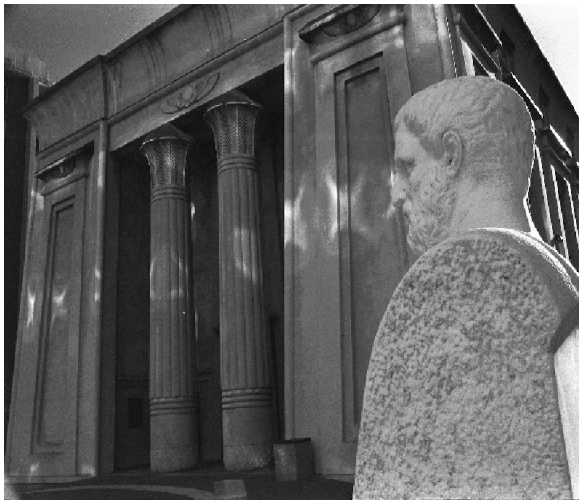
Eastern Pulmonary Conference
January 2021

Treatment and "Overtreatment" of Hypoxemic Respiratory Failure



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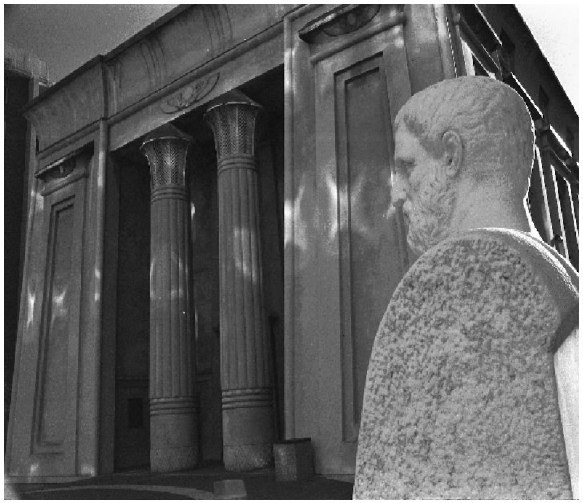

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Nothing to disclose

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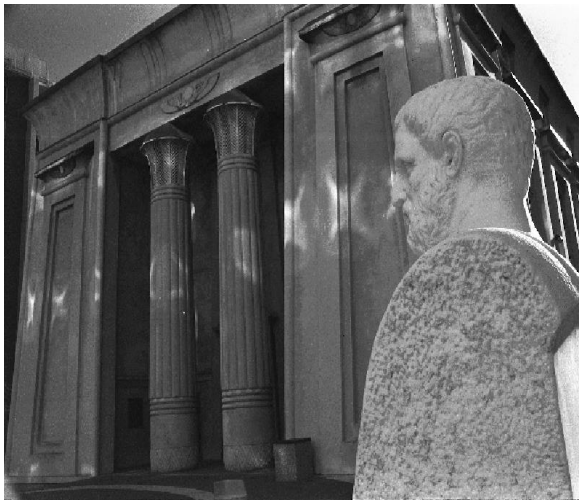
Treatment and "Overtreatment" of Hypoxemic Respiratory Failure

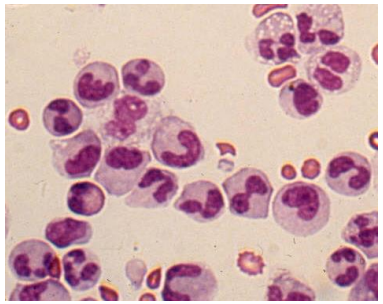


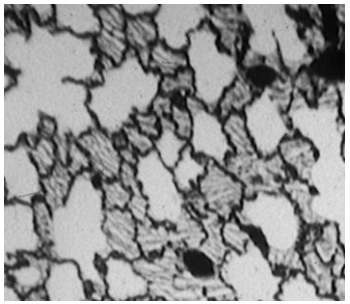
Learning Objectives: Upon completion of this learning activity, participants should be able to…

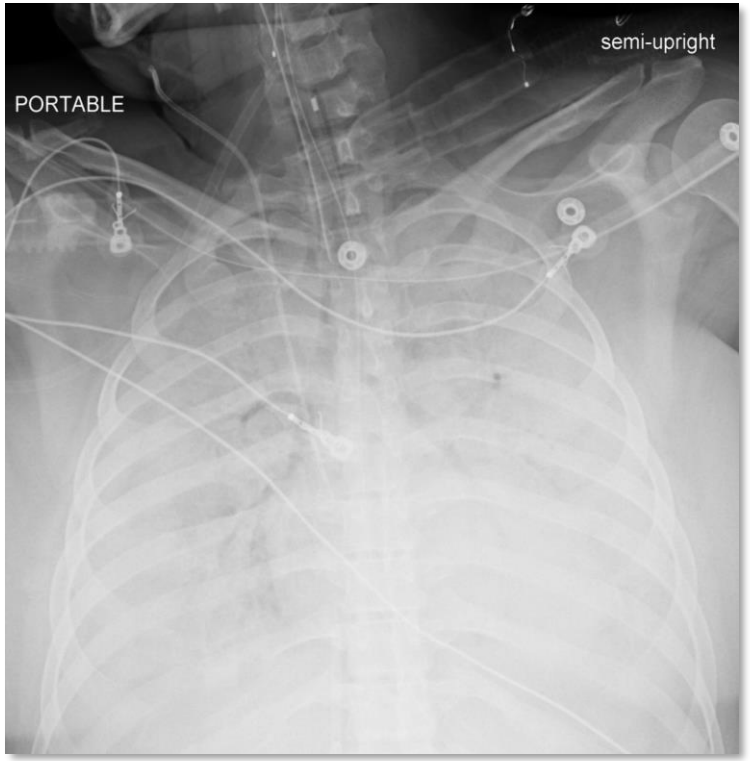
1. Apply a structured outline to managing the patient with hypoxemic respiratory failure
2. Examine the pitfalls of "over-treating" hypoxemic respiratory failure, particularly related to mechanical ventilation

Acute Hypoxemic Respiratory Failure: Often Due to ARDS

ARDS is an acute diffuse, inflammatory lung injury, leading to increased pulmonary vascular permeability, pulmonary edema, and loss of aerated lung tissue with hypoxemia and bilateral radiographic opacities, associated with reduced lung compliance.

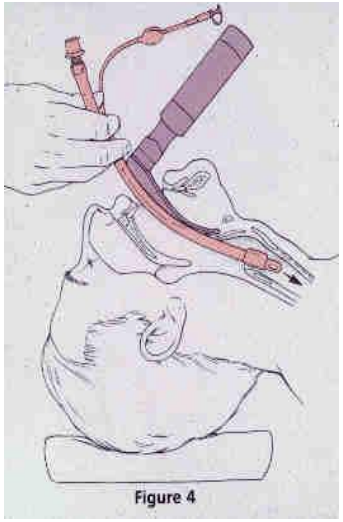


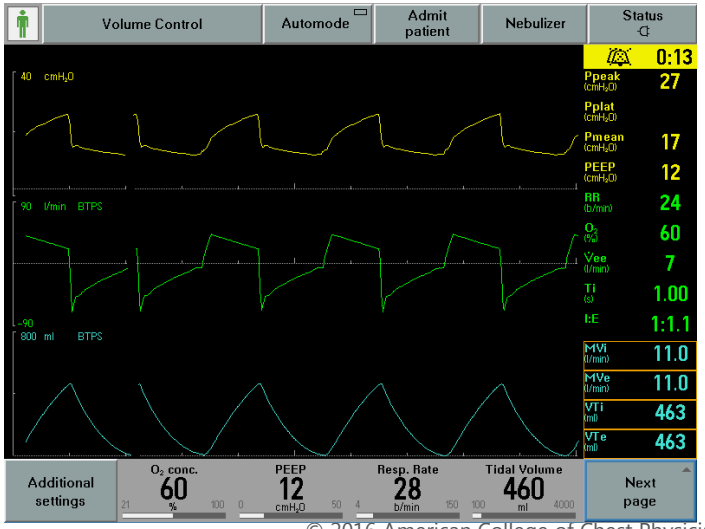




Management of Hypoxemic Respiratory Failure

- Immediate evaluation & stabilization
- Supplemental oxygen
- Mechanical ventilation*
- Supportive care
- Identification & management of causative conditions





Management of Hypoxemic Respiratory Failure

TREATMENT	"OVERTREATMENT"
High Flow Nasal Oxygen	Invasive Ventilation?

- Does your patient need invasive ventilation?
- Invasive ventilation…
  - More sedation
  - Reduce mobility
  - More tubes and lines
  - Airway and ventilator complications

High-Flow Nasal Oxygen

- High FiO2 + high flow rates (control each)
- Constant FiO2 during peak inspiratory flow
- Low level CPAP; increased end-expiratory pressure (only about 1 cmH2O/10lpm flow)
- Better oxygenation, reduced work of breathing via dead space washout and intrinsic PEEP
- Gases warmed and humidified
  - Improved comfort
  - Reduced airway inflammation
  - Improved drainage of respiratory secretions

High-Flow Nasal Oxygen > NPPV or Face Mask for Acute Hypoxemic Respiratory Failure

- Multicenter, open-label trial of 310 patients with acute hypoxemic respiratory failure (P/F < 300) in 23 ICUs
  - High flow nasal O2 at 50 lpm, FiO2 1.0 - adjusted
  - Nonrebreather face mask at 10 lpm – adjusted
  - NPPV face mask: PSV so Vt 7-10ml/kg, PEEP 2-10 cm H2O - adjusted
- Patients randomized to high-flow nasal O2…
  - More ventilator-free days (p=0.02)
  - Higher probability of survival (p=0.02)
  - Less likely to be intubated if P/F $\leq$ 200 (p=0.009)

Frat et al. N Engl J Med 2015; 372:2185

Noninvasive Ventilation for Mild ARDS?

Noninvasive Ventilation of Patients with Acute Respiratory Distress Syndrome

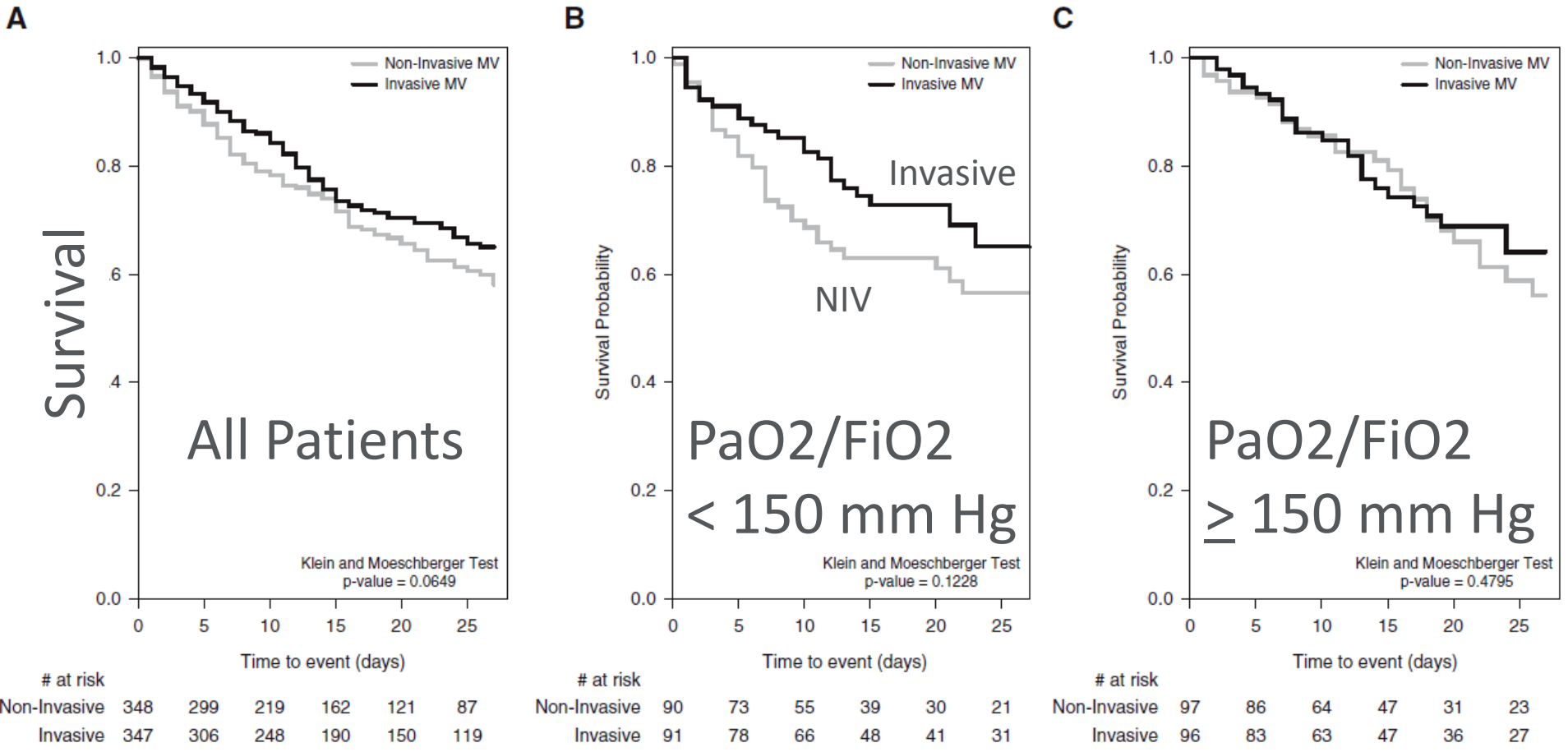
Insights from the LUNG SAFE Study

Am J Respir Crit Care Med 2017

Giacomo Bellani[1,2], John G. Laffey[3,4,5,6,7,8], Tài Pham[9,10,11], Fabiana Madotto[12], Eddy Fan[8,13,14,15], Laurent Brochard[4,5,8,14], Andres Esteban[16], Luciano Gattinoni[17], Vesna Bumbasirevic[18,19], Lise Piquilloud[20,21], Frank van Haren[22,23], Anders Larsson[24], Daniel F. McAuley[25,26], Philippe R. Bauer[27], Yaseen M. Arabi[28,29], Marco Ranieri[30], Massimo Antonelli[31], Gordon D. Rubenfeld[8,14,32], B. Taylor Thompson[33], Hermann Wrigge[34], Arthur S. Slutsky[5,8,14], and Antonio Pesenti[35,36]; on behalf of the LUNG SAFE Investigators and the ESICM Trials Group*

- Of the 2813 patient with ARDS, 436 (15%) were managed on NIV
- NIV Failure in 22% Mild, 42% Moderate, 47% Severe ARDS
- NIV use associated with increased ICU mortality (HR 1.44 (1.16-1.81)), not hospital mortality

Worse Outcomes With NIV If PaO2/FiO2 < 150 mm Hg but ok with mild ARDS



Bellani et al. Am J Respir Crit Care Med 2017

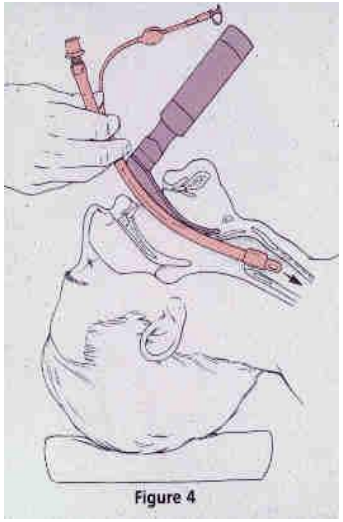
Management of Hypoxemic Respiratory Failure

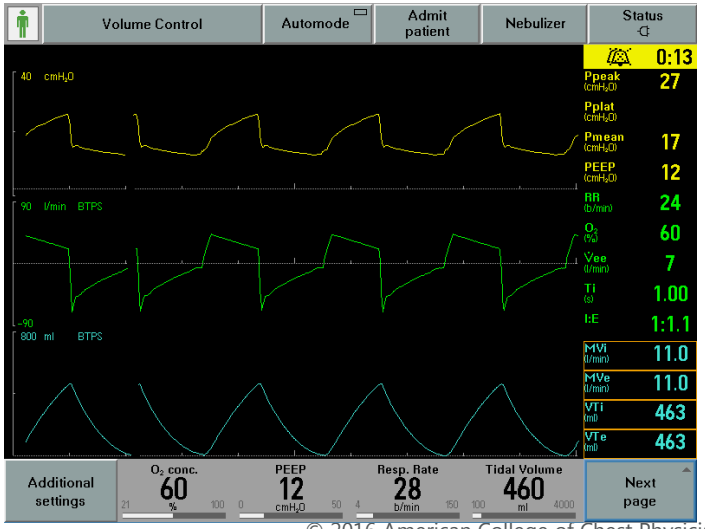
TREATMENT	"OVERTREATMENT"
High Flow Nasal Oxygen	Invasive Ventilation?

- Consider a trial of HFNO2
  - Prefer HFNO2 over NIV

Management of Hypoxemic Respiratory Failure

- Immediate evaluation & stabilization
- Supplemental oxygen
- Mechanical ventilation*
- Supportive care
- Identification & management of causative conditions





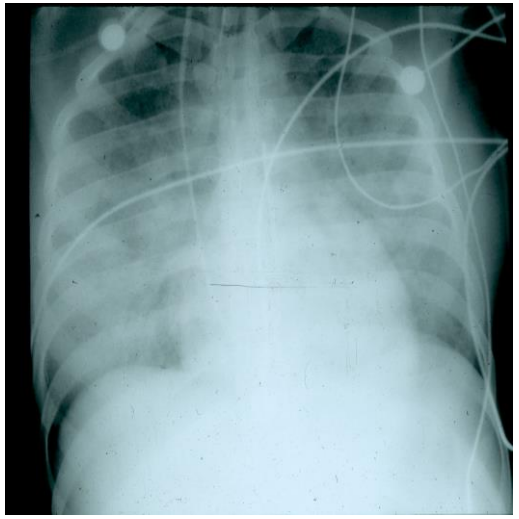
Management of Hypoxemic Respiratory Failure

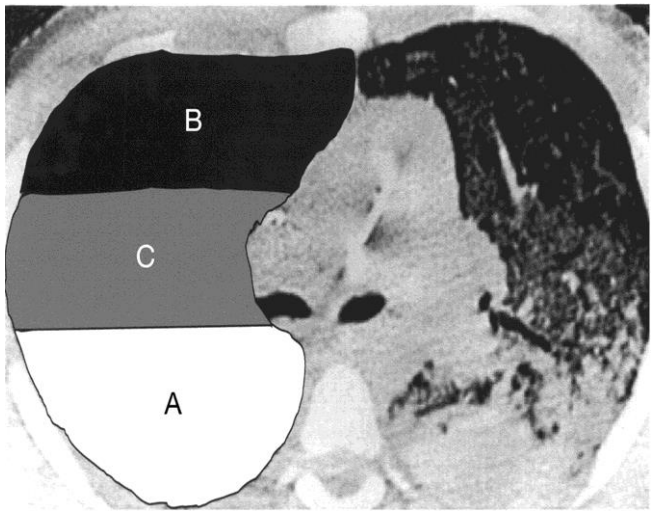
TREATMENT	"OVERTREATMENT"
High Flow Nasal Oxygen	Invasive Ventilation?
Low Tidal Volume	Conventional Tidal Volume

- Physiologic rationale and outcome studies favor smaller over larger tidal volumes during invasive ventilation of ARDS

Lung *Protective* Mechanical Ventilation for ARDS

- Lung injury is heterogeneous, but with functional "compartments":
  - Normal lung (B) – potential for over-distention
  - Atelectatic, but recruitable lung (C) – potential for cyclic recruitment / collapse
  - Densely consolidated lung (A) – poorly recruitable



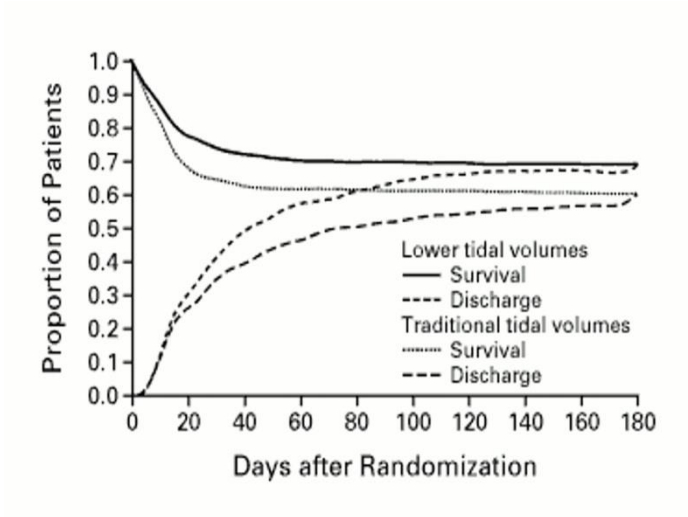


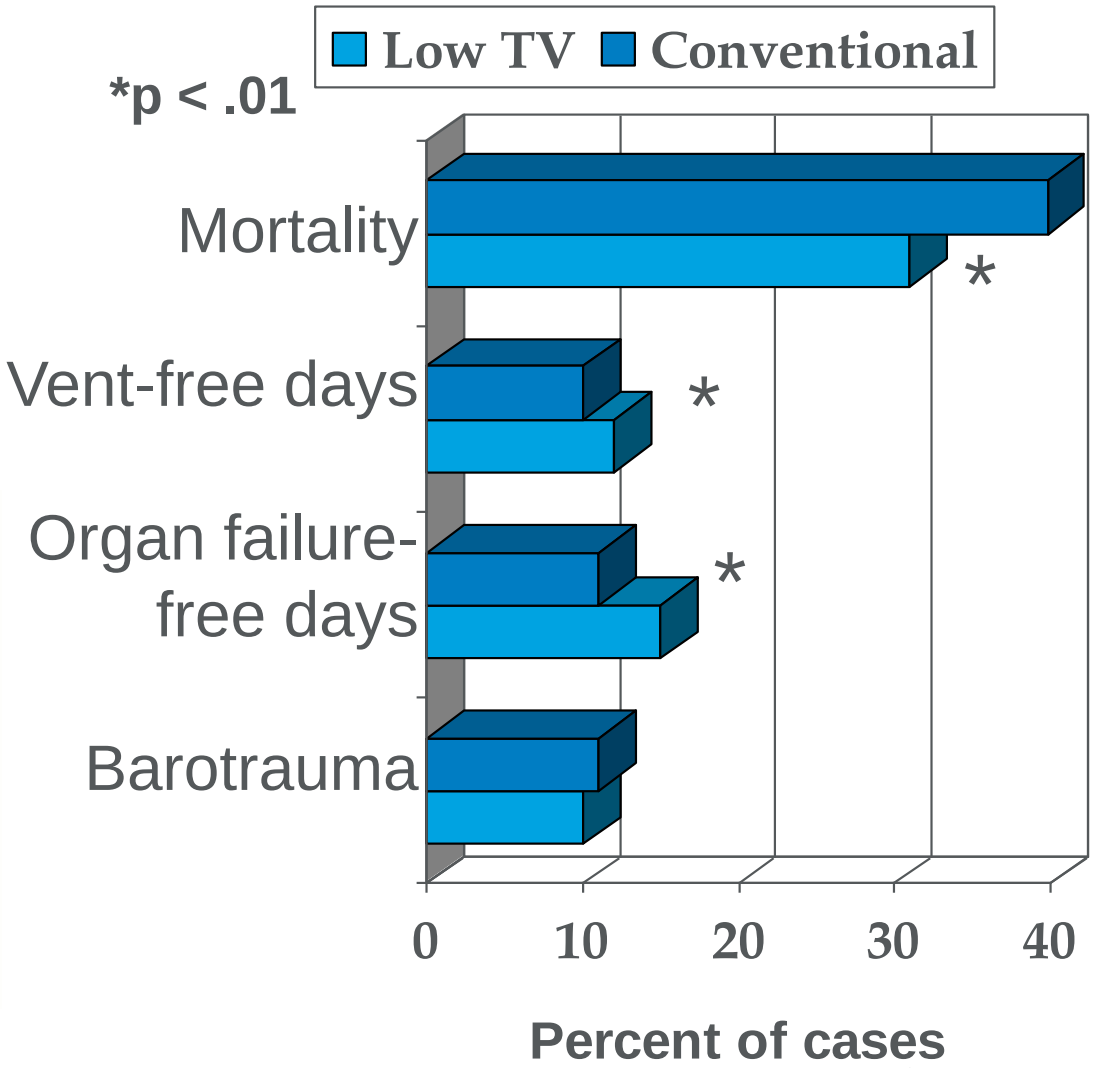
Moloney & Griffiths Br J Anaesth 2004; 92:261-70

Low Tidal Volume Ventilation

ARDS Network. N Engl J Med 2000; 342:1301

- Randomized trial of conventional TV (11.8 ml/kg) vs low TV (6.2 ml/kg) ventilation in 861 patients with ALI





ATS Guideline Recommendation

- We recommend that adult patients with ARDS receive mechanical ventilation with strategies that limit tidal volumes (4 – 8 ml/kg PBW) and inspiratory pressures (plateau pressure < 30 cm H2O)

  Strong recommendation, moderate confidence in effect estimates

VCU Health

Fan et al. Am J Respir Crit Care Med 2017

PETA People for the Ethical Treatment of Alveoli

Utilize Strategies to Improve Lung Protective Ventilation

Male		Female		Predicted body weight	6 ml/kg tidal volume
Height in inches	Height in cm	Height in inches	Height in cm	(in kg)	(in ml)
58	147	60	152	45.5	272
60	152	62	157	50	300
62	157	64	163	54.7	328
64	163	66	168	59	355
66	168	68	173	64	383
68	173	70	178	68.5	410
70	178	72	183	73	438
72	183	74	188	78	466
74	188	76	193	82	493

Sessler, C. Hypoxemic Respiratory Failure, in ACCP Pulmonary Board Review 2009

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Management of Hypoxemic Respiratory Failure

TREATMENT	"OVERTREATMENT"
High Flow Nasal Oxygen	Invasive Ventilation?
Low Tidal Volume	Conventional Tidal Volume

- Use low tidal volume ventilation avoiding OVERLY LARGE TIDAL VOLUMES

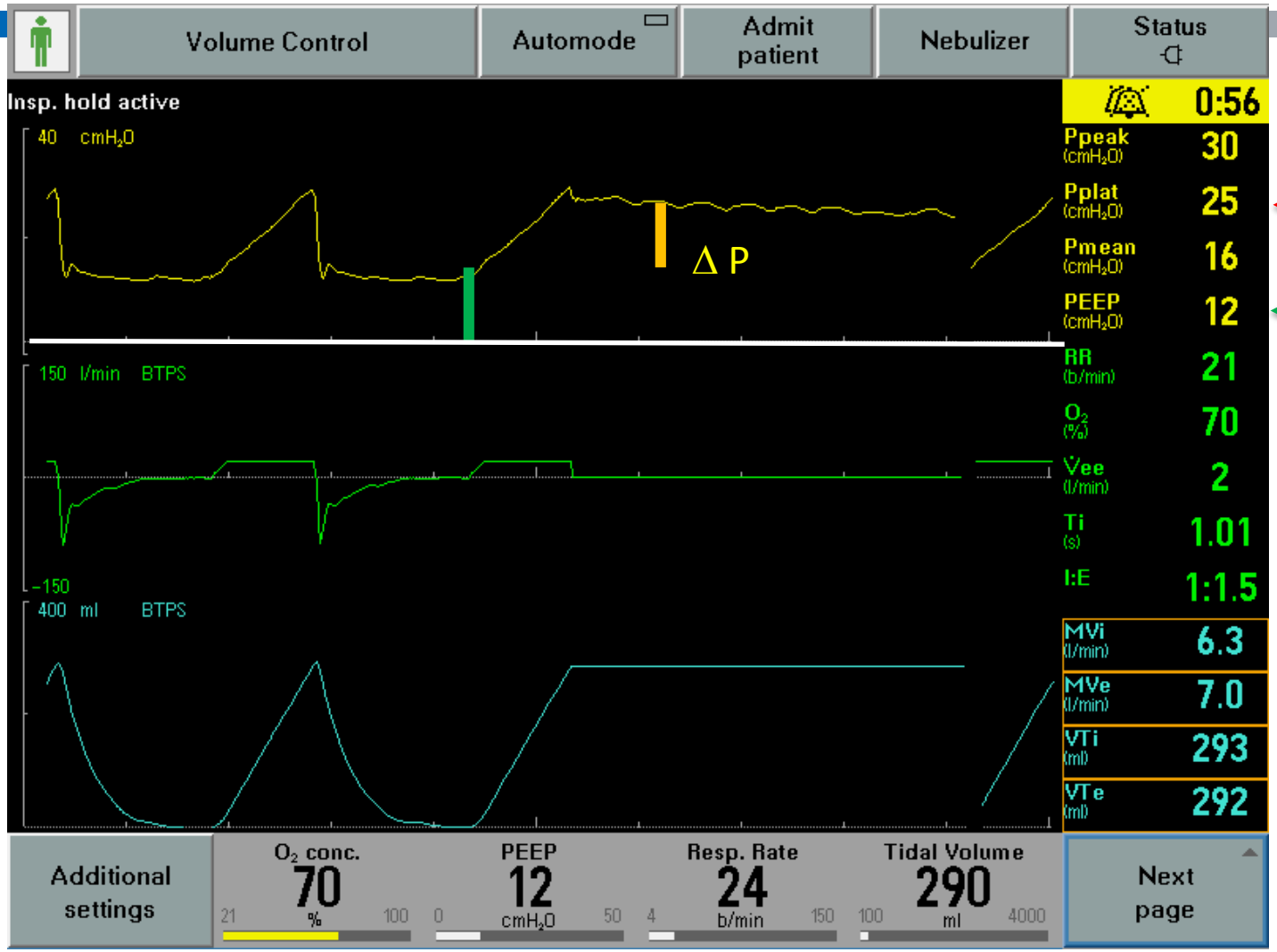
NOT TOO BIG

Management of Hypoxemic Respiratory Failure

TREATMENT	"OVERTREATMENT"
High Flow Nasal Oxygen	Invasive Ventilation?
Low Tidal Volume	Conventional Tidal Volume
Modest Inflation Pressure	High Plateau, Driving P

- Stiff, non-compliant lungs require higher inflation pressure to produce a given tidal volume.
- Evidence that higher alveolar pressure as well as "driving" pressure are bad

Avoid Excessive Plateau & Driving Pressures



Pplat

PEEP

Δ P = 13

Driving Pressure (Δ P) = Pplat-PEEP

ATS Guideline Recommendation

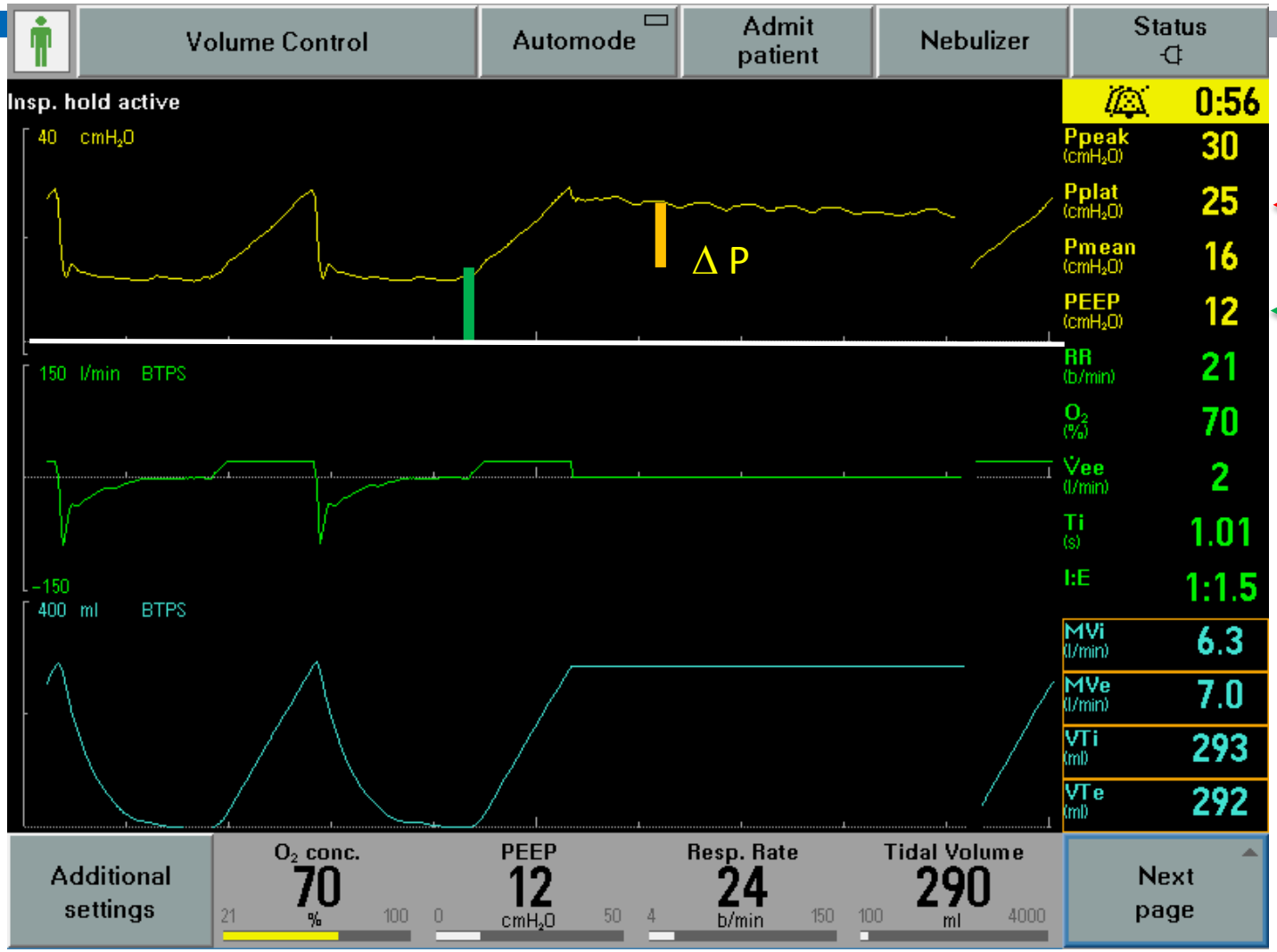
- We recommend that adult patients with ARDS receive mechanical ventilation with strategies that limit tidal volumes (4 – 8 ml/kg PBW) and inspiratory pressures (plateau pressure < 30 cm H2O)

  Strong recommendation, moderate confidence in effect estimates

VCU Health

Fan et al. Am J Respir Crit Care Med 2017

Avoid Excessive Plateau & Driving Pressures



Pplat

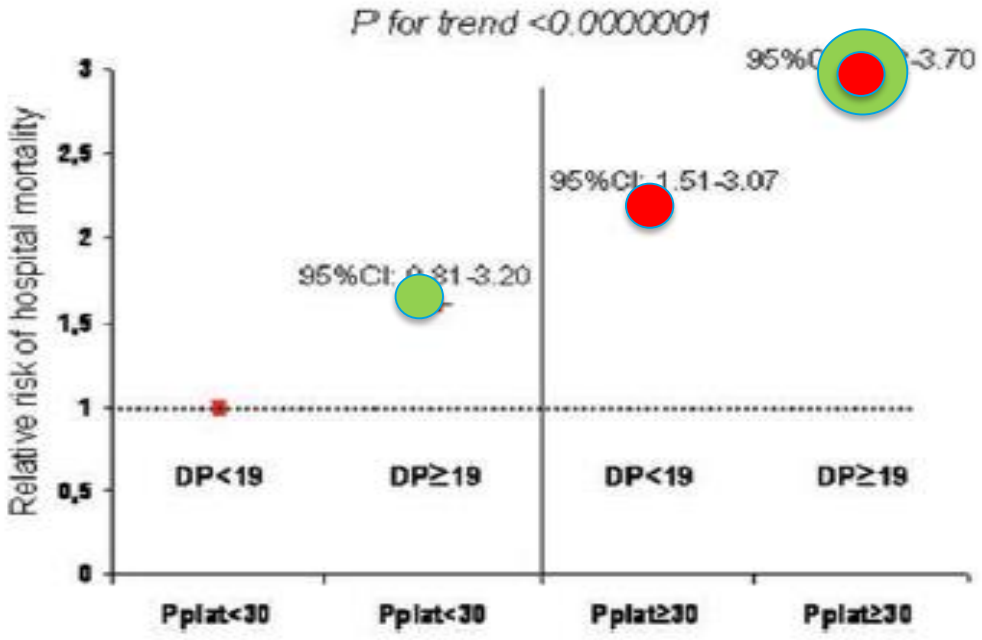
PEEP

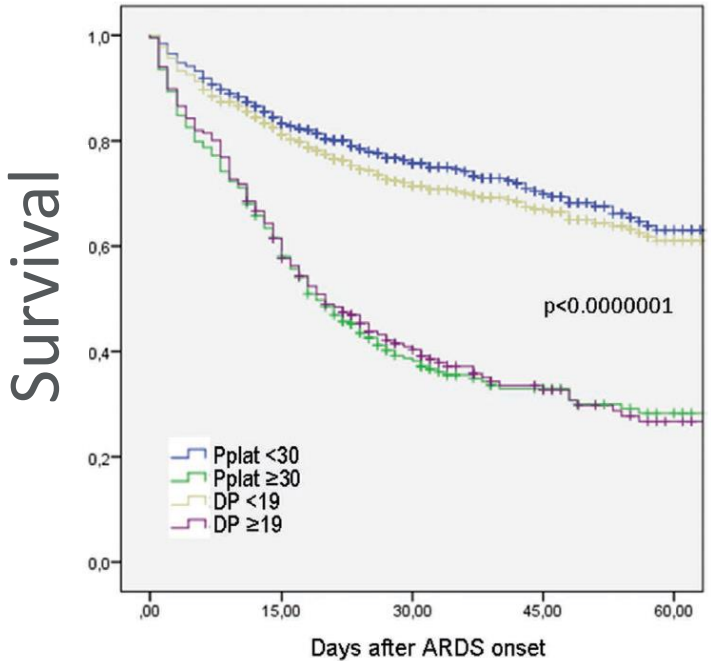
Δ P = 13

Driving Pressure (Δ P) = Pplat-PEEP

Higher Plateau & Driving Pressures = Death

- Analysis of data from 778 patients with ARDS
- Increased risk of hospital death
  - Pplat ≥ 29 or Driving Pressure ≥ 19 cm H2O





Villar et al. Crit Care Med 2017

Management of Hypoxemic Respiratory Failure

TREATMENT	"OVERTREATMENT"
High Flow Nasal Oxygen	Invasive Ventilation?
Low Tidal Volume	Conventional Tidal Volume
Modest Inflation Pressure	High Plateau, Driving P

- Monitor and control Plateau pressure (<30 cmH2O), Driving pressure (<15-19 cm H2O)

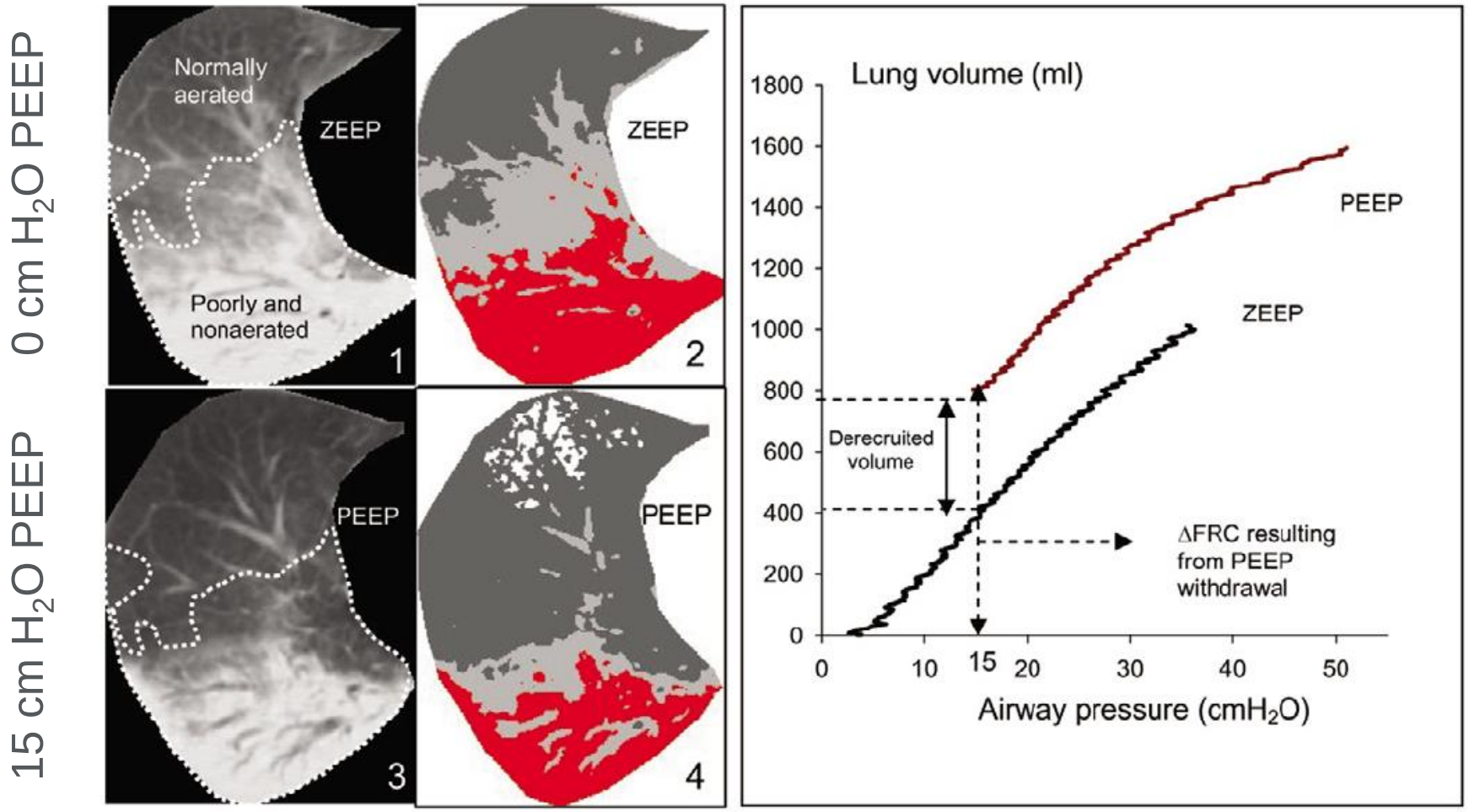
NOT TOO HARD

Management of Hypoxemic Respiratory Failure

TREATMENT	"OVERTREATMENT"
High Flow Nasal Oxygen	Invasive Ventilation?
Low Tidal Volume	Conventional Tidal Volume
Modest Inflation Pressure	High Plateau, Driving P
Use Enough PEEP	Avoid Excessive PEEP

- Positive end-expiratory pressure (PEEP) splints open alveoli improving oxygenation and reducing "atelectrauma"
- Excessive PEEP, however is detrimental

PEEP Splints Open Alveoli

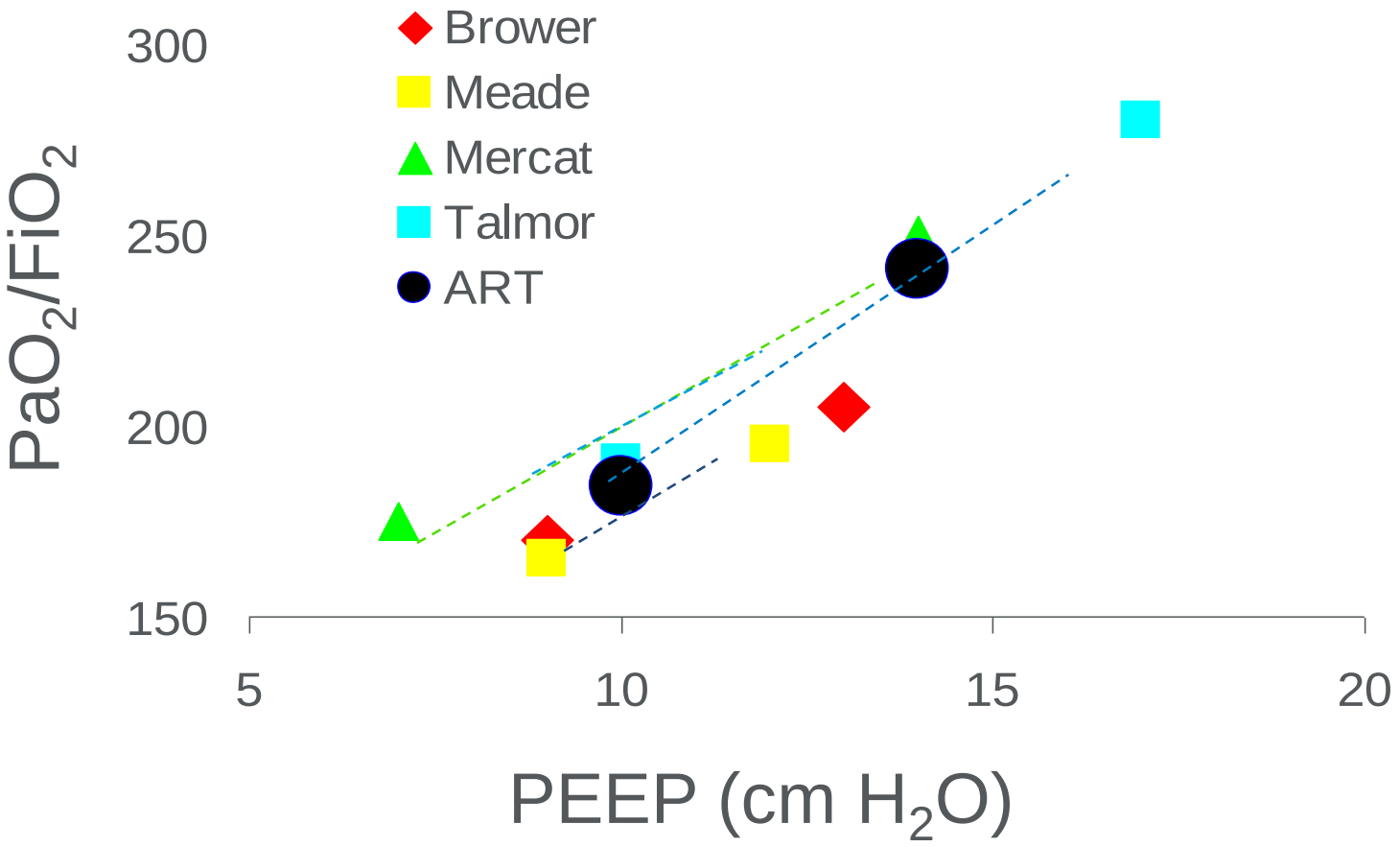


Dark gray = normal, light gray = poorly aerated, red = nonaerated

Lu et al. Crit Care 2006; 10:R95

More PEEP > Higher PaO2

Oxygenation vs PEEP (Day 3) 5 High vs Low PEEP RCTs



ATS Guideline Recommendation

- We suggest that adult patients with moderate or severe ARDS receive higher rather than lower levels of PEEP

  Conditional recommendation, moderate confidence in effect estimates

Fan et al. Am J Respir Crit Care Med 2017

High PEEP good in Moderate-Severe ARDS but potentially harmful in mild ARDS

	Mod – Severe ARDS			Mild ARDS		
	Higher PEEP	Lower PEEP	P	Higher PEEP	Lower PEEP	p
Hospital death	34%	39%	.049	27%	19%	.07
ICU death	30%	37%	.001	20%	17%	.71
Pneumothorax	8%	7%	.13	4%	5%	.33
Vent-free days	12 d	7d	.004	17d	19d	.07
Rescue therapy	14%	21%	<.001	4%	7%	.25

Briel et al. JAMA 2010;303:865-73

We suggest that adult patients with moderate or severe ARDS receive higher rather than lower levels of PEEP

Fan et al. Am J Respir Crit Care Med 2017

Recruitment Maneuvers

- Brief over-inflation to “pop open” or recruit alveoli
- Wide variety of proposed approaches
  - 40 cm H2O pressure for 40 seconds (or 30x30)
  - Ramp up and down of pressure
  - Many others
- Demonstrated to improve oxygenation
  - Transient benefit alone
  - Recommended prior to increasing PEEP
  - Beneficial for interventions that promote loss of airway pressure / PEEP (i.e. suctioning)

Risk for barotrauma, hemodynamic compromise

Hazards of Super Recruitment and Super PEEP

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Lung Recruitment and Titrated Positive End-Expiratory Pressure (PEEP) vs Low PEEP on Mortality in Patients With Acute Respiratory Distress Syndrome

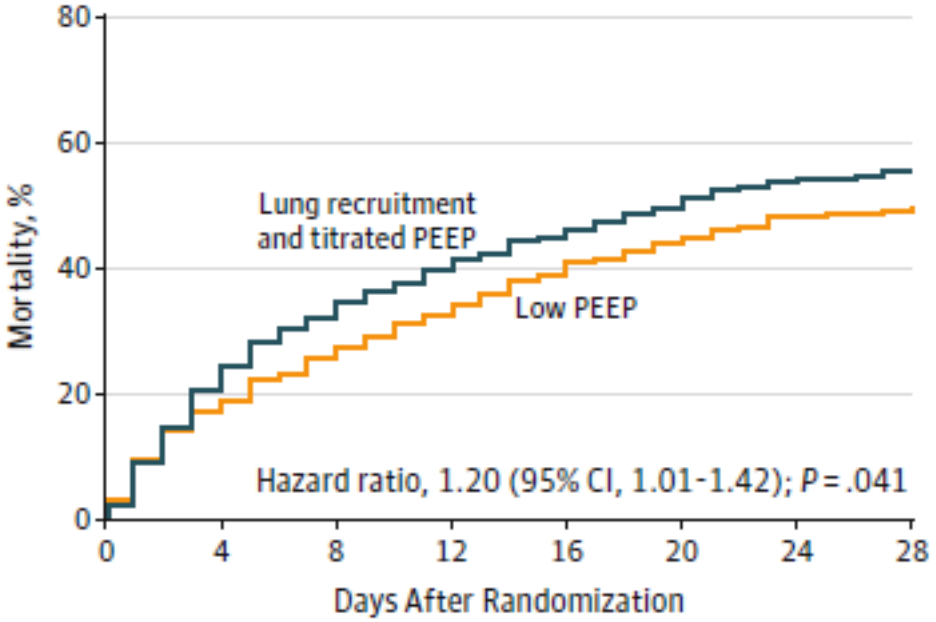
A Randomized Clinical Trial

Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART) Investigators

- Multicenter (120 ICUs) international (South American, Europe) RCT of recruitment maneuver + PEEP titration by respiratory system compliance (n = 501) vs low PEEP (n = 509) in patients with moderate to severe ARDS (P/F < 200)
- Recruitment maneuvers so Pplat as high at 60 cm H2O x 2 min, PEEP up to 23 cm H2O

Hazards of Super Recruitment and Super PEEP

- Higher 28-day Mortality with High PEEP + RM strategy (55%) vs Low PEEP strategy (49%), HR 1.20 (1.01-1.42, p = 0.04)



- Higher 6-month Mortality with High PEEP + RM strategy (65%) vs Low PEEP strategy (60%), HR 1.18 (1.01-1.38, p = 0.04)

Higher BMI – Use Higher PEEP

- Retrospective analysis of 50 patients from the ALVEOLI Trial
- Comparison of outcomes of Obese (BMI > 30 kg/m2) vs Non-obese patients
- Obese: Lower mortality with high PEEP (18% vs 32%, $p = 0.04$)
- Non-obese: Trend for higher mortality with high PEEP (34% vs 23%, $p = 0.13$)
- Interaction of obesity status and PEEP on mortality ($p < 0.01$)

Bime et al. Am J Med 2017

Lung Protective Ventilation

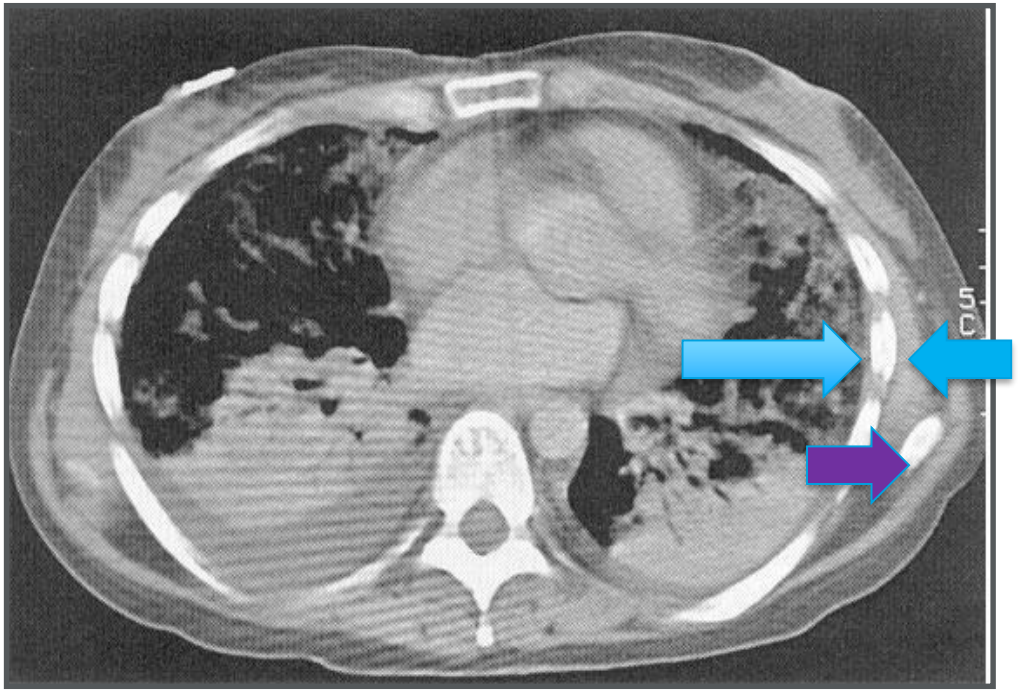
CHEST
AMERICAN COLLEGE of CHEST PHYSICIANS

- Low tidal volume ventilation
- Higher PEEP
- Avoid excessive plateau pressure and driving pressure

Pulmonary pressures

Pleural / chest wall pressure

Trans-alveolar pressure



Best PEEP for ARDS?

- Consider impact of PEEP on oxygenation, ventilation, oxygen delivery, risk of barotrauma, extra-pulmonary pressure (obesity)
- Increasing PEEP trial – positive effects…
  - Better oxygenation (↑ SpO2 and/or PaO2)
  - Better ventilation / compliance / recruitment (↓ or no Δ PaCO2, or ↑ or no Δ in tidal volume (pressure-targeted mode))
  - Indirect evidence that DO2 does not worsen
    - ↓ CO, BP, PvO2
  - Stress Index < 1

Esan et al. Chest 2010; 137:1203-1216
Narendra et al. Chest 2017

Management of Hypoxemic Respiratory Failure

TREATMENT	"OVERTREATMENT"
High Flow Nasal Oxygen	Invasive Ventilation?
Low Tidal Volume	Conventional Tidal Volume
Modest Inflation Pressure	High Plateau, Driving P
Use Enough PEEP	Avoid Excessive PEEP

- Use higher PEEP (12-20 cm H2O) for moderate-severe, but not mild ARDS; avoid extreme PEEP & recruitment

KEEP ALVEOLI FULL, BUT NOT TOO FULL

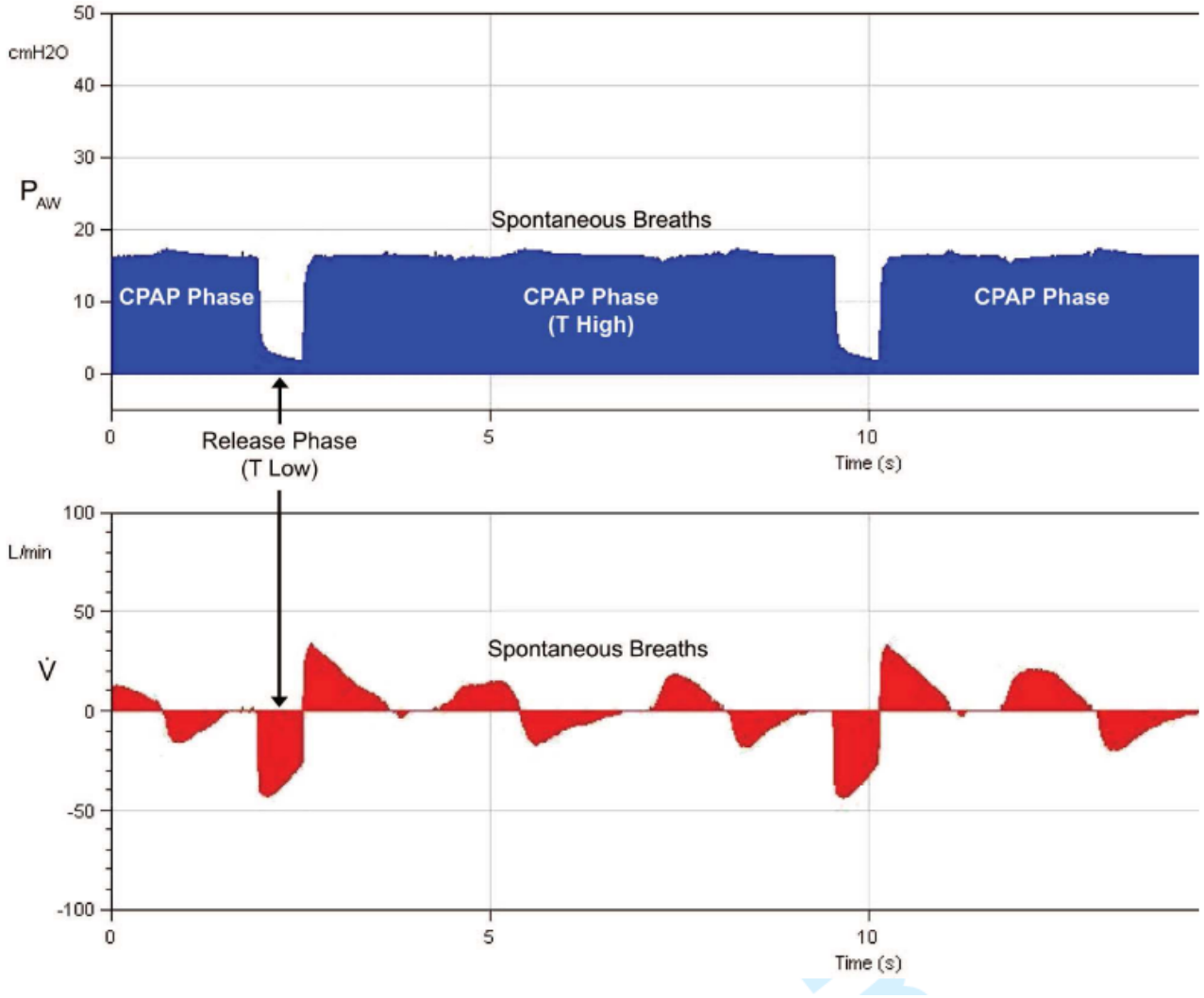
Management of Hypoxemic Respiratory Failure

TREATMENT	"OVERTREATMENT"
High Flow Nasal Oxygen	Invasive Ventilation?
Low Tidal Volume	Conventional Tidal Volume
Modest Inflation Pressure	High Plateau, Driving P
Use Enough PEEP	Avoid Excessive PEEP
Adjust Inspiratory Time	Be Careful with APRV

Longer Inspiratory Time

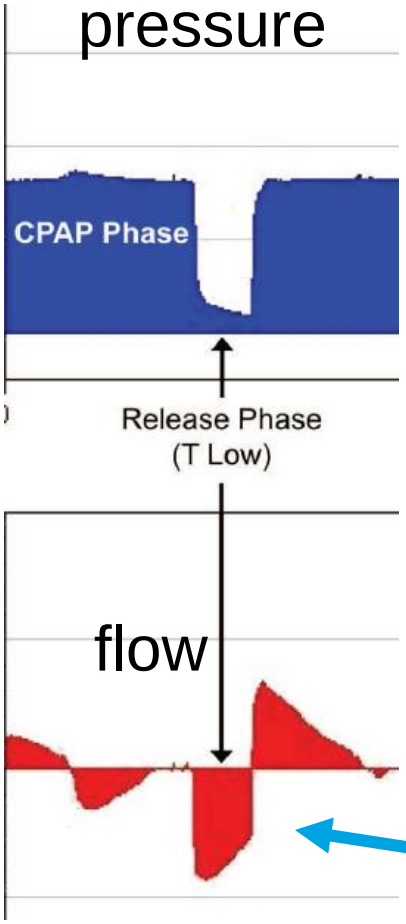
- Allows more effective distribution of breath
- Might allow lower driving pressure
- Most easily done with pressure-targeted modes
- Pressure controlled inverse ratio ventilation (PC-IRV)
  - No spontaneous breaths
- “BiLevel” permits spontaneous breaths
- Airway pressure release ventilation (APRV) in U.S. = long inspiratory time and very short expiratory time
- Few Outcome RCTs for APRV in ARDS
- Potential for complications

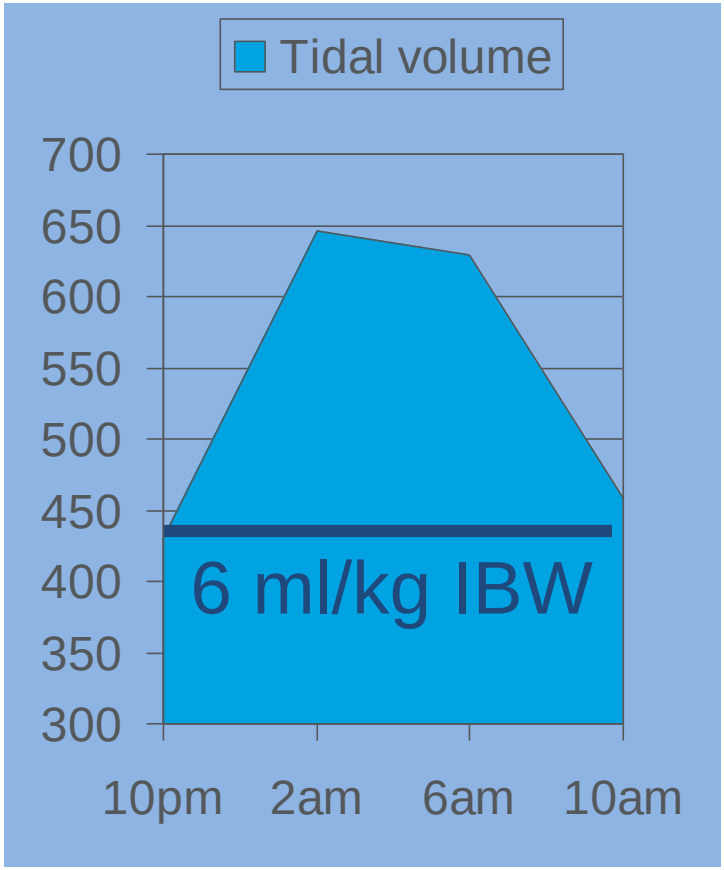
(Airway Pressure Release Ventilation (APRV)



APRV Concerns

AutoPEEP & Tidal Volume Creep





Incomplete emptying (i.e. autoPEEP)

Management of Hypoxemic Respiratory Failure

TREATMENT	"OVERTREATMENT"
High Flow Nasal Oxygen	Invasive Ventilation?
Low Tidal Volume	Conventional Tidal Volume
Modest Inflation Pressure	High Plateau, Driving P
Use Enough PEEP	Avoid Excessive PEEP
Adjust Inspiratory Time	Be Careful with APRV

- Avoid excessively brief exhalation, watch Vt

BREATHS NOT TOO LONG

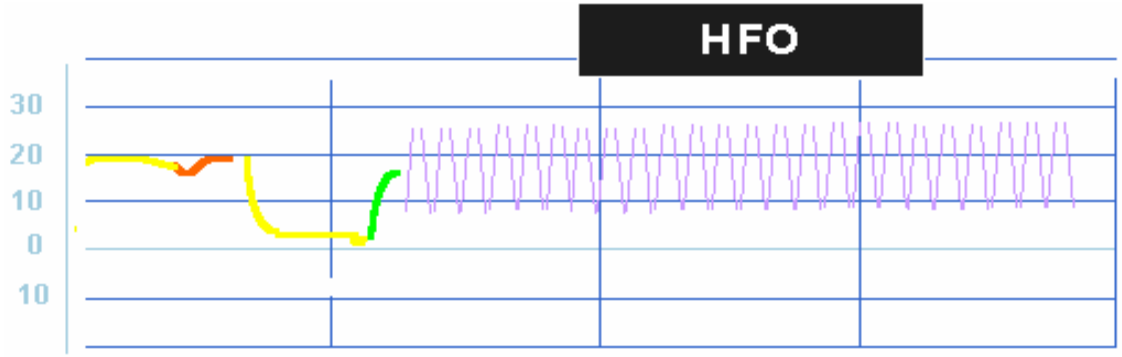
Management of Hypoxemic Respiratory Failure

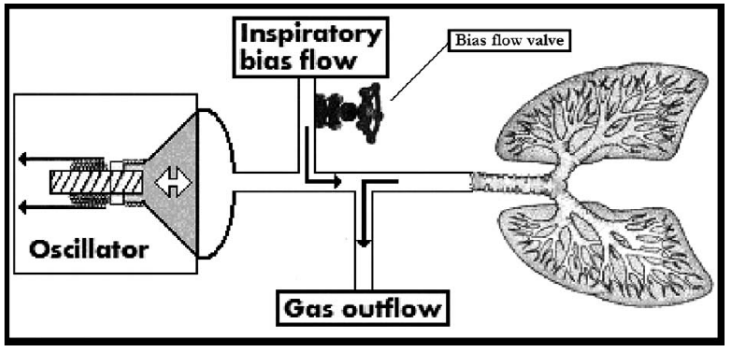
TREATMENT	"OVERTREATMENT"
High Flow Nasal Oxygen	Invasive Ventilation?
Low Tidal Volume	Conventional Tidal Volume
Modest Inflation Pressure	High Plateau, Driving P
Use Enough PEEP	Avoid Excessive PEEP
Adjust Inspiratory Time	Be Careful with APRV
Can increase f to 35/min	Avoid High Frequency Vent

- How fast to ventilate?

High Frequency Oscillation in ARDS: The Ultimate Lung Protective Ventilation?

- HFV proposed as a form of lung protective strategy
- High frequency oscillation ventilation (HFOV)
  - Active inspiratory and expiratory phases
  - Frequency = 3-15 Hz, tidal volumes < dead space
  - Parameters controlled: power (affects pressure amplitude), inspiratory time, bias flow rate, FiO2
  - Puritan Bennett 3100B FDA approved for adults





HFOV for Severe ARDS: Not So Fast

- Multicenter RCT of 548 patients of HFOV vs LTVV (Vt 6 ml/kg, high PEEP) for ARDS (PaO2:FiO2 ≤ 200 mmHg)
- Stopped early for harm
- HFOV associated with:
  - Higher mortality (ICU, hosp)
  - More sedation, NMBA
  - More vasopressors
  - Less refractory hypoxemia

Ferguson et al. N Engl J Med 2013

- Multicenter RCT of 795 UK patients of HFOV vs usual care for ARDS (PaO2:FiO2 ≤ 200 mmHg)
  - Vt = 8.3 ml/kg, PEEP 11 cm H2O
- No difference in:
  - 30 day all cause mortality
  - ICU, Hosp LOS
  - Vent-free days

Young et al. N Engl J Med 2013

ATS Guideline Recommendation

- We recommend that HFOV **not** be used routinely in patients with moderate or severe ARDS

Strong recommendation, moderate-high confidence in effect estimates

Fan et al. Am J Respir Crit Care Med 2017

Management of Hypoxemic Respiratory Failure

TREATMENT	"OVERTREATMENT"
High Flow Nasal Oxygen	Invasive Ventilation?
Low Tidal Volume	Conventional Tidal Volume
Modest Inflation Pressure	High Plateau, Driving P
Use Enough PEEP	Avoid Excessive PEEP
Adjust Inspiratory Time	Be Careful with APRV
Can increase f to 35/min	Avoid High Frequency Vent

- Avoid HFOV in most ARDS patients

NOT TOO FAST

Treat, but Do Not Over-Treat, Hypoxemic Respiratory Failure

- Trial of High Flow Nasal Oxygen may help avoid intubation and invasive ventilation in some patients
- Avoid the many forms of excessive ventilation for Hypoxemic Respiratory Failure, delivering ventilation that is…
  - Not too big (low tidal volume ventilation)
  - Not too forceful (avoid high inflating pressures)
  - Not overly full (use high (but not too high) PEEP)
  - Not too long (caution with APRV)
  - Not too fast (avoid routine use of HFOV)