



# (Excessive) Spontaneous Efforts May be Dangerous

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To breath or not to breath (spontaneously)  
That is the question



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## Equation of motion

### Equation of Motion

**ventilation pressure** = **elastic pressure** + **resistive pressure**  
 (to deliver tidal volume)      (to inflate lungs and chest wall)      (to make air flow through the airways)

$$P_{\text{mus}} + P_{\text{vent}} = P_{\text{elastic}} + P_{\text{resistive}}$$

$$P_{\text{mus}} + P_{\text{vent}} = E \times V + R \times \dot{V}$$

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## Benefits

### Spontaneous breathing

- Reduced dependent lung collapse
- Reduce diaphragmatic disuse atrophy
- Reduce the use of sedatives and NM blockers (Delerium and muscle weakness)
- Hemodynamic advantages
- Improved gas exchange ?
- Decreased VILI ?
- Early mobility



### Passive breathing

- Reduce Asynchronies
- Reduce PSILI
- Decreased VILI ?
- Lower oxygen consumption
- Easier to adjust the ventilator, monitoring of static conditions
- Improved oxygenation ?

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TRANSLATIONAL  
MEDICINE

## Spontaneous breathing: a double-edged sword to handle with care

Key physiologic findings on spontaneous breathing	First author, year
<b>Pro</b> —supporting spontaneous breathing	
Active diaphragmatic contraction, reduced diaphragmatic atrophy	Pellegrini 2017, Vassilakopoulos 2004, Yonis 2015
Improved ventilation/perfusion matching	Putensen 1999
Improvement of dorsal ventilation	Wrigge 2003, Langer 2016, Mauri 2015
Improvement of gas-exchange	Putensen 2001
Reduction of sedative drugs and their side effects	Hansen-Flaschen 1991
Hemodynamic improvement (increase in venous return)	Putensen 2001
Potentially reduction of pneumonia (better secretions clearance) in extubated patients	Mauri 2017
<b>Cons</b> —against spontaneous breathing	
Diaphragmatic atrophy	Dot 2017, Levine 2008
High risk of patient-ventilator asynchrony	Colombo 2011, Thille 2006, Spahija 2010, Tassaux 2005
Risk of uncontrolled, high, potentially injurious tidal volume	Yoshida 2017, Marini 2011
Risk of regional increase of transpulmonary pressure in the presence of safe average values that generates "occult pendelluft"	Yoshida 2013, Yoshida 2012
Higher dose of sedative and muscle relaxant to avoid spontaneous effort; collateral effects of high sedation drug dosage (stress disorders, delirium etc.)	Hansen-Flaschen 1991
Hemodynamic instability (increase filling of the right heart and dysfunction of left heart)	Eckstein 1958
Interstitial and alveolar edema	Perlman 2011, Kallet 1999

Mauri T, et al. Spontaneous breathing: a double-edged sword to handle with care. *Ann Transl Med.* 2017 Jul;5(14):292.

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## Spontaneous breathing

### Diaphragm Muscle Tone

Controlled mechanical ventilation (i.e., no spontaneous breathing) induces diaphragmatic muscle dysfunction and atrophy. This is a serious problem, especially for subsequent weaning; it is detectable in patients within as little as 18 hours, and can be ameliorated by preservation of spontaneous effort

### Cardiovascular Effects

Increase preload might improve Cardiac output and Hemodynamics

### Pulmonary Function

Spontaneous breathing increases aeration in dependent lung, as well as increasing lung perfusion. Thus intrapulmonary shunt is reduced and V/Q matching and oxygenation increased

Yoshida T, et al. Fifty Years of Research in ARDS. Spontaneous Breathing during Mechanical Ventilation. Risks, Mechanisms, and Management. *Am J Respir Crit Care Med.* 2017 Apr 15;195(8):985-992.

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## Spontaneous breathing

### APRV

Spontaneous breathing, accounting for 10–30% of  $\dot{V}_E$  during APRV, leads to improved ventilation-perfusion matching, decreased intrapulmonary shunt, and decreased dead space, through improvement of transpulmonary pressure in the juxtadiaphragmatic lung regions, with alveolar recruitment, and without raising peak Furthermore, regular spontaneous breathing maintains diaphragmatic muscle condition.

Putensen and colleagues<sup>18</sup> have documented the benefits of spontaneous breathing during APRV, which has increased the respiratory-system compliance, PaO<sub>2</sub>, cardiac index, and oxygen delivery, compared to patients who were paralyzed during mechanical ventilation.

### Outcome

Reduced length of intensive care unit stay

In severe ARDS, avoidance of spontaneous effort reduces injury and improves outcome. By contrast, in milder disease, the presence of spontaneous effort has little impact on outcome, but may prevent worsening of lung injury, improve pulmonary function and in some patients, reduce duration of mechanical ventilation

Daoud EG, et al. Airway pressure release ventilation: what do we know? Respir Care. 2012 Feb;57(2):282-92.

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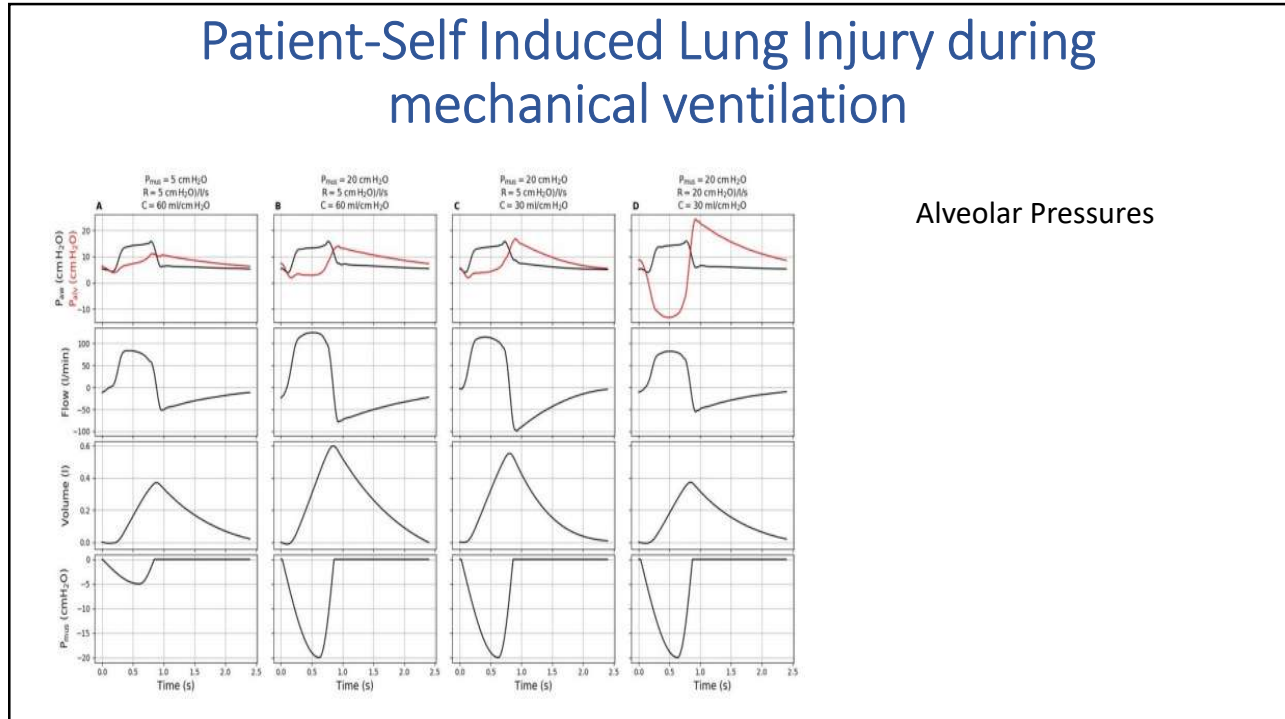
## Patient-Self Inflicted Lung Injury during mechanical ventilation (P-SILI)

- (A) Swings in transpulmonary pressure (lung stress) causing the inflation of big volumes in an aerated compartment markedly reduced by the disease-induced aeration loss
- (B) Abnormal increases in transvascular pressure, favoring negative-pressure pulmonary edema
- (C) Intra-tidal shift of gas between different lung zones, generated by different transmission of muscular force (pendelluft)
- (D) Diaphragm injury.
- (E) Patient-Ventilator Asynchrony

Patient self-inflicted lung injury: implications for acute hypoxemic respiratory failure and ARDS patients on non-invasive support. Minerva Anestesiologica 2019 September;85(9):1014-23

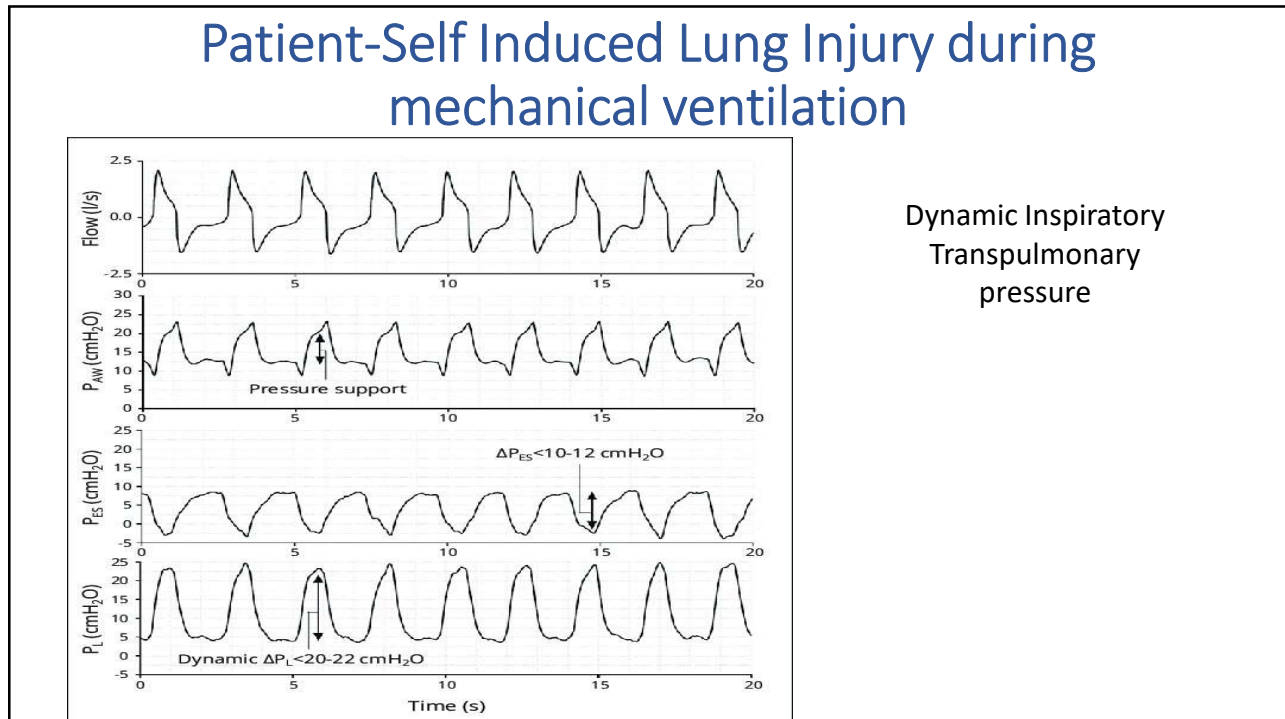
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## Patient-Self Induced Lung Injury during mechanical ventilation



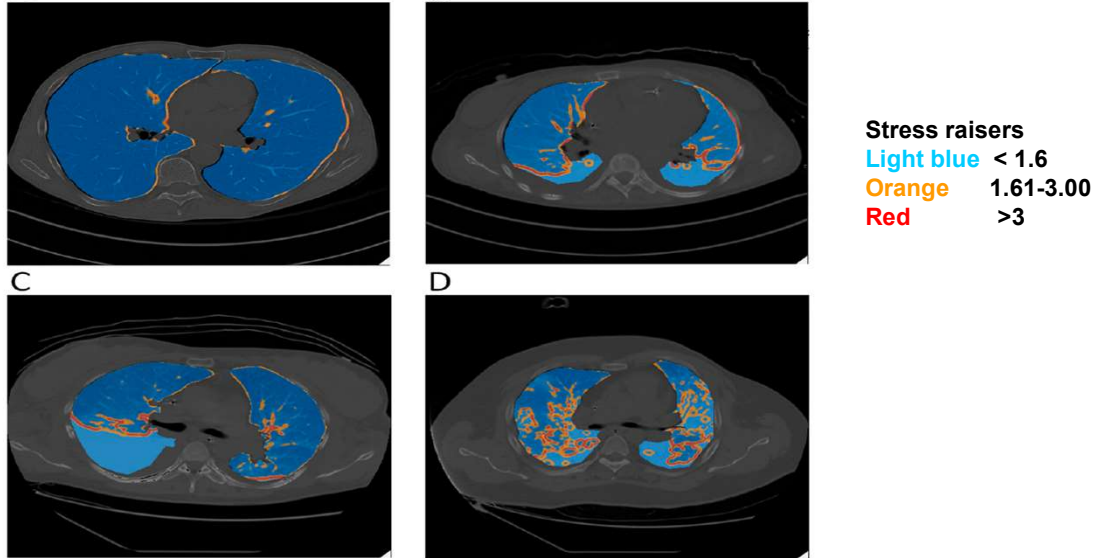
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## Patient-Self Induced Lung Injury during mechanical ventilation



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## Patient-Self Induced Lung Injury

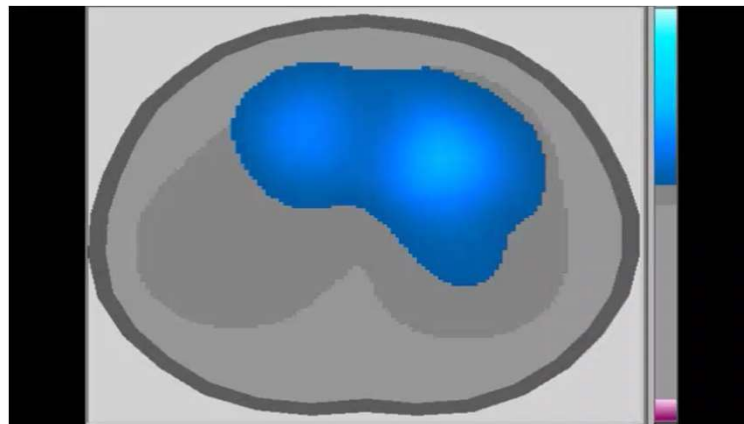


Cressoni et al. Am J Respir Crit Care Med 2014, 189:149-58

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## Patient-Self Induced Lung Injury

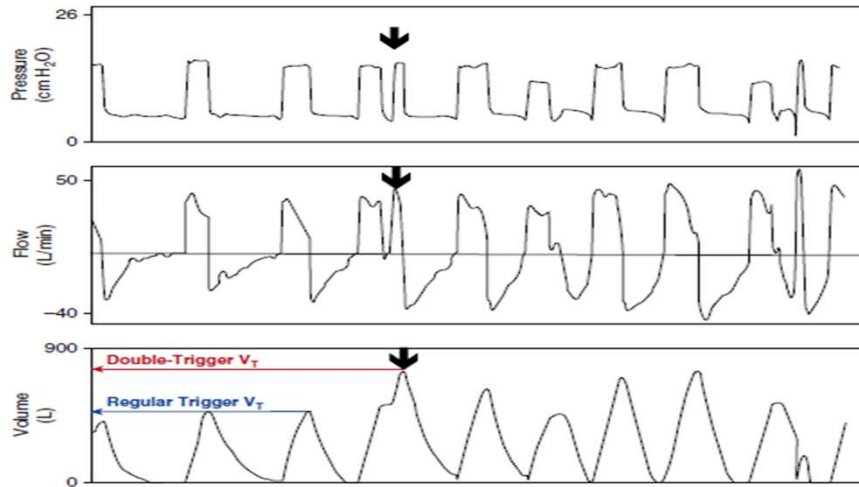
Large vertical pressure gradient of Ppl "swings" from nondependent (less negative) to dependent (more negative) regions



Su PL, et al. Spontaneous Breathing and Pendelluft in Patients with Acute Lung Injury: A Narrative Review. J Clin Med. 2022 Dec 15;11(24):7449.

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## Patient-Self Induced Lung Injury Patient-Ventilator Asynchronies

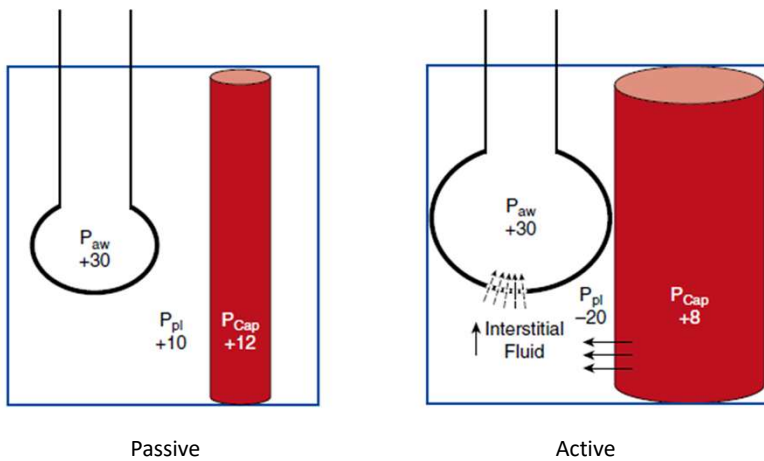


Increased Tidal volume (Strain)

Yoshida et al. Am J Respir Crit Care Med. 2017, 195(8):985-992

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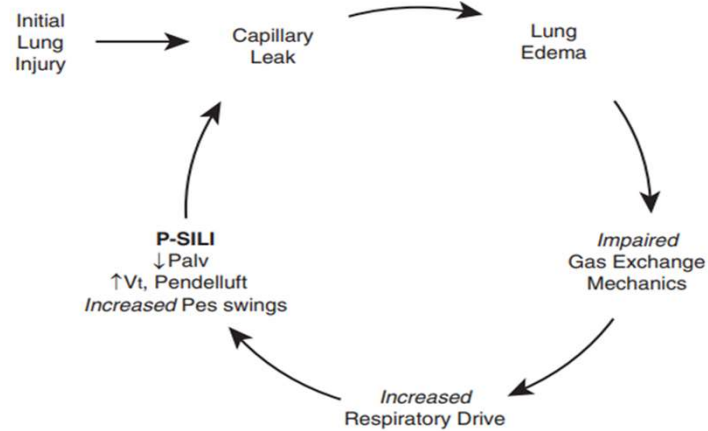
## Patient-Self Induced Lung Injury Trans-vascular pressure



Increased Lung perfusion and edema

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## Patient-Self Induced Lung Injury Vicious Cycle



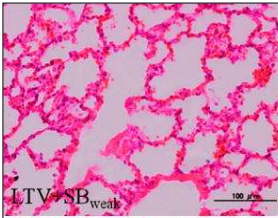
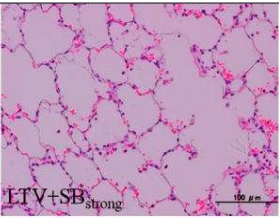
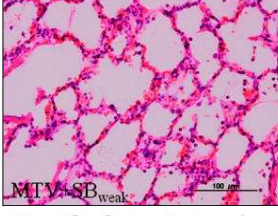

**Figure 2.** Illustration of the vicious cycle of injury present in patients with acute respiratory failure. Palv = alveolar pressure; Pes = esophageal pressure swings; P-SILI = patient self-inflicted lung injury.

Brochard et al. *Am J Respir Crit Care Med* Vol 195, Iss 4, pp 438–442

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Weak Spontaneous breaths	Strong Spontaneous breaths	
		Low Tidal Volume
		Medium Tidal Volume

**Conclusions:** Even when plateau pressure is limited to <30 cm H<sub>2</sub>O, combined with increased respiratory rate and tidal volume, high transpulmonary pressure generated by strong spontaneous breathing effort can worsen lung injury. When spontaneous breathing is preserved during mechanical ventilation, transpulmonary pressure and tidal volume should be strictly controlled to prevent further lung injury.

Yoshida, T et al Spontaneous breathing during lung-protective ventilation in an experimental acute lung injury model: High transpulmonary pressure associated with strong spontaneous breathing effort may worsen lung injury. *Critical Care Medicine*. 40(5):1578-1585, May 2012.

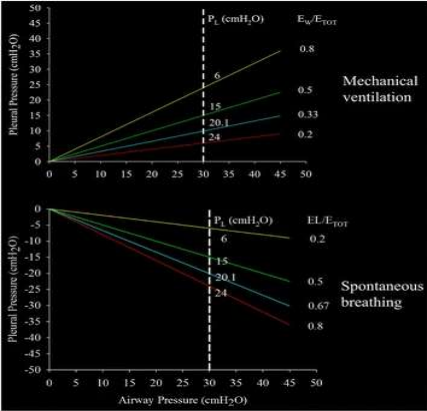
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*Intensive Care Med* (2017) 43:256–258  
DOI 10.1007/s00134-016-4483-4

**EDITORIAL**

**Ventilation-induced lung injury exists in spontaneously breathing patients with acute respiratory failure: We are not sure**

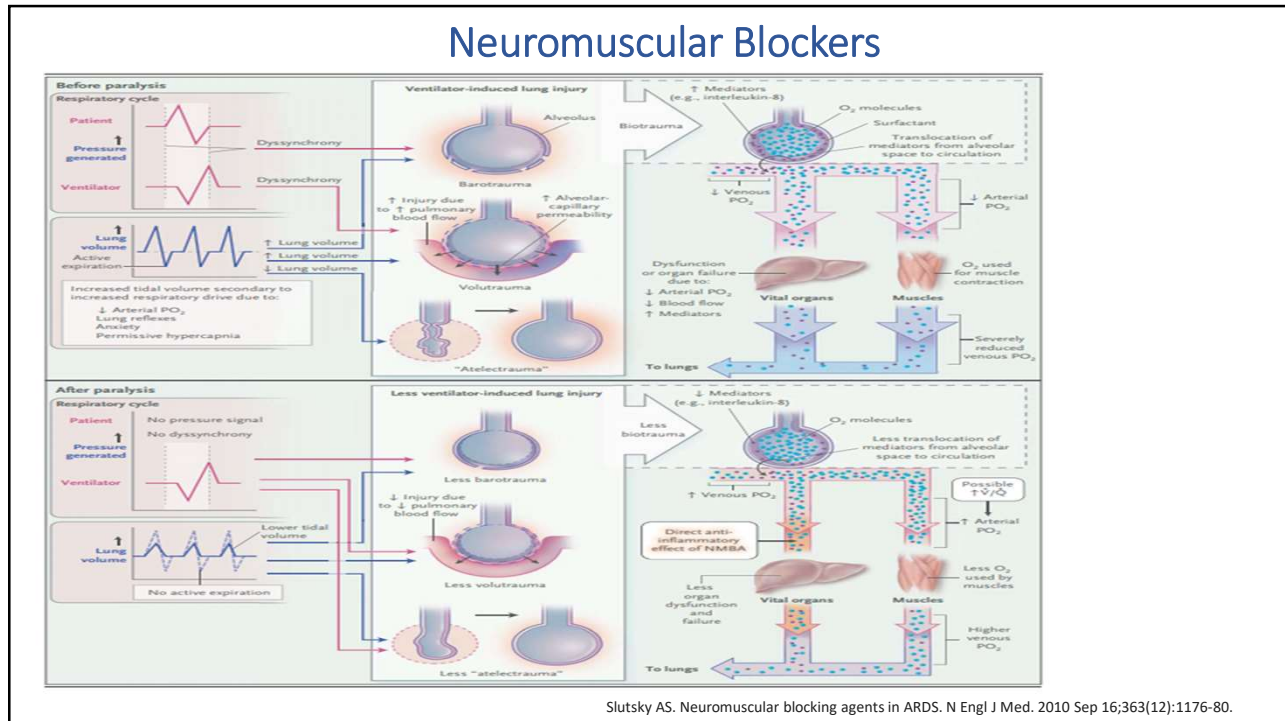
Luciano Gattinoni\*



Gattinoni L. Ventilation-induced lung injury exists in spontaneously breathing patients with acute respiratory failure: We are not sure. *Intensive Care Med*. 2017 Feb;43(2):256-258.

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## Neuromuscular Blockers



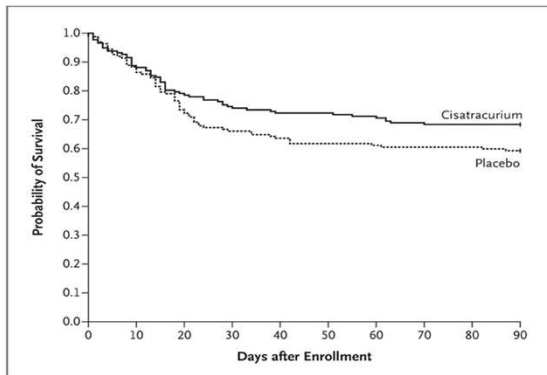
Slutsky AS. Neuromuscular blocking agents in ARDS. N Engl J Med. 2010 Sep 16;363(12):1176-80.

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## Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome ACURASYS Study

### CONCLUSIONS

In patients with severe ARDS, early administration of a neuromuscular blocking agent improved the adjusted 90-day survival and increased the time off the ventilator without increasing muscle weakness. (Funded by Assistance Publique-Hôpitaux de



### ventilator free days

	Cisatracurium (n=177)	Placebo (n=162)	P
From day 1 to day 28	10.6 ± 9.7	8.5 ± 9.4	0.04
From day 1 to day 90	53.1 ± 35.8	44.6 ± 37.5	0.03

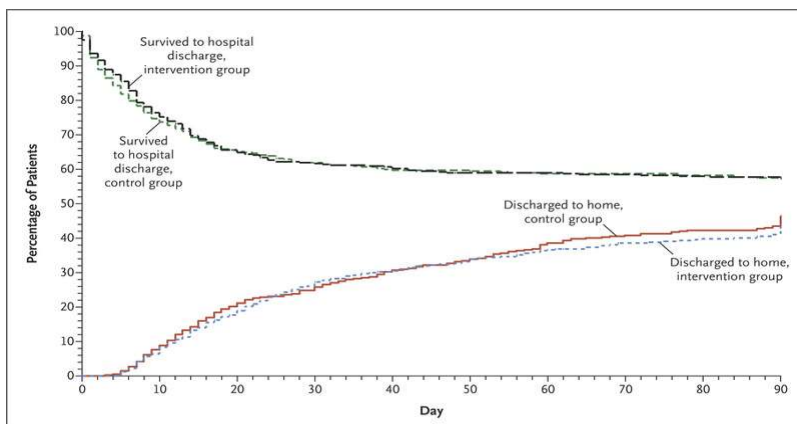
Papazian L, et al. N Engl J Med 2010; 363:1107-1116

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## Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome Rose Trial

### CONCLUSIONS

Among patients with moderate-to-severe ARDS who were treated with a strategy involving a high PEEP, there was no significant difference in mortality at 90 days between patients who received an early and continuous cisatracurium infusion and those who were treated with a usual-care approach with lighter sedation targets.



Papazian L, et al. N Engl J Med 2010; 363:1107-1116

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## Neuromuscular Blockers

### Recommendations for acute respiratory distress syndrome in major guidelines

	JRS/JSICM/JSRCM-GL2021	SSCq 2021	SRLF-GL 2019	FICM/ICS-GL 2018	ATS/ESICM/SCCM-GL2017	SSAI-ARDS-GL2016	KSCCM/KATRD-ARDS-GL2016
Lower SpO <sub>2</sub> (PaO <sub>2</sub> ) target	D for excess control	-				-	
HFNC	B						
NPPV	B					-	
Lung protective ventilation							
Low tidal volume	A	A	A	A	A	A	A
Low plateau pressure	B	A Severe	A		A	A	-
High level PEEP	B	A: Moderate-severe	A	B: P/F ≤ 200	C: Moderate-severe	B	B
Recruitment maneuver	D	B: Moderate-severe traditional	E: routine use		C	B	B
Prone position	B: Long hours	A: Moderate-severe, ≥ 12 h	A: P/F < 150, ≥ 16 h	A: P/F < 150, ≥ 12 h	A: ≥ 12 h	B	A
High-frequency oscillatory ventilation (HFOV)	D		E	E	E	E	E
Limited muscle relaxants use	B: Moderate-severe	B: Moderate-severe, intermittent use	A: P/F < 150, ≤ 48 h	B: P/F ≤ 150, ≤ 48 h		B	B
Weaning protocolization	B						
Early tracheotomy	B						D

Fujishima, S. Guideline-based management of acute respiratory failure and acute respiratory distress syndrome. *J Intensive Care* 11, 10 (2023).

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## Neuromuscular Blockers in Acute Respiratory Distress Syndrome

### ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies

We **recommend against** the *routine* use of continuous infusions of NMBA to reduce mortality in patients with moderate-to-severe ARDS not due to COVID-19.

*Strong recommendation, moderate level of evidence.*

We are **unable to make a recommendation** for or against the *routine* use of continuous infusions of NMBA to reduce mortality in patients with moderate-to-severe ARDS due to COVID-19.

*No recommendation; no evidence.*

Grasselli G, et al. ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies. *Intensive Care Med* 49, 727–759 (2023)

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## Neuromuscular Blockers in Acute Respiratory failure & Septic Shock

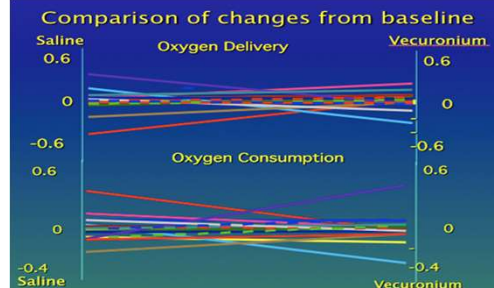
### Oxygen delivery, oxygen consumption, and gastric intramucosal pH are not improved by a computer-controlled, closed-loop, vecuronium infusion in severe sepsis and septic shock

#### Conclusions

In these patients, vecuronium infusion achieved the targeted level of paralysis and improved respiratory compliance but did not alter intramucosal pH,  $VO_2$ ,  $DO_2$ , or oxygen extraction ratios. With deep sedation, neuromuscular blockade in severe sepsis/septic shock does not significantly influence oxygen flux and should be abandoned as a routine method of improving tissue oxygenation in these patients. (*Crit Care Med* 1997; 25:72-77)

#### Differences: Saline vs Vecuronium (One tailed t- test)

Mean Airway Press	0.312	ns
Static Compliance	0.036	$p \leq 0.05$
O <sub>2</sub> Content	0.098	ns
DO <sub>2</sub>	0.334	ns
VO <sub>2</sub>	0.350	ns
pHi	0.365	ns



Freebairn RC, et al. Oxygen delivery, oxygen consumption, and gastric intramucosal pH are not improved by a computer-controlled, closed-loop, vecuronium infusion in severe sepsis and septic shock. *Crit Care Med*. 1997 Jan;25(1):72-7.

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**NARRATIVE REVIEW**

**Clinical strategies for implementing lung and diaphragm-protective ventilation: avoiding insufficient and excessive effort**

**MINIMIZING (BABY) LUNG STRESS & STRAIN**

**OPTIMIZING DIAPHRAGM EFFORT & SYNCHRONY**

breath-stacking dyssynchrony  
 ↓  
 excessive inspiratory assist → high  $V_T$ ,  $\Delta P$   
 excessive PEEP → overdistention  
 insufficient PEEP → derecruitment

“VILI”

“P-SILI”

insufficient assist, high effort/drive  
 ↓  
 injurious efforts

eccentric injury ← expiratory dyssynchrony  
 longitudinal atrophy ← excessive PEEP  
 disuse atrophy ← excessive assist, low effort/drive

diaphragm injury

Goligher, E., et al. Clinical strategies for implementing lung and diaphragm-protective ventilation: avoiding insufficient and excessive effort. *Intensive Care Med* 46, 2314–2326 (2020).

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So what is the answer  
 Spontaneously Breath or Not

Don't know But:

Balance  
 Personalized Ventilation

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