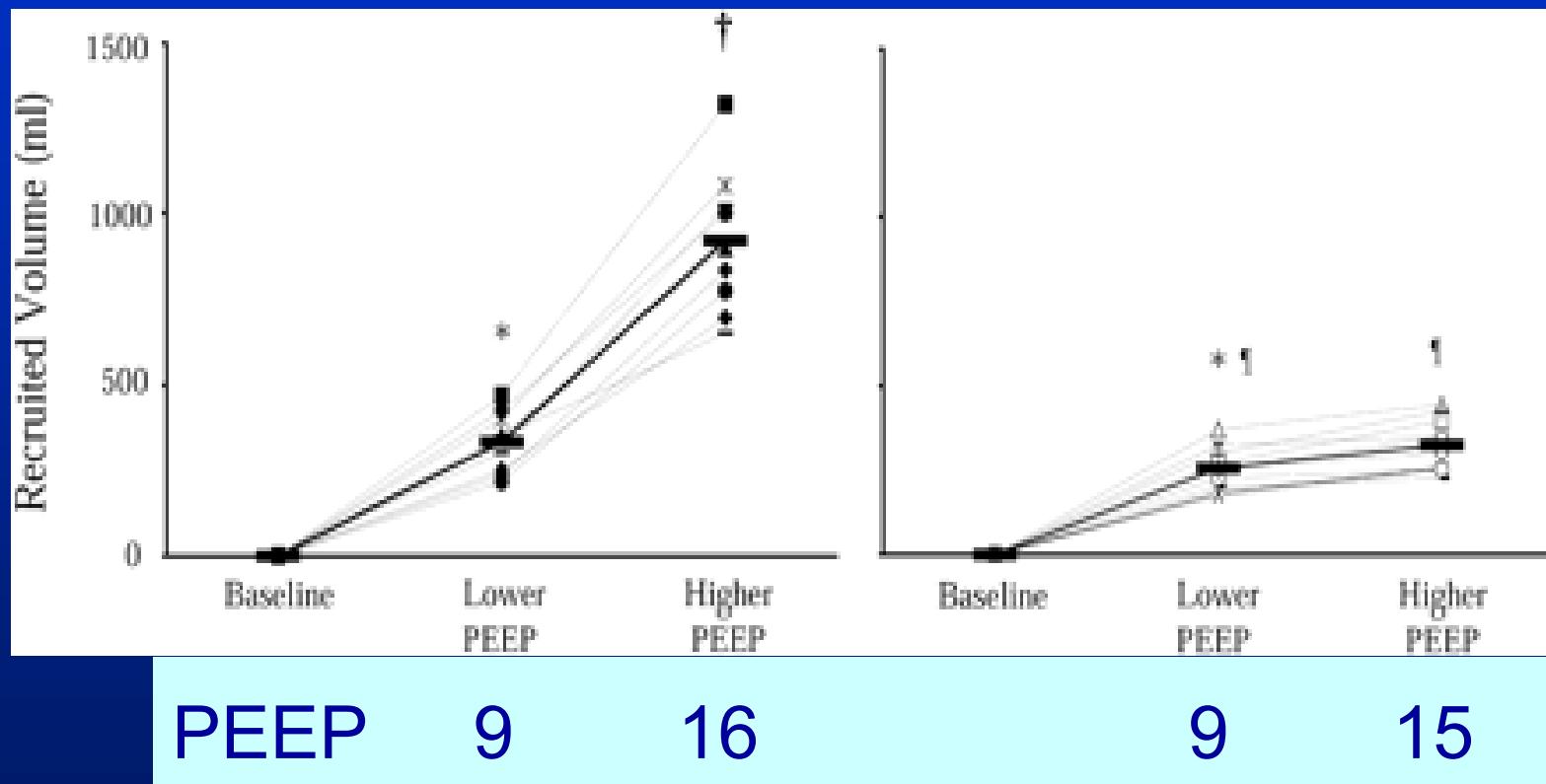
Anesthesiology 1964; 312-316



Effects of PEEP

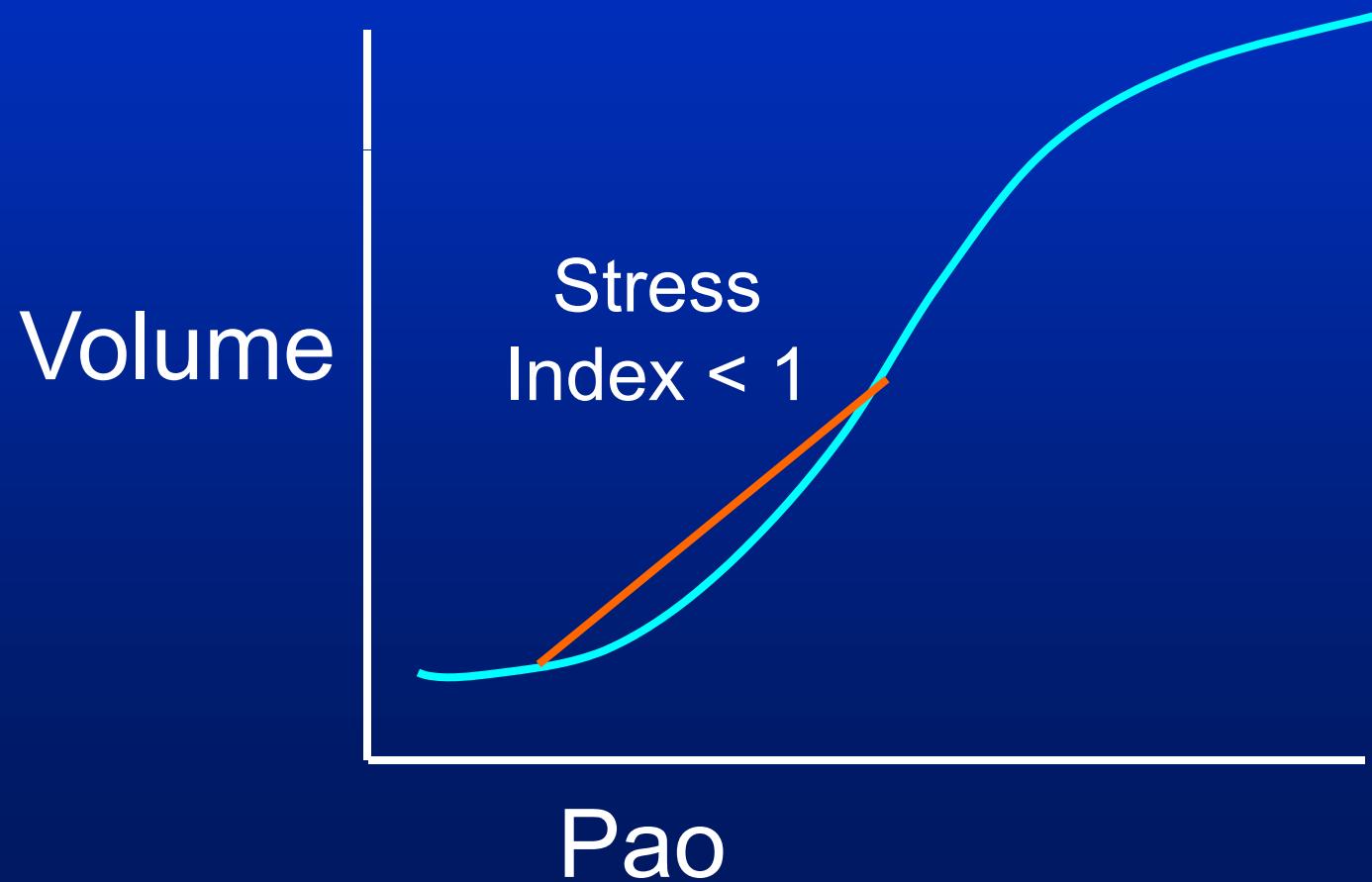
Responders

Nonresponders

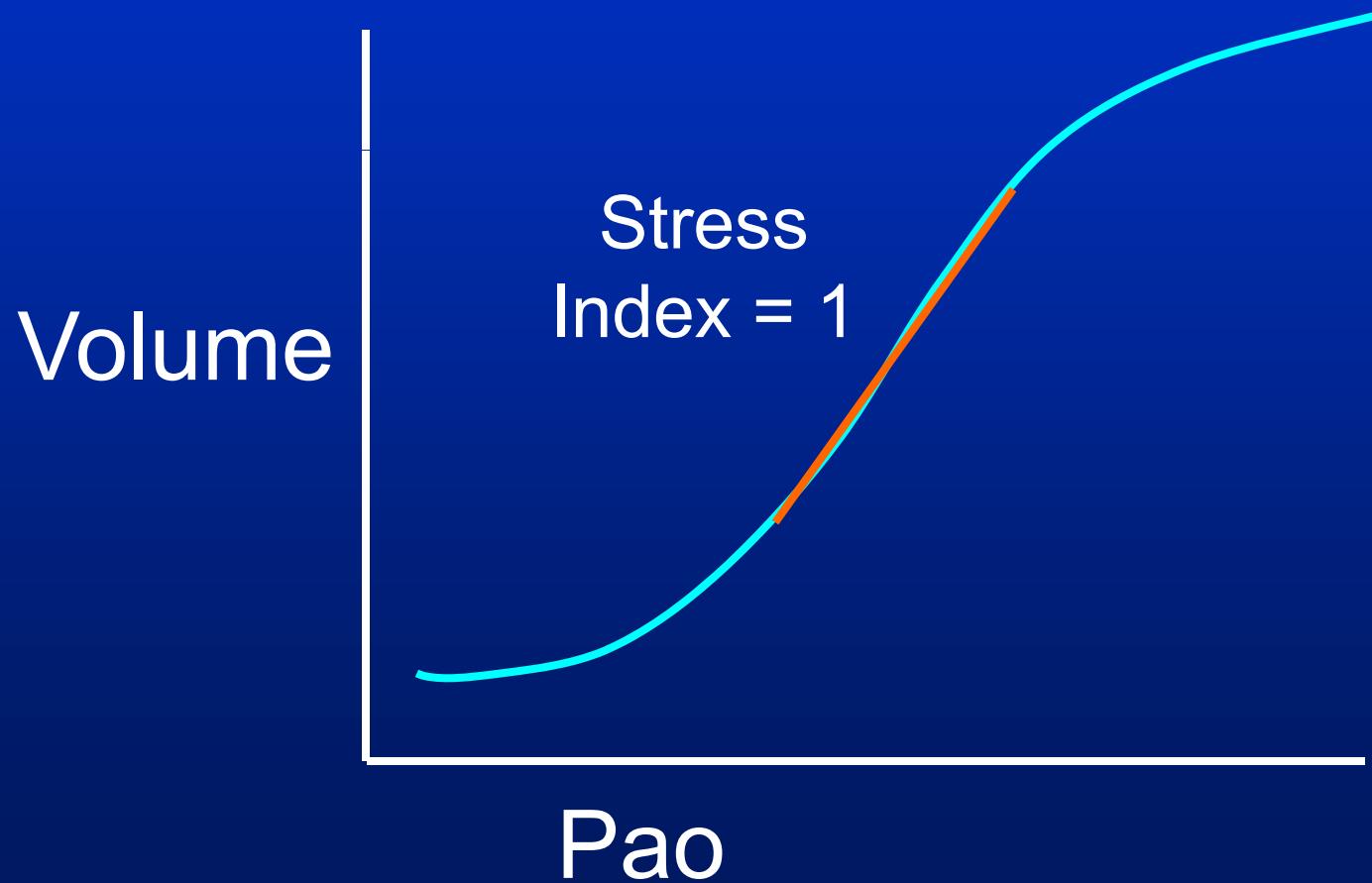


Grasso et al. Am J Resp Crit Care Med 2005; 171: 1002-1008

Pressure Volume Curve Stress Index



Pressure Volume Curve Stress Index



Pressure Volume Curve Stress Index

