Covid-ARDS Physiology

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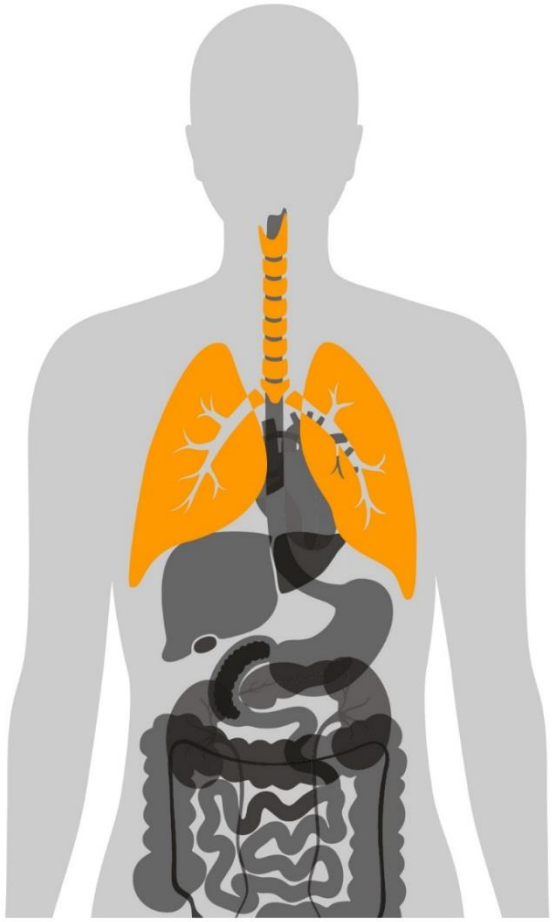
COVID-19

Clinical presentation



Most common symptoms: [1]

- Fever
- Fatigue
- Dry cough

Some patients may also have:

- Aches and pains
- Runny nose
- Sore throat
- Shortness of breath
- Diarrhoea

Two clinical scenarios:

Based on Chinese Centers for Disease Control report on 72,314 patients[2]

Mild disease (81%): non-pneumonia and mild pneumonia

Severe disease (14%): dyspnea, respiratory frequency ≥ 30/min, blood oxygen saturation (SpO2) ≤ 93%, PaO2/FiO2 ratio*< 300 and/or lung infiltrates > 50% within 24 to 48 hours

Critical disease (5%): respiratory failure, septic shock and/or multiple organ dysfunction (MOD) or failure (MOF)

* the ratio between the blood pressure of the oxygen (PaO2) and the percentage of oxygen supplied (FiO2)

1. Wang D, et al. *JAMA*. 2020;323:1061-1069. 2. Wu Z, et al. *JAMA*. 24 February 2020. doi:10.1001/jama.2020.2648

“This Is Not ARDS”

People are saying this without appreciating Berlin definition

JAMA 2012


ONLINE FIRST

Acute Respiratory Distress Syndrome

The Berlin Definition

The ARDS Definition Task Force*

The acute respiratory distress syndrome (ARDS) was defined in 1994 by the

NYC hospitals presented different phenotypes locally

a) Vascular clot (giving heparin and lytics)
b) Mucus hypersecretion – bronching
c) Capillary leak – unclear
d) Alveolar flooding with high surface tension- recruitment
e) CHF from myocarditis


HIGH ALTITUDE MEDICINE & BIOLOGY
Volume 00, Number 0, 2020
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DOI: 10.1089/ham.2020.0055

COVID-19 Lung Injury is Not High Altitude Pulmonary Edema

Andrew M. Luks, MD,[1] Luanne Freer, MD,[2] Colin K. Grissom, MD,[3] Scott E. McIntosh, MD, MPH,[4] Robert B. Schoene, MD,[5] Erik R. Swenson, MD[1,6] and Peter H. Hackett, MD[7]

Research Question: perhaps Covid is affecting different cells in different patients e.g. non ACE2 mechanisms

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.

activity. Overinflation of the lung results in depletion or alteration in surfactant which is essential to the maintenance of expanded alveoli at end-expiratory pressures. Prolonged positive pressure ventilation at normal pressure and volume does not alter surfactant and did not result in atelectasis in this study.

Anesthesiology 1964

Experimental Pulmonary Edema due to Intermittent Positive Pressure Ventilation with High Inflation Pressures. Protection by Positive End-Expiratory Pressure[1-4]

HERBERT H. WEBB and DONALD F. TIERNEY

ARRD 1974

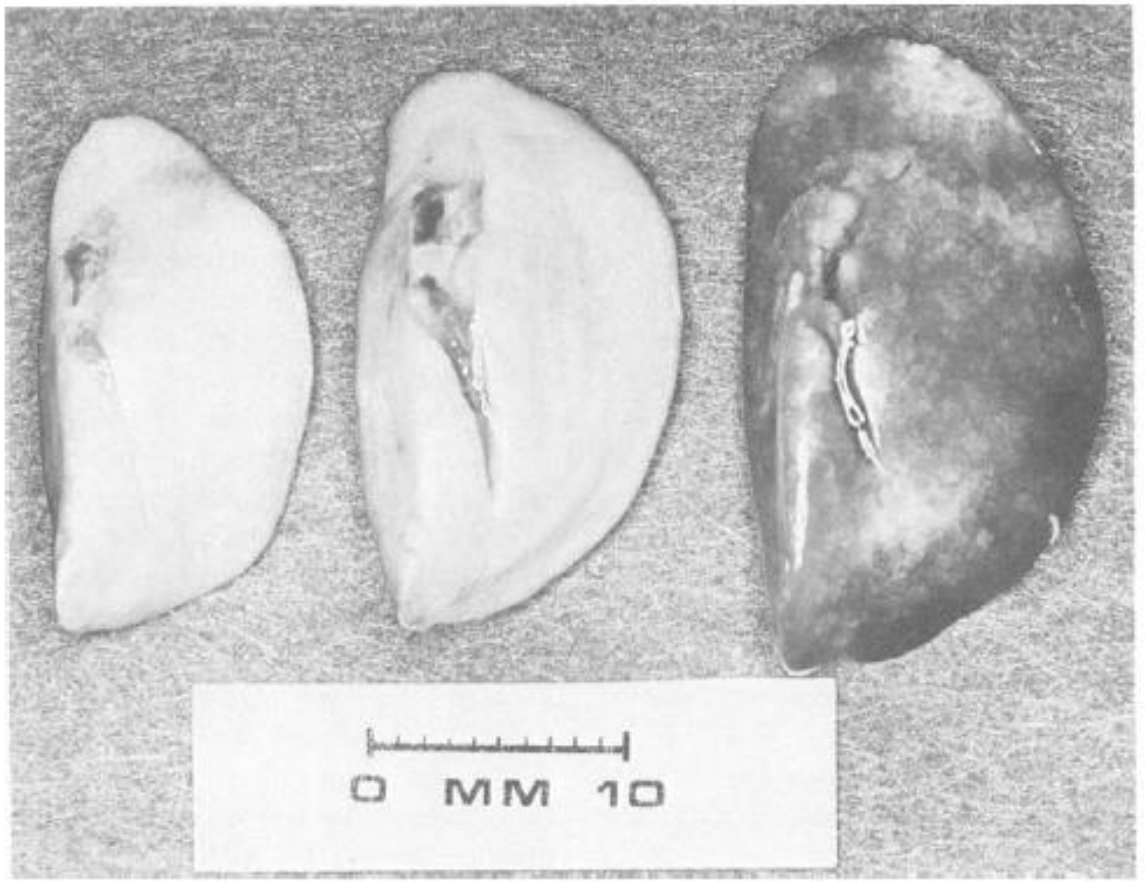
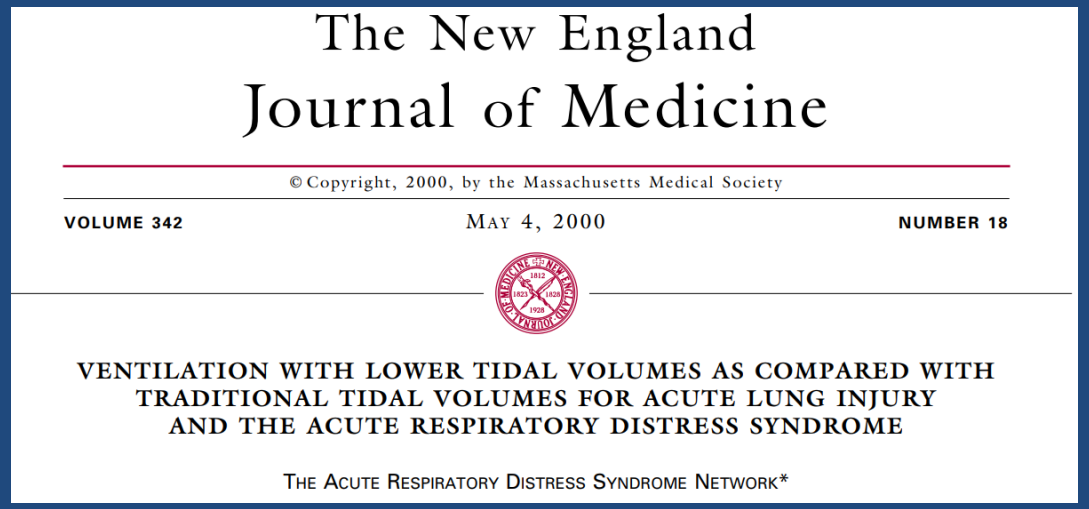


Fig. 3. Comparison of left lungs from rats ventilated with IPPB 14/0, PEEP 45/10, and HIPPB 45/0 (left to right). The perivascular groove is distended with edema in the lungs from rats ventilated with inspiratory pressure of 45 cm H_2O. The dark congested appearance of the lung ventilated with 45/0 is apparent.

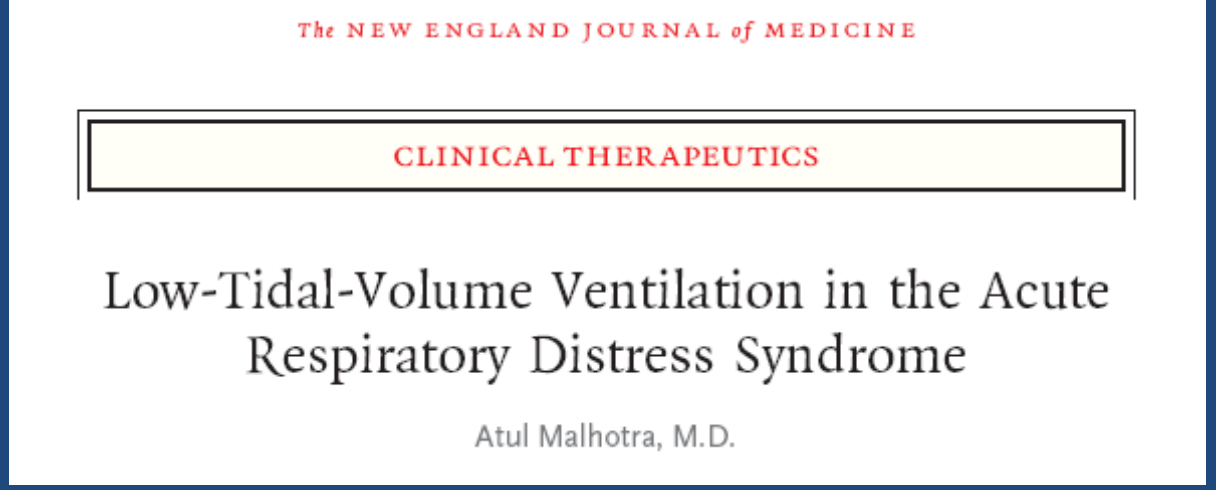


The New England
Journal of Medicine

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*



The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL THERAPEUTICS

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

Atul Malhotra, M.D.

ARDSNET

6 cc/kg ideal body weight

40% vs. 30% mortality comparing 12 cc/kg vs. 6 cc/kg

Lower is better

Goal is to do no mechanical harm with ventilator

NEJM 9/07

Driving Pressure for Ventilation of Patients with Acute Respiratory Distress Syndrome

Angela Meier, M.D., Ph.D., Rebecca E. Sell, M.D., Atul Malhotra, M.D.

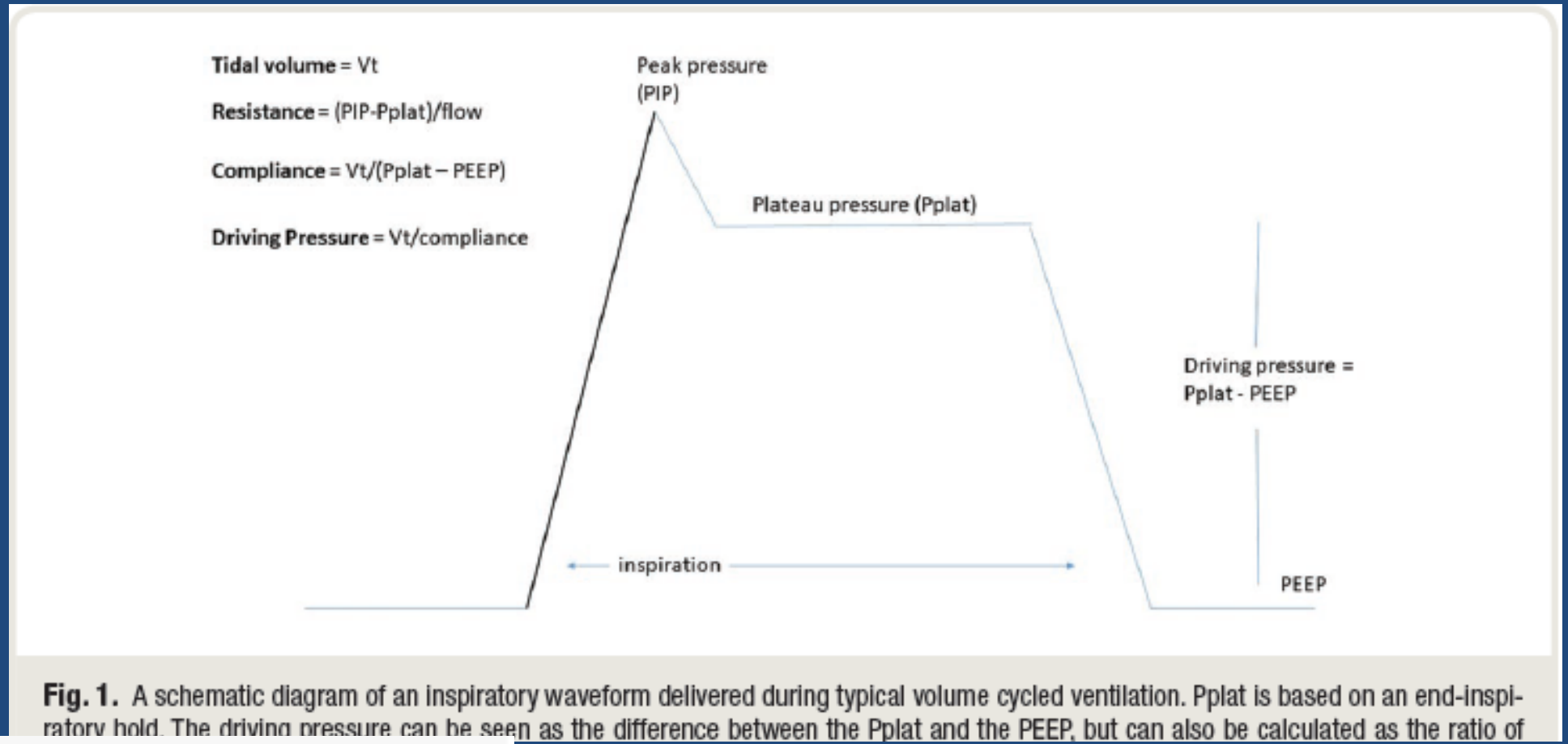


Fig. 1. A schematic diagram of an inspiratory waveform delivered during typical volume cycled ventilation. Pplat is based on an end-inspiratory hold. The driving pressure can be seen as the difference between the Pplat and the PEEP, but can also be calculated as the ratio of

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Driving Pressure and Respiratory Mechanics in ARDS

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

Anesthesiology 2020 in press

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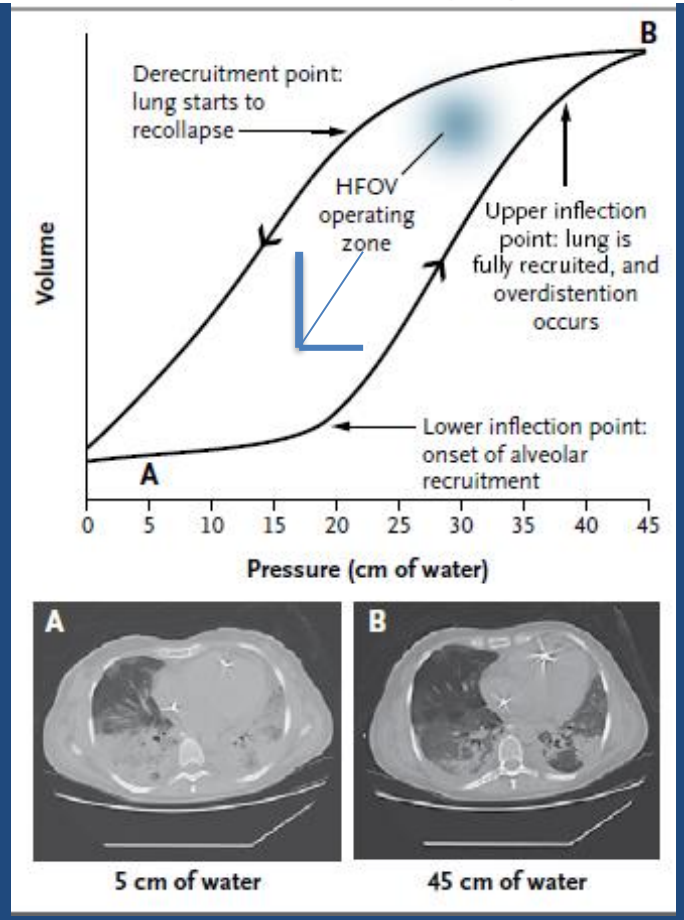
EDITORIAL

High-Frequency Oscillatory Ventilation on Shaky Ground

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



Covids are ‘recruitable’ by some reports

Recruitment is a vertical line on the PV Curve; overdistension is horizontal

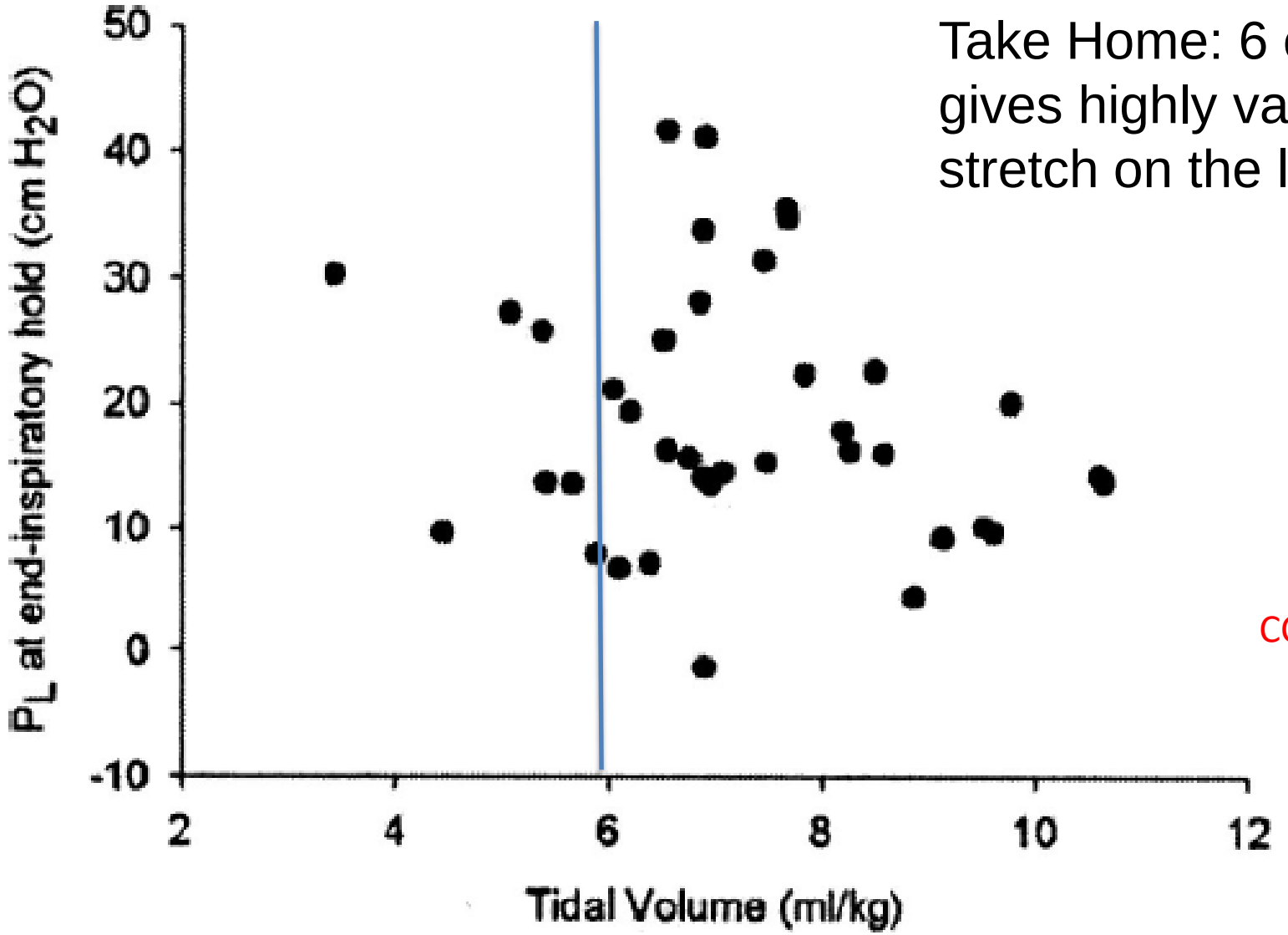
Concomitant COPD increases compliance

Spontaneous breathing complicates matters

NEJM 2013

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



Take Home: 6 cc/kg gives highly variable stretch on the lung

CCM 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	

Self Inflicted Lung Injury

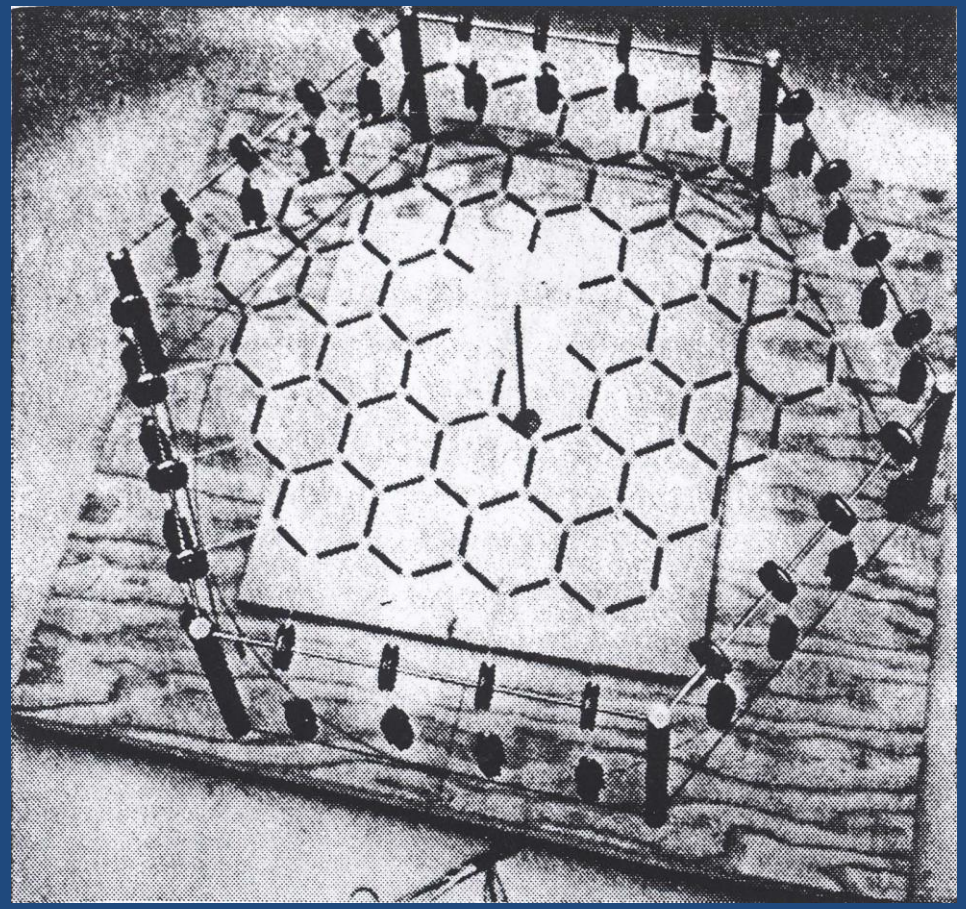
- Traditional teaching is that you can't pop your own lung
- High shear forces can occur at junctions of normal and abnormal lung – so called stress amplification
- Spontaneous breathing can generate lung stress even with atmospheric pressure at mouth (P_L = Pao-Ppl)
- Kolobow ICM 1988 Induced lung injury by injecting salicylate into cisterna magna to stimulate ventilation but no lung injury when sheep were sedated and paralyzed.

Stress Concentration

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

Stress distribution in lungs: a model of pulmonary elasticity

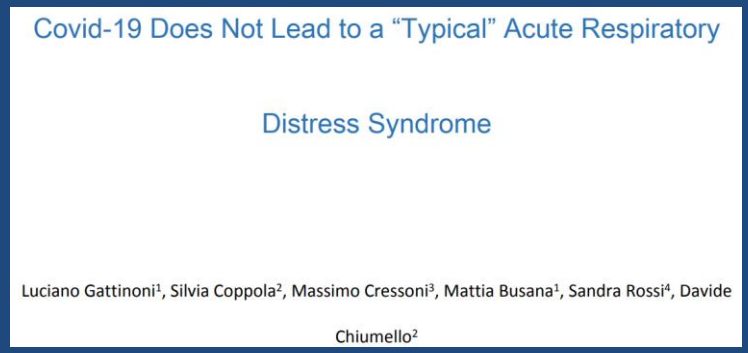
JERE MEAD, TAMOTSU TAKISHIMA, AND DAVID LEITH
Department of Physiology, Harvard University School of Public Health, Boston, Massachusetts 02115



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

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

Gattinoni AJRCCM 2020


Covid-19 Does Not Lead to a "Typical" Acute Respiratory

Distress Syndrome

Luciano Gattinoni[1], Silvia Coppola[2], Massimo Cressoni[3], Mattia Busana[1], Sandra Rossi[4], Davide Chiumello[2]

-Some of this is interesting but wild speculation:

-Initial lesion is vasoplegia i.e. loss of hypoxic vasoconstriction (HPV)

-Robust ventilatory response to hypoxia drives big tidal volumes

With very compliant lungs (relief of dyspnea, corollary discharge)

-Lung injury is 'self-infected' based on stress (transpulmonary pressure) and strain (overcoming TLC locally)

-starts to look like typical ARDS

His solution: ICU in Switzerland intubated and paralyzed very early and had 0/40 deaths compared to neighbors with >50% dead

Gattinoni et al. AJRCCM 2020

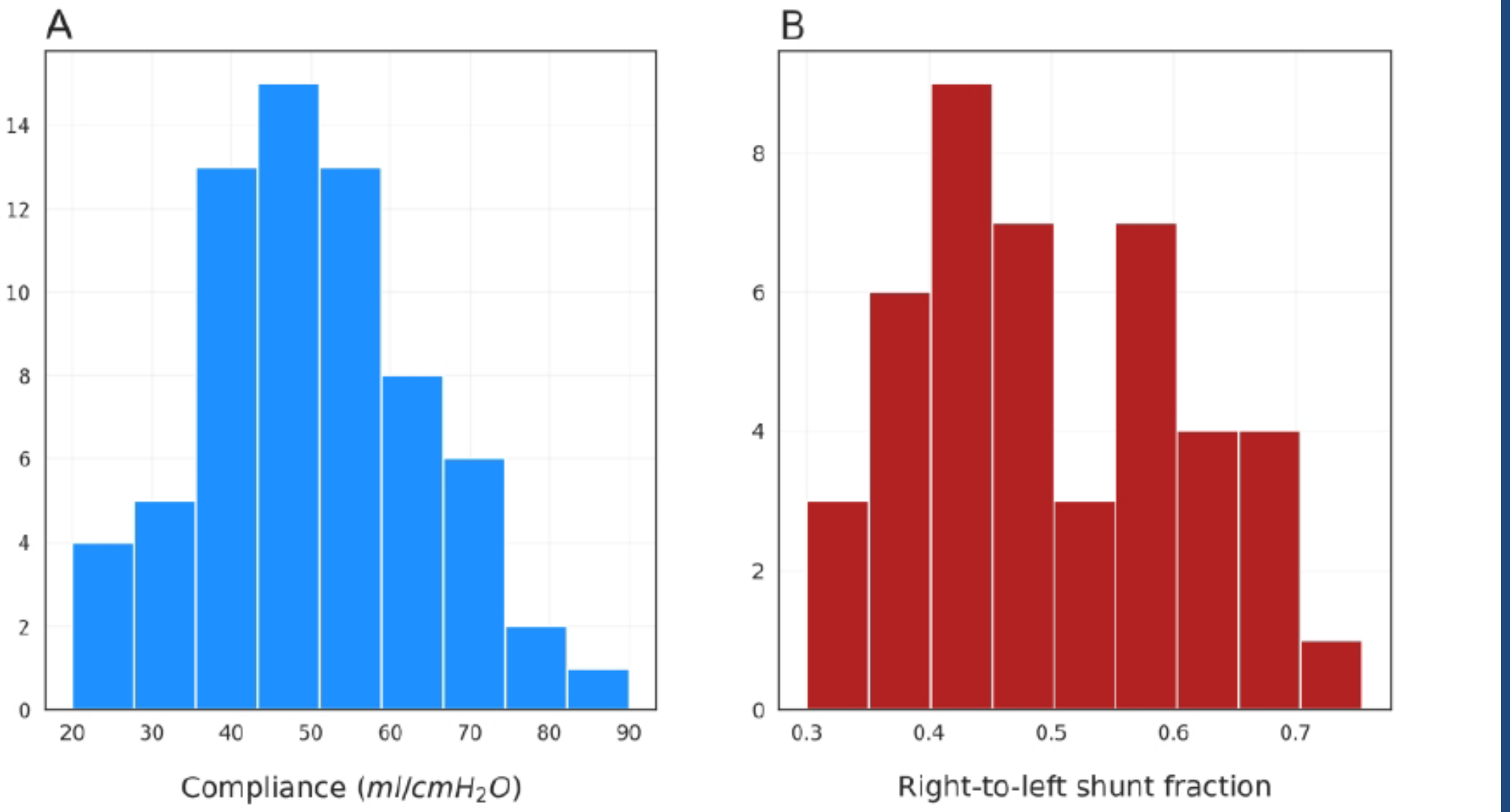


Figure 1

We are given insufficient information about how/when these measurements were made to draw real conclusions

Summary: Clinical Observations So Far for Covid and possible research ideas

- Hypoxemia out of proportion to lung infiltrates (? HPV problem)
- Compliance of lungs higher than expected (occasionally measured during spontaneous breathing giving spurious values)
- Cardiac function has been fairly normal by echo, central venous oxygen saturations and pressor requirements are ok
- Some patients abruptly deteriorate
- We have seen 3 ventilator induced pneumothorax which is typically rare in usual ARDS
- Response to inhaled pulmonary vasodilators has been generally poor
- Perhaps different cells are being affected in different patients (endothelial vs. vascular smooth muscle vs. T2 pneumocyte, goblet)
- Abnormalities in gas exchange, mechanics and control all seen

- Speculation among friends :
- I wonder if proteases which are released in Covid pneumonia are degrading parenchyma leading to high compliance and pneumothorax
- I have a theory about extremes of HPV (gas exchange vs. infection control)
- I have a theory about extremes of chemosensitivity (severe asthma vs. ARDS)

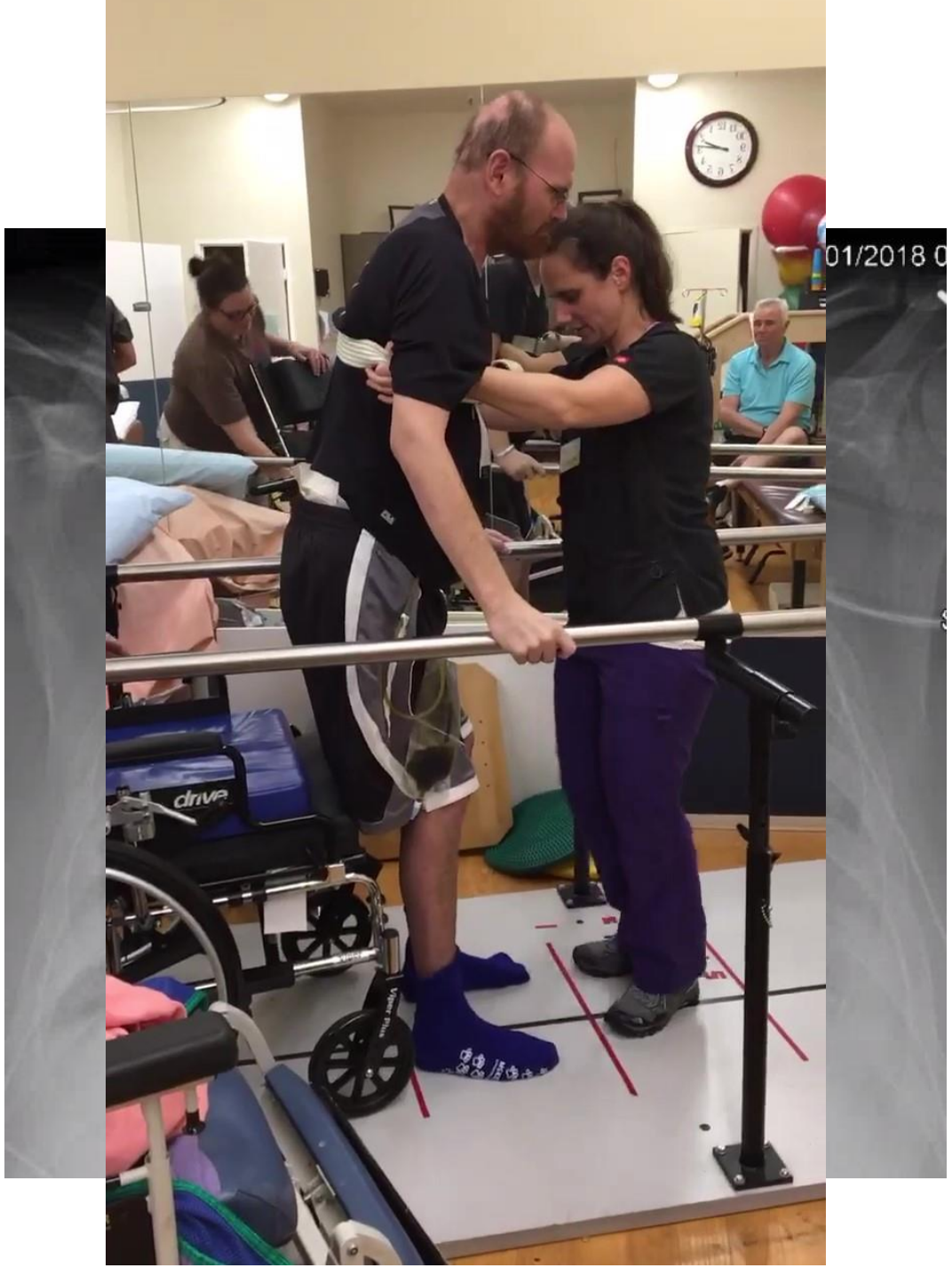
Post-ICU Syndrome: Implications in the COVID-19 era

Amy Bellinghausen, MD, PGY6, PCCM fellow, UCSD

I have no conflicts of interest to disclose

PICS

- 42 previously healthy male
- Influenza pneumonia
- ~65 days in intensive care
  - Extracorporeal Membrane Oxygenation (ECMO) x17 days
- Multiple procedures
  - Tracheostomy, gastrostomy, central & arterial lines, percutaneous cholecystostomy and chest tube
- Discharged to nursing home
- Unable to walk

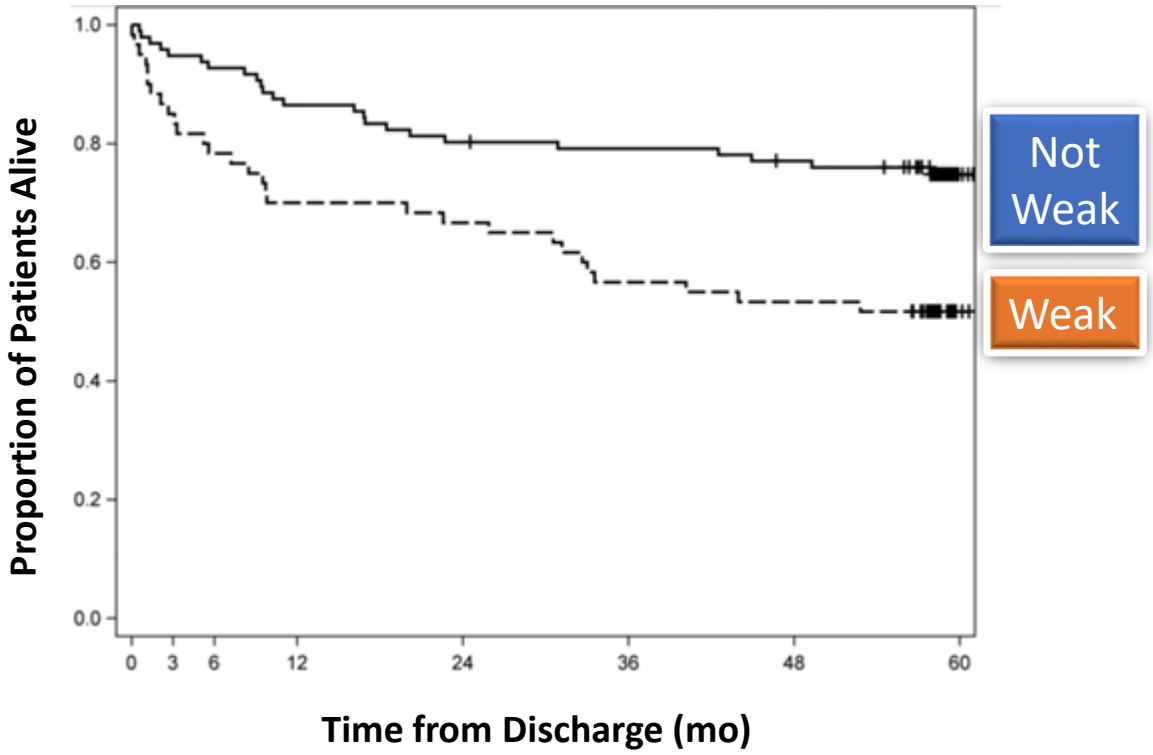


ICU Acquired Weakness

Common

- 38-51% of ARDS patients

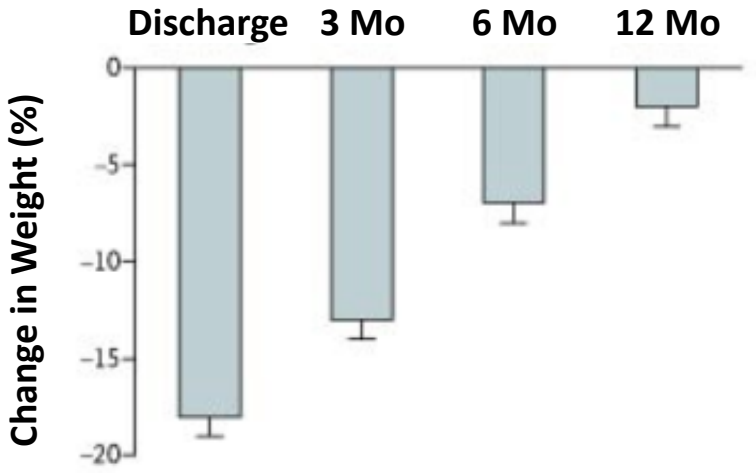
- Multifactorial
  - Myopathy and/or Polyneuropathy



ORIGINAL ARTICLE

One-Year Outcomes in Survivors of the Acute Respiratory Distress Syndrome

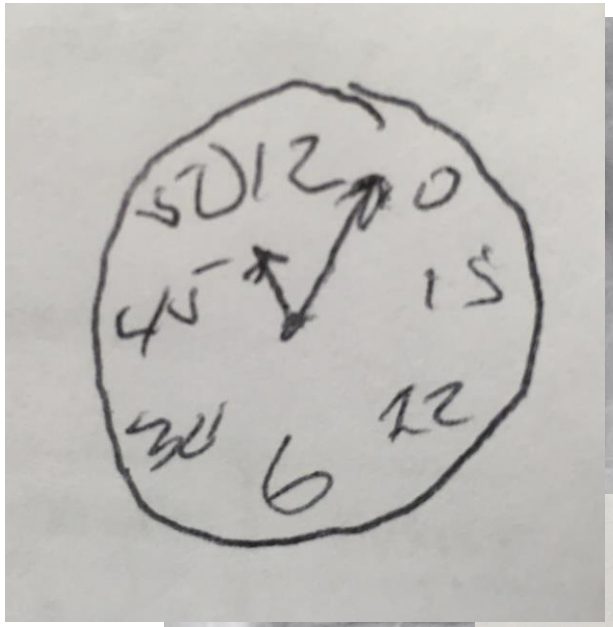
Margaret S. Herridge, M.D., M.P.H., Angela M. Cheung, M.D., Ph.D., Catherine M. Tansey, M.Sc., Andrea Matte-Martyn, B.Sc., Natalia Diaz-Granados, B.Sc., Fatma Al-Saidi, M.D., Andrew B. Cooper, M.D., Cameron B. Guest, M.D., C. David Mazer, M.D., Sangeeta Mehta, M.D., Thomas E. Stewart, M.D., Aiala Barr, Ph.D., et al., for the Canadian Critical Care Trials Group

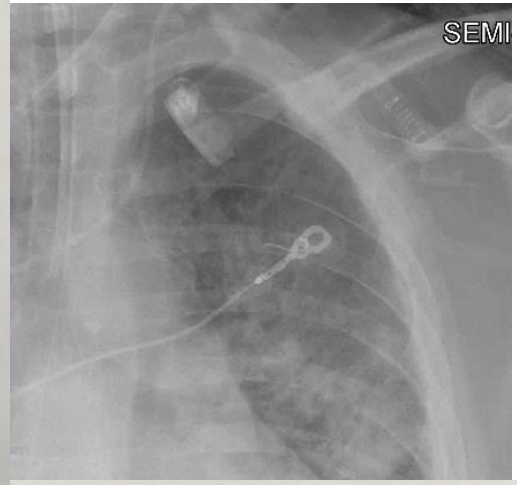


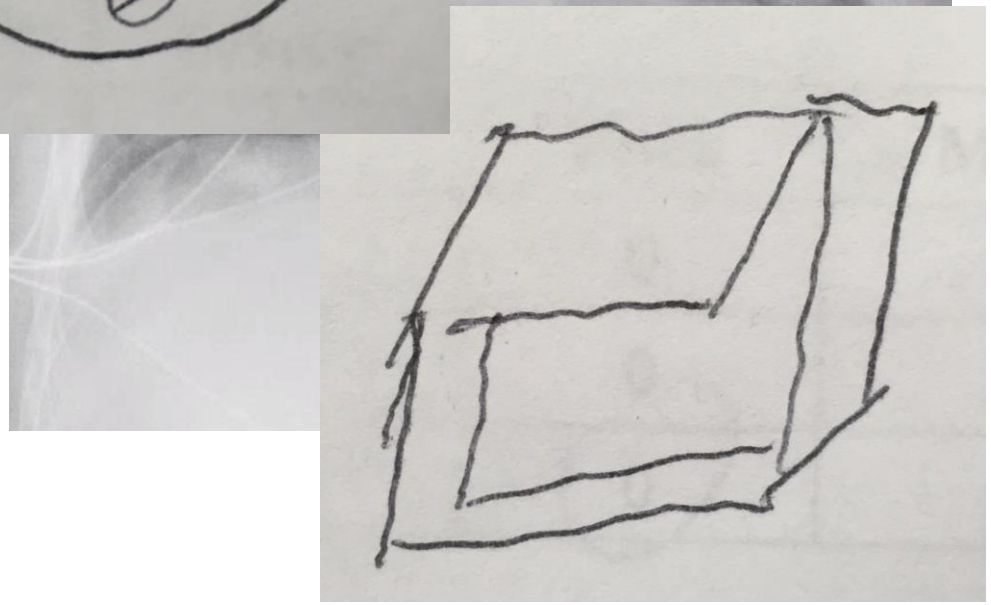
Muscle Weakness and 5-Year Survival in Acute Respiratory Distress Syndrome Survivors

Victor D. Dinglas, MPH[1,2], Lisa Aronson Friedman, ScM[1,2], Elizabeth Colantuoni, PhD[1,3], Pedro A. Mendez-Tellez, MD[1,4], Carl B. Shanholtz, MD[5], Nancy D. Ciesla, DPT, MS[1,2], Peter J. Pronovost, MD, PhD[1,4], and Dale M. Needham, FCPA, MD, PhD[1,2,6]

ICU Recovery Clinic: Mr. G







- 45M with very severe ARDS
  - Paralyzed & proned, sent to UCSD for ECMO
  - Ambulated on ventilator, awake & communicative
  - Extubated after 5 days at UCSD, +delirium
- ICU Recovery Clinic - 20 days post discharge
  - Minimal complaints
  - Wife reported “He’s a little more forgetful”
  - Previously worked as aerospace machinist
- Cognitive testing – **MoCA 11/30 (nl ≥ 26)**
  - <u>Sent for neuropsych testing</u>
  - <u>Cognitive rehab referral</u>

ICU Recovery Clinic Visit = Hub and Spoke

- **Check in**
  - Screen for anxiety, depression, PTSD, insomnia
- **Critical Care MD**
  - Hear the ICU story
  - Cognitive testing
  - Identify functional deficits
- **Critical Care Pharmacist**
  - Reconcile medications
  - Review vaccines
- Referrals as needed
- Letter sent to primary MD