DRIVING PRESSURE AND LUNG MECHANICS

Atul Malhotra, MD
UC San Diego
Professor of Medicine and Sleep Specialist

Friday, January 18, 2019 – 10:00 a.m. – 10:45 a.m.

Atul Malhotra, MD, is a board-certified pulmonologist, intensivist and chief of Pulmonary, Critical Care and Sleep Medicine. He is active clinically in pulmonary, critical care and sleep medicine. In the sleep clinic, he provides a full spectrum of diagnostic and therapeutic services to patients with sleep-related disorders, including sleep apnea, insomnia, restless leg syndrome, narcolepsy and sleep disorders associated with medical or psychiatric conditions. He has a special interest in the treatment of sleep apnea.

Dr. Malhotra is the president of the American Thoracic Society. He has taught and presented his research on sleep-related disorders locally, regionally, nationally and internationally. He has published more than 200 original manuscripts in leading journals. He is a principal- and co-investigator on numerous projects relating to sleep apnea and serves as an ad hoc reviewer for many leading journals including the New England Journal of Medicine, Mayo Clinic Proceedings, Sleep and the Journal of American Medical Association. To view a full list of his publications, visit PubMed.

As a professor in the Department of Medicine, Dr. Malhotra is involved in training medical students, residents and fellows at UC San Diego School of Medicine.

Before joining UC San Diego Health, Dr. Malhotra practiced pulmonary, critical care and sleep medicine at Massachusetts General Hospital, Beth Israel Deaconess Medical Center and Brigham and Women's Hospital. He also served as attending physician in intensive care at King Faisal Hospital in Rwanda. He was associate professor at Harvard Medical School and medical director of the Brigham and Women's Hospital Sleep Disorders Research Program.

Dr. Malhotra completed his fellowship training in pulmonary and critical care medicine at Harvard Medical School and a residency in internal medicine at the Mayo Clinic. He completed an internship at St. Thomas Medical Center in Akron, OH and received his medical degree from the University of Alberta in Canada. Dr. Malhotra is triple board-certified in pulmonary disease, sleep medicine and critical care medicine.

Acute Respiratory Distress Syndrome
Lung Mechanics and Driving Pressure

Atul Malhotra, MD

Pulmonary, Critical Care and Sleep Medicine
UC San Diego

Obesity and the lung: 3 · Obesity, respiration and intensive care

A Malhotra,[1] D Hillman[2]

Outline

- 1. Obesity effects on the abdomen
- 2. Obesity effects on the respiratory system
- 3. Implications for mechanical ventilation

Thorax 2008

Abdominal Compartment Syndrome

- **Syndrome well recognized by surgeons**
- **Increasing evidence in Medical ICU patients**
- **Transduce Foley catheter or paracentesis needle or measure gastric pressure**

Intensive Care Med (2004) 30:822–829
DOI 10.1007/s00134-004-2169-9

ORIGINAL

Manu L. N. G. Malbrain
Davide Chiumello
Paolo Pelosi
Alexander Wilmer
Nicola Brienza
Vincenzo Malcangi

Prevalence of intra-abdominal hypertension in critically ill patients: a multicentre epidemiological study

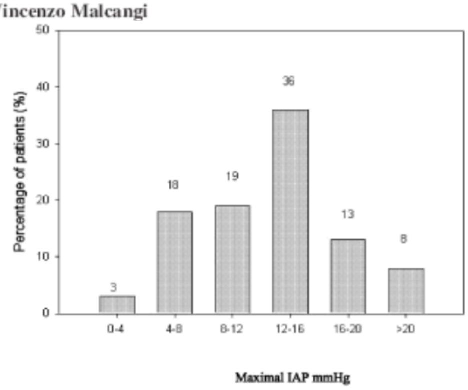
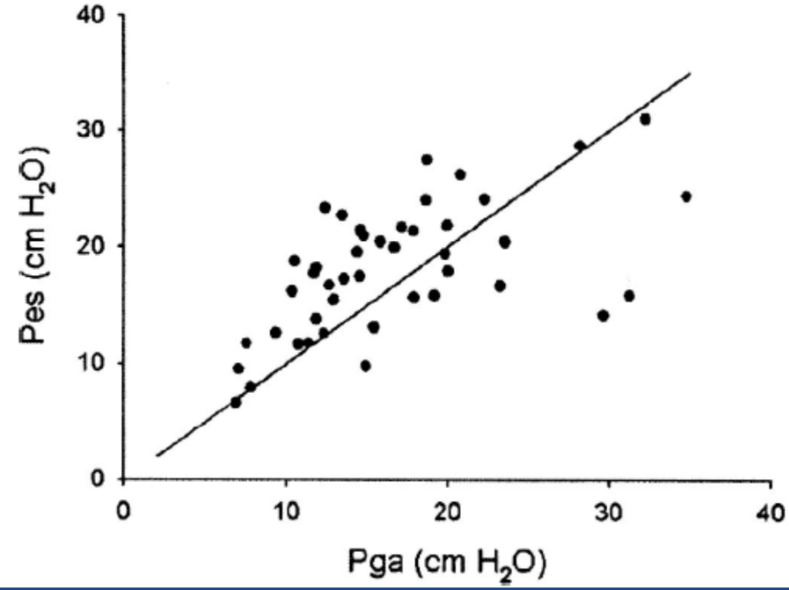


Fig. 1 Gaussian distribution of maximal intra-abdominal pressure (IAP) during the study day

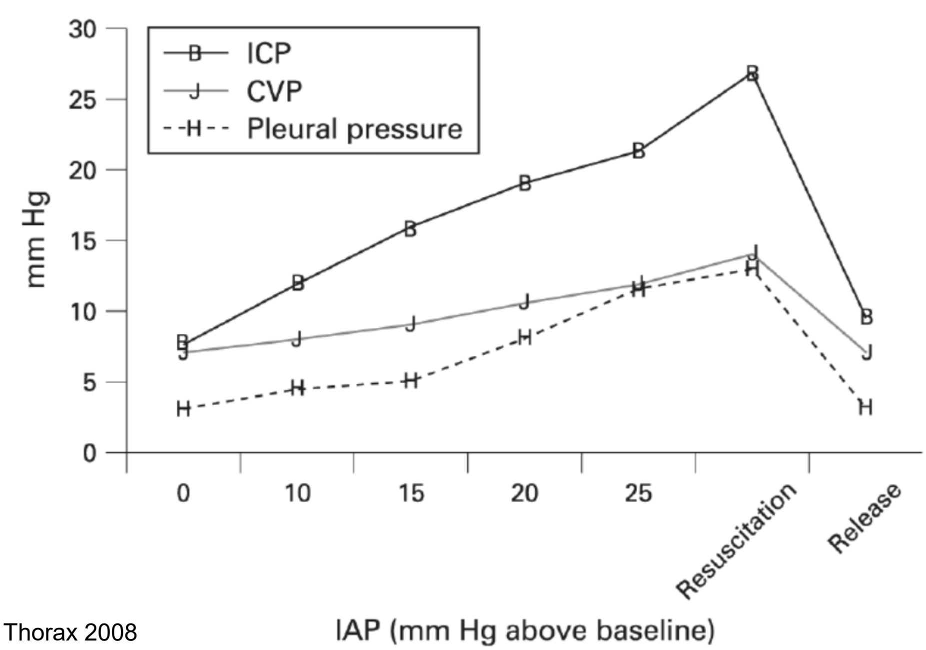
- **50% had IAP > 12 mmHg**
- **8% had ACS**
- **BMI was the <u>only</u> significant independent predictor of IAP in multivariate analysis**



Critical Care Medicine 2006

Malhotra and Hillman

Page 16



Thorax 2008

Summarize ACS

- **Elevated IAP is common in obesity**
- **Important effects on abdominal viscera**
- **Raised pleural pressure has implications for mechanical ventilation**
- **Awareness of pleural pressure is critical for interpretation of CVP and Wedge**
- **Raised ICP may respond to laparotomy**

Outline

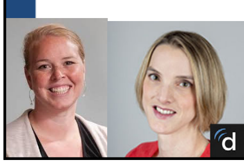
- 1. Obesity effects on the abdomen
- 2. Obesity effects on the chest wall/lung
- 3. Implications for mechanical ventilation

CHEST Postgraduate Education Corner

CONTEMPORARY REVIEWS IN CRITICAL CARE MEDICINE

Obesity and ARDS

Kathryn Hibbert, MD; Mary Rice, MD; and Atul Malhotra, MD, FCCP

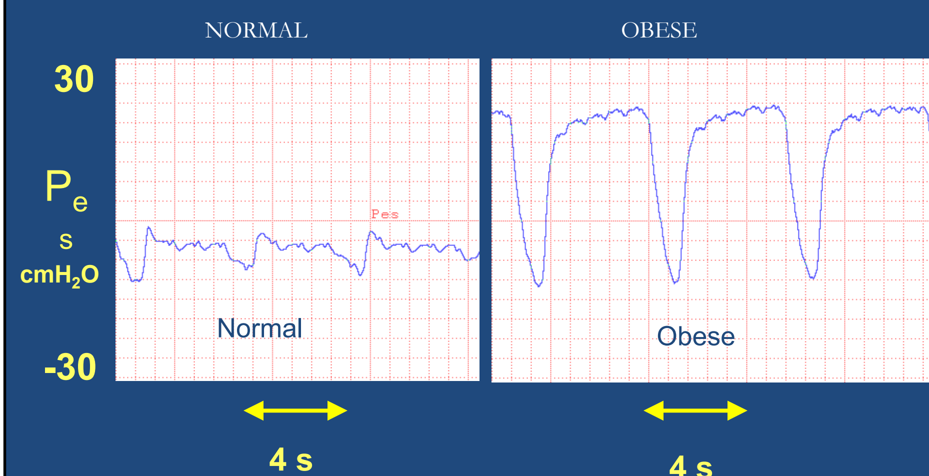


Thorax 2008; Chest 2012

Obesity Effects on Chest Wall

- **Compliance of the lung but not the chest wall is reduced in a number of obesity studies.**
- **Baseline position is altered i.e. pleural pressure is positive but pressure/volume characteristic is preserved.**

Pes in normal and obese subjects at rest, lateral recumbent.



Owens et al. Obesity 2012

Compliance of the respiratory system and its components in health and obesity[1]

A. NAIMARK[2] AND R. M. CHERNIACK[3]
Faculty of Medicine, University of Manitoba; and Clinical Investigation Unit, Department of Medicine, Winnipeg General Hospital, Winnipeg, Canada

- **Studied modest obesity by today's standards**
- **Normal lung compliance**
- **Reduced chest wall compliance**
- **Likely confounded by behavioral influences during wakefulness i.e chest wall muscle activity**

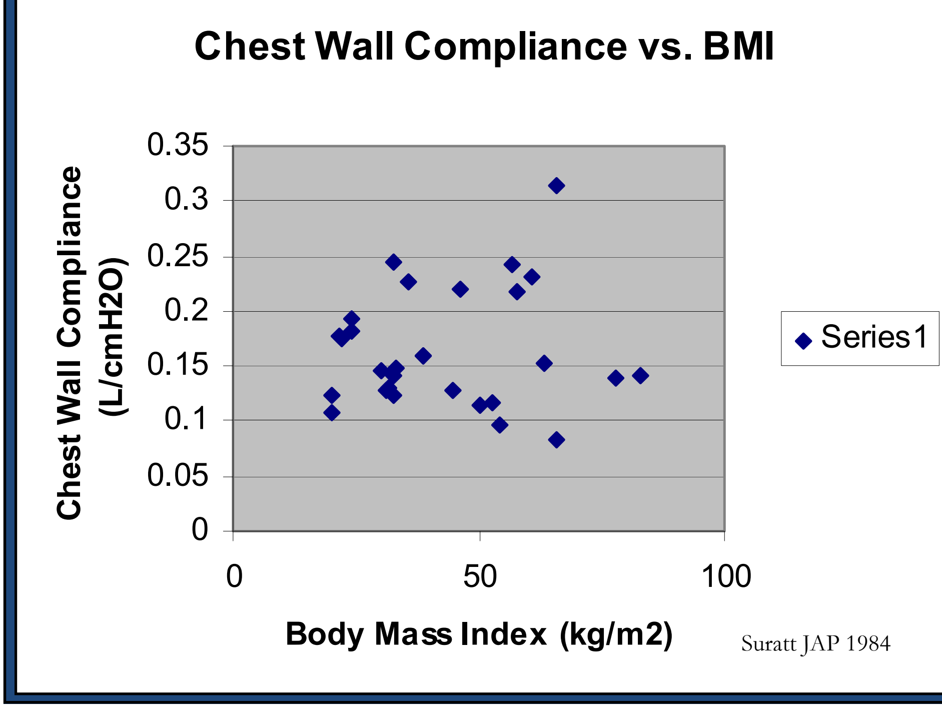
JAP 1960 Cherniack

Compliance of chest wall in obese subjects

PAUL M. SURATT, STEPHEN C. WILHOIT, HENRY S. HSIAO, RICHARD L. ATKINSON, AND DUDLEY F. ROCHESTER
Department of Internal Medicine, University of Virginia School of Medicine and Pulmonary Function Laboratory, University of Virginia Hospital, Charlottesville, Virginia 22908; and Department of Surgery, University of North Carolina, Chapel Hill, North Carolina 27514

- **Early chest wall studies were likely confounded by behavioral influences**
  e.g. muscle activity during wakefulness
- **Subsequent studies done during relaxed wakefulness or paralysis or sleep**
- **Chest wall compliance is likely normal in obesity**

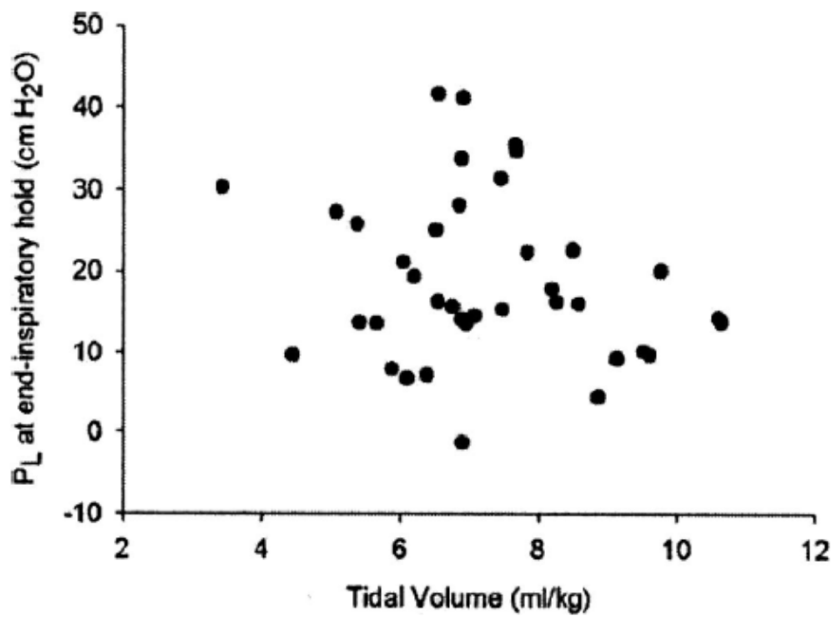
JAP 1984



Esophageal and transpulmonary pressures in acute respiratory failure*

Daniel Talmor, MD, MPH; Todd Sarge, MD; Carl R. O'Donnell, ScD; Ray Ritz, RRT; Atul Malhotra, MD; Alan Lisbon, MD; Stephen H. Loring, MD

CCM 2006



Summarize Obesity and Chest Wall

- Most data indicate that the lung not the chest wall is stiff
- Evidence of alveolar collapse suggests benefits to PEEP
- Airway opening pressures tell us little about distending pressures across the lung.
- 6 cc/kg tidal volume gives variable lung stretch.


ARTICLES
INTEGRATIVE PHYSIOLOGY
nature publishing group

Sitting and Supine Esophageal Pressures in Overweight and Obese Subjects

Robert L. Owens[1], Lisa M. Campana[1,2], Lauren Hess[1], Danny J. Eckert[1], Stephen H. Loring[3] and Atul Malhotra[1]

Obesity 2012

Outline

- 1. Obesity effects on the abdomen
- 2. Obesity effects on the chest wall/lung
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Thorax 2008

How Many Have a Good Sense How to Ventilate this patient ?

- 45 year old with bilateral infiltrates has ABG of pH=7.35 PaCO2=43 mmHg, PaO2=70 mmHg on FIO2=0.6
- Who would give PEEP=8 cmH2O vs. 15 cmH2O?

Malhotra et al, NEJM CPC 2003

Table 4. Effects of Positive End-Expiratory Pressure in Patients with Congestive Heart Failure.

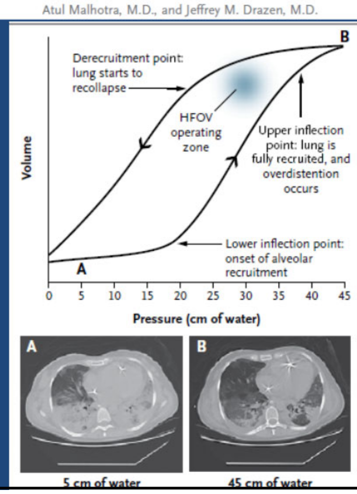
Reduced preload due to increased vena caval resistance
Reduced left ventricular afterload due to reduced wall stress
Reduced myocardial oxygen consumption due to decreased ventricular size
Increased lung compliance due to reduced extravascular lung fluid
Decreased negative pleural pressure with inspiration
Suppressed catecholamines due to improved cardiac output and oxygenation
Reduced mitral regurgitation

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIAL

High-Frequency Oscillatory Ventilation on Shaky Ground

Atul Malhotra, M.D., and Jeffrey M. Drazen, M.D.



NEJM 2013

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CLINICAL THERAPEUTICS

Low-Tidal-Volume Ventilation in the Acute Respiratory Distress Syndrome

Atul Malhotra, M.D.

Conservative views expressed

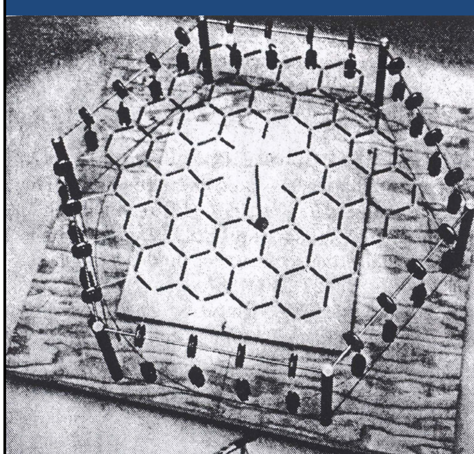
6 cc/kg volume pre-set is the gold standard

Lower is better

Goal is to do no harm with ventilator i.e. prevent mechanical injury

NEJM 9/07

Stress Concentration



- Estimated concentration of stress could be > 4 times that applied to the airway
- Airway pressure of 30 $cmH_2O \approx 140$ cm H_2O in some regions

Mead, *JAP* 1970, 28(5):596

JOURNAL OF APPLIED PHYSIOLOGY
Vol. 28, No. 5, May 1970. *Printed in U.S.A.*

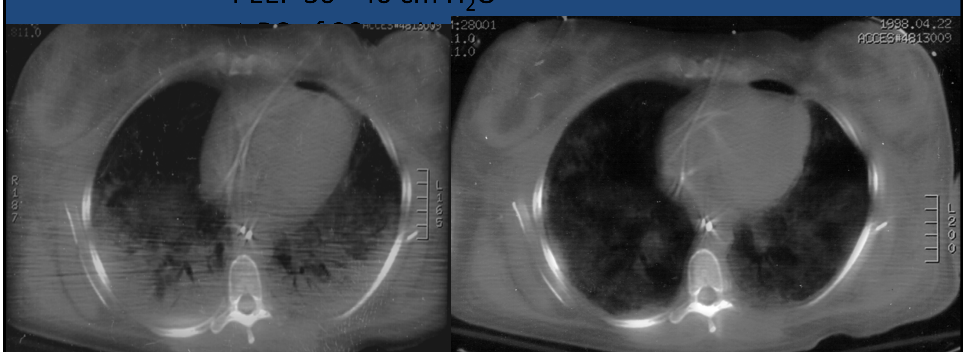
Stress distribution in lungs: a model of pulmonary elasticity

JERE MEAD, TAMOTSU TAKISHIMA, AND DAVID LEITH
Department of Physiology, Harvard University School of Public Health, Boston, Massachusetts 02115

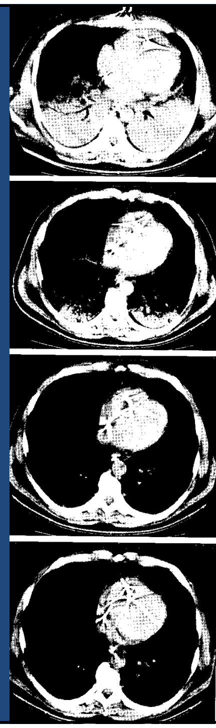
- **Very high shear forces can occur at junctions of normal and abnormal lung**
- **No safe pressure (AJRCCM 2007)**
- **Strategies to promote homogeneity may promote lung protection**
- **"get it open, leave it open"**
- **Homogeneity is everything**

Cytokine Release Following Recruitment Maneuvers*

Daniel Talmor, MD, MPH, FCCP; Todd Sarge, MD; Anna Legedza, ScD; Carl R. O'Donnell, ScD; Ray Ritz, RRT; Stephen H. Loring, MD; and Atul Malhotra, MD, FCCP



Crit Care Med 2000, Chest 2007



PEEP = 5 cmH_2O

collapsed Area = 54.3%
collapsed Mass = 69.2%

PEEP = 19 cmH_2O
(OLA)

collapsed Area = 21.9%
collapsed Mass = 36.8%

PEEP = 25 cmH_2O
(after P_{PLAT} = 55)

collapsed Area = 0.4%
collapsed Mass = 0.9%

PEEP = 23 cmH_2O
(30 minutes later)

collapsed Area = 0.5%
collapsed Mass = 1.8%

Baptista et al AJRCCM 2006

EFFECT OF A PROTECTIVE-VENTILATION STRATEGY ON MORTALITY IN THE ACUTE RESPIRATORY DISTRESS SYNDROME

MARCELO BRITTO PASSOS AMATO, M.D., CARMEN SILVIA VALENTE BARBAS, M.D., DENISE MACHADO MEDEIROS, M.D., RICARDO BORGES MAGALDI, M.D., GUILHERME DE PAULA PINTO SCHETTINO, M.D., GERALDO LORENZI-FILHO, M.D., RONALDO ADIB KAIRALLA, M.D., DANIEL DEHEINZELIN, M.D., CARLOS MUNOZ, M.D., ROSELAINE OLIVEIRA, M.D., TERESA YAE TAKAGAKI, M.D., AND CARLOS ROBERTO RIBEIRO CARVALHO, M.D.

- **Open Lung Ventilation**
- **PEEP > Pflex and Plateau < UIP**
- **Permissive hypercapnia and recruitment maneuvers**
- **Studied n=53 RCT sick patients**
- **28 day survival 71% vs 38%**

Amato et al NEJM 1998; Ranieri JAMA 1999

Amato – caveats?

- Some have argued 71% control mortality too high (3.6 organ failures)
- Small sample size???
- Findings confirmed by Ranieri et al. who demonstrated lower cytokines using lung protective strategy

Ranieri JAMA 1999

A high positive end-expiratory pressure, low tidal volume ventilatory strategy improves outcome in persistent acute respiratory distress syndrome: A randomized, controlled trial*

Jesús Villar, MD, PhD, FCCM; Robert M. Kacmarek, PhD, FCCM; Lina Pérez-Méndez, MD, PhD; Armando Aguirre-Jaime, PhD; for the ARIES Network

- Set ventilator based on PV curves
- Similar to Amato's strategy

Table 2. Main outcome variables

	Control	P_{flex}/LTV	p Value
Ventilator-free days	6.0 ± 7.9	10.9 ± 9.4	.008
Barotrauma, n (%)	4 (8.4)	2 (4)	.418
No. of organ failures: post-pre randomization	1.2 (0.7–1.6)	0.3 (0–0.7)	<.001
ICU mortality rate, %	53.3	32.0	.040

P_{flex}, lower inflection point of the pressure volume curve of the respiratory system; LTV, low tidal volume; ICU, intensive care unit.

- one protocol violation kept this out of NEJM

CCM May 2006

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 13, 2008 VOL. 359 NO. 20

Mechanical Ventilation Guided by Esophageal Pressure in Acute Lung Injury

Daniel Talmor, M.D., M.P.H., Todd Sarge, M.D., Atul Malhotra, M.D., Carl R. O'Donnell, Sc.D., M.P.H., Ray Ritz, R.R.T., Alan Lisbon, M.D., Victor Novack, M.D., Ph.D., and Stephen H. Loring, M.D.

Table 4. Clinical Outcomes.*

Outcome	Esophageal-Pressure–Guided (N=30)	Conventional Treatment (N=31)	P Value
28-Day mortality — no. (%)	5 (17)	12 (39)	0.055
180-Day mortality — no. (%)	8 (27)	14 (45)	0.13
Length of ICU stay — days			0.16
Median	15.5	13.0	
Interquartile range	10.8–28.5	7.0–22.0	

Transpulmonary Pressure

- Transpulmonary pressure (P_L) is the pressure actually distending the lung.

$$P_L = P_{ao} - P_{pl}$$

- Knowing <u>pleural pressure</u> (P_{pl}) could allow calculation of transpulmonary pressure (P_L) to individualize pressures appropriate to the lungs.

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.

CONCLUSIONS

We found that ΔP was the ventilation variable that best stratified risk. Decreases in ΔP owing to changes in ventilator settings were strongly associated with increased survival. (Funded by Fundação de Amparo e Pesquisa do Estado de São Paulo and others.)

NEJM 2015

Critique of Amato et al.

- Driving pressure independent of tidal volume predictive value is surprising if not implausible
- Statistics were robust but complex
- Primary studies had relatively fixed tidal volume diminishing its predictive value

Driving Pressure and Respiratory Mechanics in ARDS

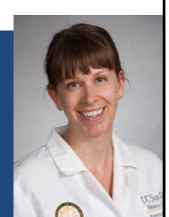
Stephen H. Loring, M.D., and Atul Malhotra, M.D.

- Plateau pressure minus PEEP predicts mortality in lots of different trials
- Incorporates scaling based on lung compliance
- Still emphasize importance of transpulmonary pressure in determining lung stress

NEJM 2015

EDITORIAL

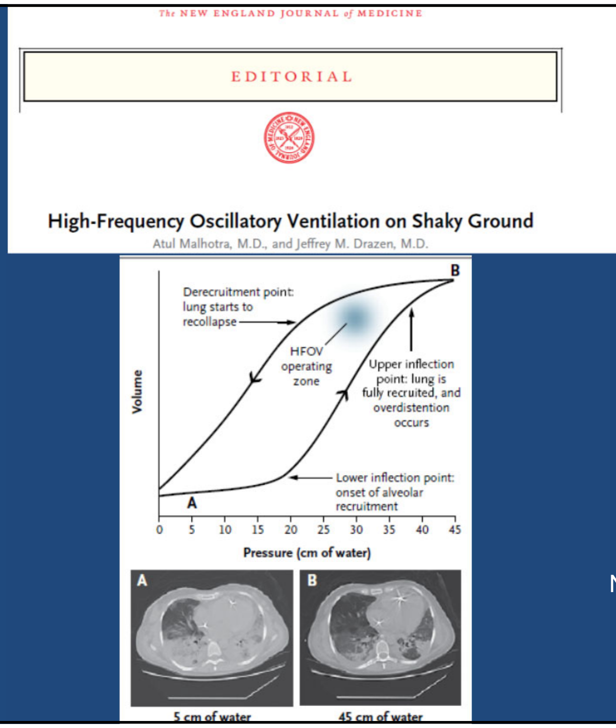
Acute respiratory distress syndrome and the promise of driving pressure



- Limiting driving pressure may help in preventing ARDS (Blondonnet et al.)
- Caution if spontaneous breathing
- Raising PEEP is not the same as lowering tidal volume even though similar driving pressure
- Tidal recruitment may maximize atelectrauma but could lower driving pressure

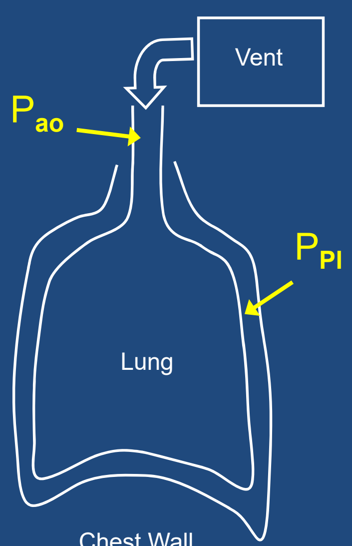
Respirology in press

Rebecca E. Sell, MD and Atul Malhotra, MD
Division of Pulmonary and Critical Care Medicine, Department of Medicine, University of California San Diego, San Diego, CA, USA



NEJM 2013

Did Prior Studies Use the Right Target?

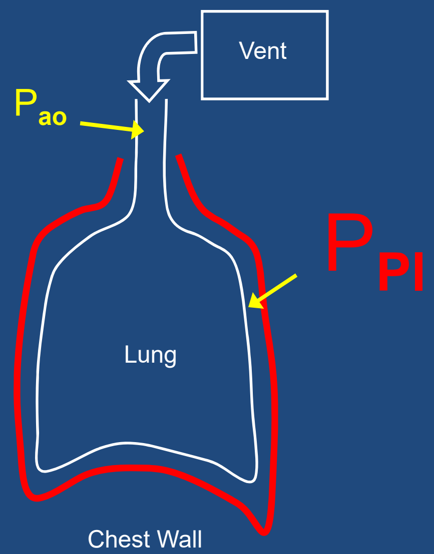


$$P_L = P_{ao} - P_{Pl}$$

P_L is the pressure actually distending the lung.

This may be very different from the pressure measured at the airway.

P_L May be Very Different then P_{ao}



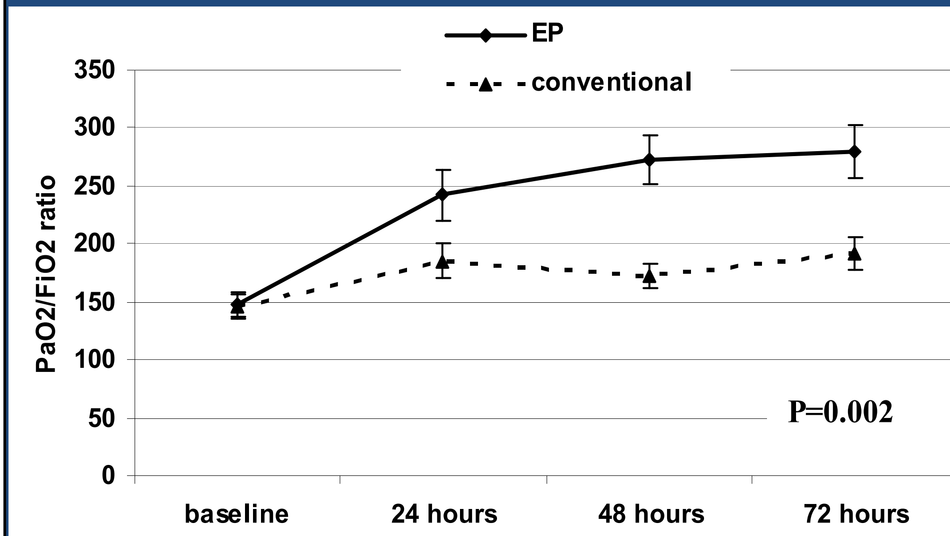
$$P_L = P_{ao} - P_{Pl}$$

Titrating ventilation based on ventilator pressures does not allow us to take this variability into account

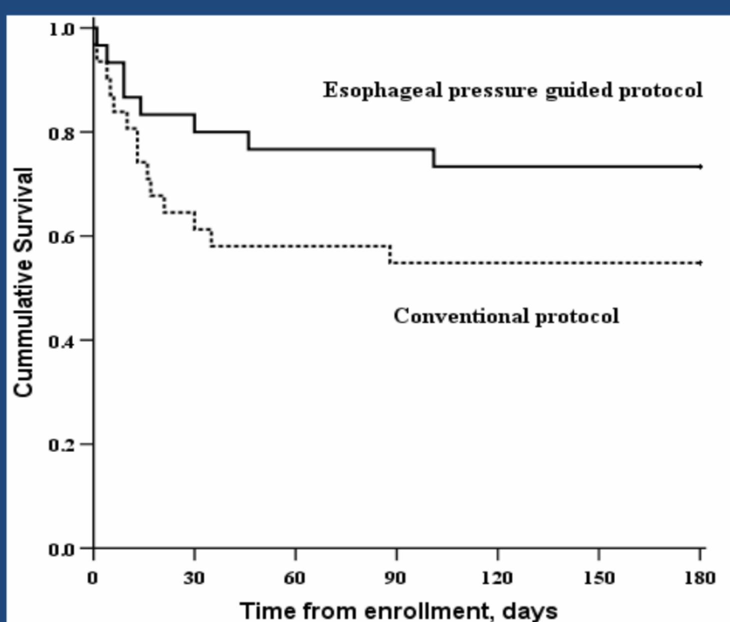
In Humans

Gattinoni. Am J Respir Crit Care Med Vol 164. pp 1701–1711, 2001

Patient Oxygenation- Repeated Measures



6- Month Survival



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 22, 2004 VOL. 351 NO. 4

Higher versus Lower Positive End-Expiratory Pressures in Patients with the Acute Respiratory Distress Syndrome

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

- **Studied high vs. low PEEP and showed no difference**
- **PEEP set based on oxygenation tables which were reasonably arbitrary.**

NEJM July 2004

Clinical Trial Oxygenation vs. Mechanics

Oxygenation
ALVEOLI - negative
LOVS - negative
Mechanics
Amato - positive
Villar - positive
EpVent - positive

? Express - equivocal

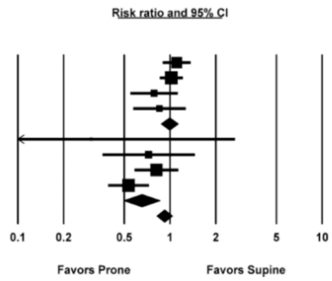
Intensive Care Med (2014) 40:332–341
DOI 10.1007/s00134-013-3194-3

SYSTEMATIC REVIEW

Jeremy R. Beitler
Shahzad Shaefi
Sydney B. Montesi
Amy Devlin
Stephen H. Loring
Daniel Talmor
Atul Malhotra

Prone positioning reduces mortality from acute respiratory distress syndrome in the low tidal volume era: a meta-analysis

Group by High vs Low Vt	Study name	Risk ratio	Lower limit	Upper limit	p-Value	Relative weight
High	Gattinoni, 2001	1.106	0.900	1.360	0.337	32.46
High	Guerin, 2004	1.020	0.862	1.207	0.819	45.08
High	Mancebo, 2006	0.786	0.551	1.120	0.183	12.30
High	Taccone, 2009 (mod)	0.852	0.575	1.262	0.424	10.15
High		0.996	0.876	1.132	0.949	
Low	Voggenreiter, 2005	0.304	0.035	2.659	0.282	1.56
Low	Fernandez, 2008	0.724	0.362	1.446	0.360	13.40
Low	Taccone, 2009 (sev)	0.814	0.588	1.128	0.216	40.82
Low	Guerin, 2013	0.534	0.394	0.724	0.000	44.23
Low		0.655	0.499	0.860	0.002	
Overall		0.834	0.683	1.017	0.073	



VIEWPOINT Open Access

PEEP titration during prone positioning for acute respiratory distress syndrome

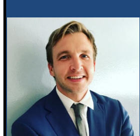
Jeremy R. Beitler[1*], Claude Guérin[2,3], Louis Ayzac[4], Jordi Mancebo[5], Dina M. Bates[1], Atul Malhotra[1] and Daniel Talmor[6]

ICM 2014, Crit Care 2015

Prone positioning in acute respiratory distress syndrome: why aren't we using it more?

Mark L. Hepokoski, Mazen Odish, Atul Malhotra

- Convenience
- Debate over mechanism
- Likely not just a function of paralytics
- Patient ventilator synchrony may be important
- It may be the only thing that works !



JTD 2018

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
Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART) Investigators, Alexandre Biasi Cavalcanti, MD, PhD, [...], and Carlos Roberto Ribeiro de Carvalho, MD, PhD

Increased mortality using strategy I recommend

Ouch

Maybe some design flaws e.g. best compliance

JAMA 2017

Rethinking the ARDS Lung

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Ventilator-induced Lung Injury

Jeremy R. Beitler, MD, MPH[a,*], Atul Malhotra, MD[a], B. Taylor Thompson, MD[b]

Clinics Chest Medicine 2016

The ARDS "Baby Lung"

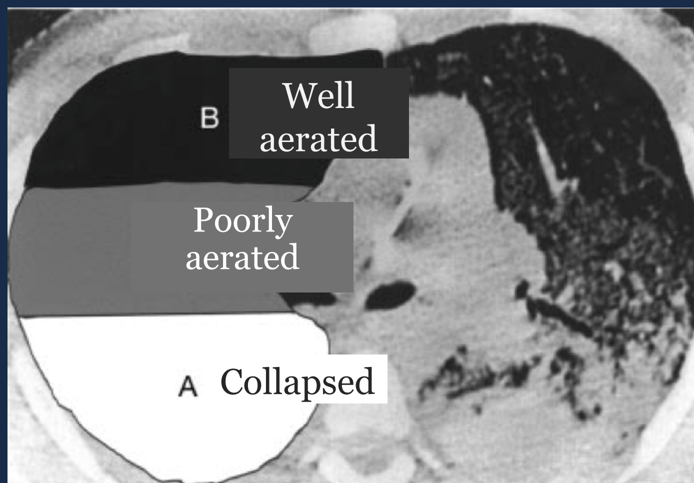

Figure from: Moloney. *Br J Anaeth.* 2004;92:261-270.

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Baby Lung: Implications for Lung Injury

• **Well-aerated regions**	Risk of overdistension (volutrauma/barotrauma)
• **Poorly aerated regions**	Risk of cyclic atelectasis
• **Collapsed regions**	Decrease lung volume available for ventilation
• **Inhomogeneity (border zones)**	High shear forces

Best evidence: therapies targeting optimal mechanics

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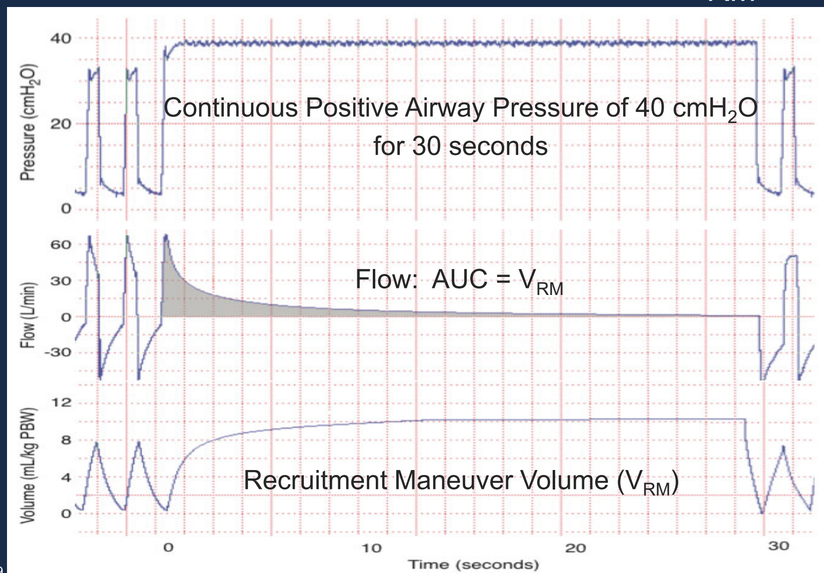
Recruitment Maneuver Volume (V_{RM})



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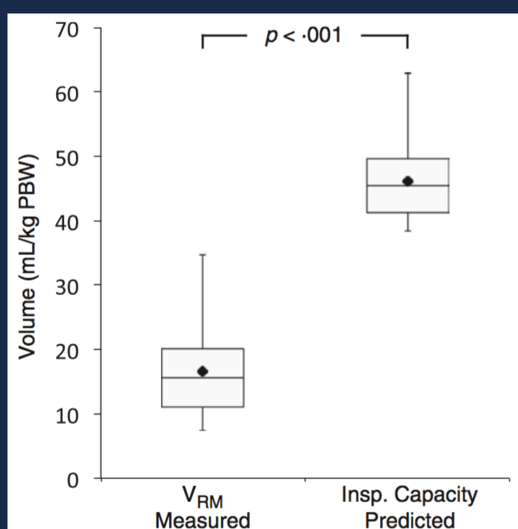
Beitler et al. *Crit Care Med.* 2016;44:91-99

Recruitment Maneuver Volume (V_{RM})



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Beitler et al. *Crit Care Med.* 2016;44:91-99

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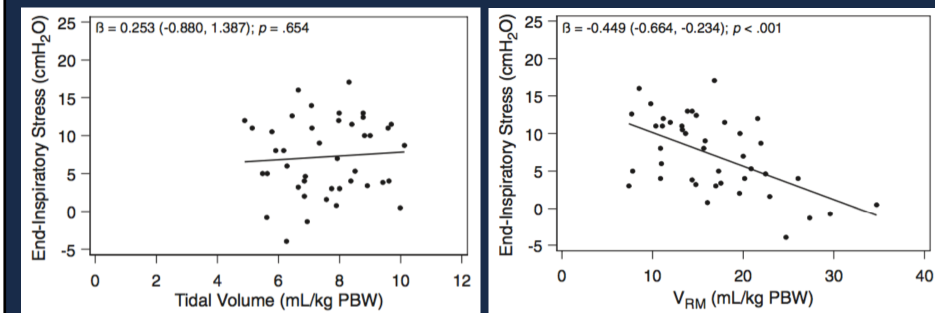
Predicting Lung Stress & Mortality

- End-inspiratory stress: Ptp = Paw – Ppl



  - V_{RM} predicts risk of death (OR 0.84, 95% CI 0.71-1.00; *p* = .02)

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Beitler et al. *Crit Care Med.* 2016;44:91-99

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V_T/V_{RM}: Scaling V_T to Baby Lung Size

- V_{RM} = maximum insufflation volume achievable under clinically plausible conditions
  - Analogous to relative inspiratory capacity measured beginning from PEEP

- V_T/V_{RM} = fraction of the potentially available lung volume that is insufflated with each tidal breath

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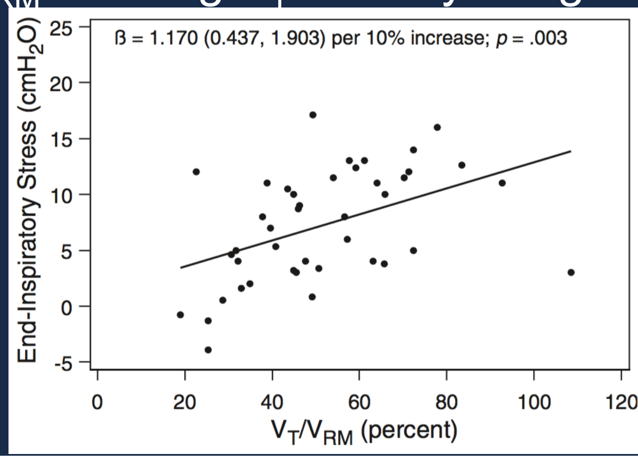
Beitler et al. *Crit Care Med.* 2016;44:91-99

UC San Diego SCHOOL OF MEDICINE

V_T/V_{RM}: Scaling V_T to Baby Lung Size



Volume Delivered During Recruitment Maneuver Predicts Lung Stress in Acute Respiratory Distress Syndrome*

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Summary

- Oxygenation is one of many factors that influences ventilator settings
- Mechanics may be more important than oxygenation since patients rarely die from low PO2 and the goal is to do no mechanical harm with ventilator
- Multiple factors including individual's hemodynamics and mechanics should influence PEEP decisions as well as response to therapy (recruitability)
- We need more RCTs but small existing studies which have titrated ventilator settings based on lung and chest wall mechanics have succeeded.
- Providing tidal volume consistent with the available lung for gas exchange deserves further study

- EPVENT 2 and ROSE are soon to release

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