



# **ARDS:** WHEN CAN WE ALLOW **SPONTANEOUS BREATHING?**



#### Niall D. Ferguson, MD, FRCPC, MSc

Head of Critical Care Medicine University Health Network & Mount Sinai Hospital

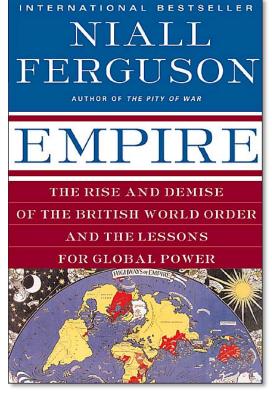
Professor, Departments of Medicine & Physiology, Institute of Health Policy, Management and Evaluation Interdepartmental Division of Critical Care Medicine University of Toronto

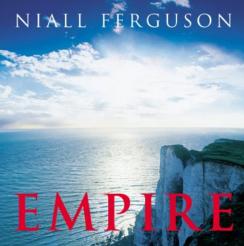




## **Disclosures**

- Consultant for Xenios
- Speaker fees from Getinge





#### HOW BRITAIN MADE The modern world

NOW A MAJOR CHANNEL FOUR SERIES

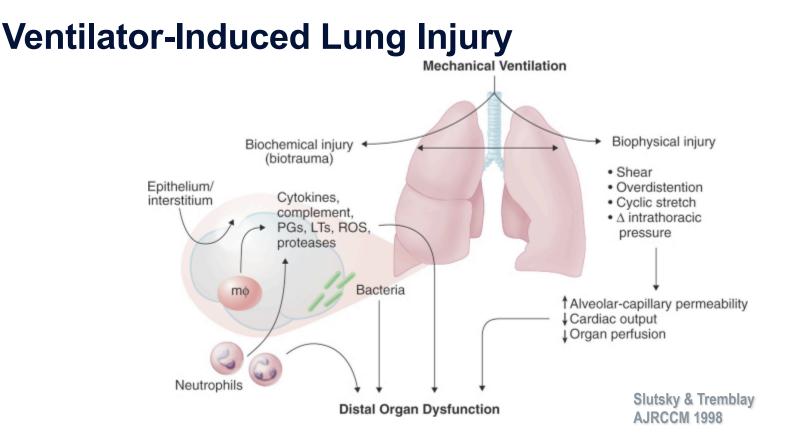














UNIVERSITY OF Interdepartmental Division of Critical Care Medicine

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#### 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\*

#### **High Stretch**

- V<sub>T</sub>: 11.8
- P<sub>PLAT</sub>: 32-34
- RR: 18
- V<sub>MIN</sub>: 13
- PEEP: 8

#### Low Stretch

- V<sub>T</sub>: 6.2 ml/kg
- P<sub>PLAT</sub>: 25 cm H<sub>2</sub>O
- RR: 29
- V<sub>MIN</sub>: 13 L/min
- PEEP: 9 cm H<sub>2</sub>O

#### Mortality 40%



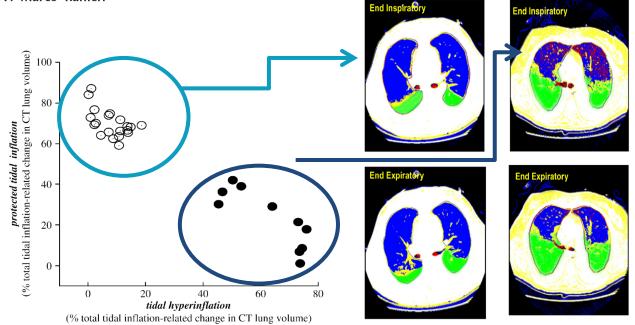






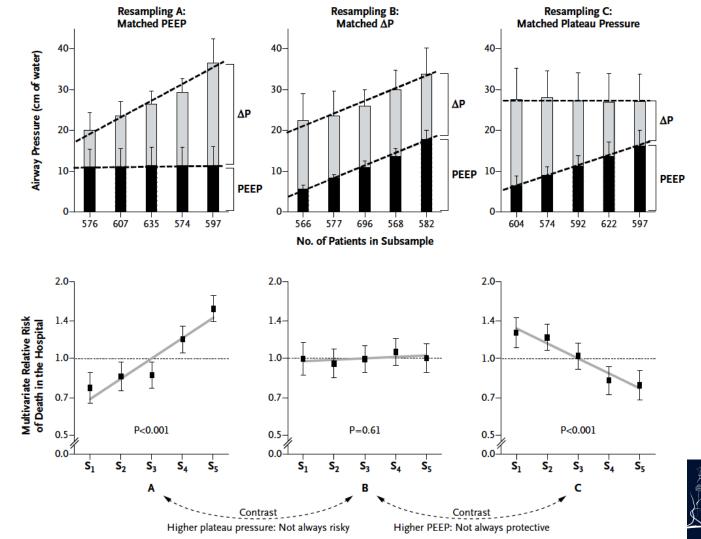
#### **Tidal Hyperinflation during Low Tidal Volume Ventilation in Acute Respiratory Distress Syndrome**

Am J Respir Crit Care Med Vol 175. pp 160–166, 2007 Pier Paolo Terragni, Giulio Rosboch, Andrea Tealdi, Eleonora Corno, Eleonora Menaldo, Ottavio Davini, Giovanni Gandini, Peter Herrmann, Luciana Mascia, Michel Quintel, Arthur S. Slutsky, Luciano Gattinoni, and V. Marco Ranieri





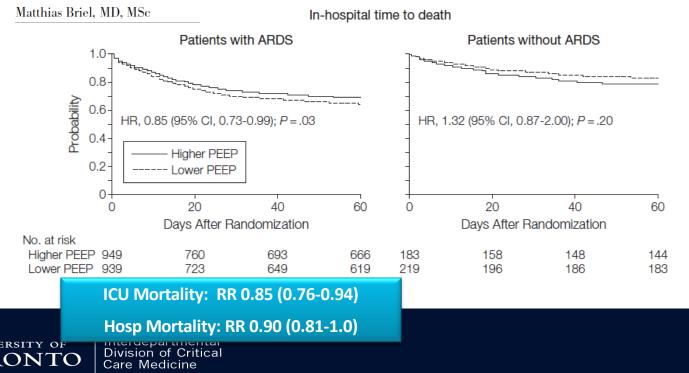






# Higher vs Lower Positive End-Expiratory Pressure What in Patients With Acute Lung Injury and Acute Respiratory Distress Syndrome

Systematic Review and Meta-analysis JAMA. 2010;303(9):865-873



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End
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A Ra

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	Day 1			Day 3			Day 7			
Variables	Lung Open Ventilation	Control	P Value	Lung Open Ventilation	Control	P Value	Lung Open Ventilation	Control	P Value	
Tidal volume, mean (SD), mL/kg predicted body weight	6.8 (1.4)	6.8 (1.3)	.76	6.9 (1.5)	6.7 (1.5)	.02	6.9 (1.3)	7.0 (1.6)	.53	ur
No. of patients	436	469		337	395		177	243		
Total respiratory rate, mean (SD), /min	25.2 (6.6)	26.0 (6.5)	.08	25.1 (6.6)	27.1 (8.0)	<.001	25.5 (8.0)	26.1 (7.6)	.26	
No. of patients	471	507		447	479		316	351		
Plateau pressure, mean (SD), cm H <sub>2</sub> O	30.2 (6.3)	24.9 (5.1)	<.001	28.6 (6.0)	24.7 (5.7)	<.001	28.8 (6.3)	25.1 (6.8)	<.001	
No. of patients	435	424		334	380		174	232		537-
30.1-35.0	112	33		76	38		37	27		
35.1-40.0	88	4		41	12		27	13		
>40.0	8	1		8	3		4	4		
FIO2, mean (SD)	0.50 (0.16)	0.58 (0.17)	<.001	0.41 (0.12)	0.52 (0.16)	<.001	0.39 (0.12)	0.48 (0.17)	<.001	
No. of patients	471	507		447	482		319	356		
Set PEEP, mean (SD), cm H <sub>2</sub> O All patients	15.6 (3.9)	10.1 (3.0)	<.001	11.8 (4.1)	8.8 (3.0)	<.001	10.3 (4.3)	8.0 (3.1)	<.001	
No. of patients	471	507		447	479		316	348		
First 161 patients	15.3 (3.6)	10.6 (2.9)	<.001	12.1 (4.1)	9.3 (3.0)	<.001	10.4 (4.3)	8.2 (3.1)	.005	
No. of patients	77	82		72	79		47	63		
Subsequent 822 patients	15.7 (4.0)	10.0 (3.0)	<.001	11.8 (4.1)	8.7 (3.0)	<.001	10.3 (4.3)	8.0 (3.1)	<.001	
No. of patients	394	425		375	400		269	285		
I:E ratio, mean (SD)	0.62 (0.19)	0.56 (0.19)	<.001	0.64 (0.21)	0.56 (0.21)	<.001	0.64 (0.19)	0.59 (0.22)	.02	
No. of patients	410	420		329	373		170	212		
PaO <sub>2</sub> /FIO <sub>2</sub> , mean (SD)	187.4 (68.8)	149.1 (60.6)	<.001	196.8 (60.6)	164.1 (63.5)	<.001	212.7 (70.5)	180.8 (73.0)	<.001	

#### For tidal volume, data exclude patients weaning in pressure support mode, with $FiO_2 \le 0.4$ and $PEEP \le 10$

pri, 110011 (00)	1.00 (0.10)	1.00 (0.00)		1.00 (0.01)	1.01 (0.00)		1.10 (0.01)	1.00 (0.00)	
No. of patients	464	498		444	472		314	342	
24-h fluid balance, mean (SD), mL	2131.4 (2506.6)	2110.6 (2641.7)	.90	1029.0 (2222.9)	722.9 (2201.4)	.04	270.6 (2078.2)	102.4 (1808.4)	.26
No. of patients	465	500		445	473		326	363	

Abbreviations: FIO2, fraction of inspired oxygen; I:E, inspiration:expiration; PEEP, positive end-expiratory pressure; PaO2, partial pressure of arterial oxygen; PaCO2, partial pressure of arterial carbon dioxide.

<sup>a</sup> Data shown were derived from the average value obtained for each patient over 3 measurements each day. Values were recorded on days 1, 3, and 7 after enrollment. For tidal volume and plateau airway pressure measurements, data exclude patients weaning in pressure support mode, with FIO2 less than or equal to 0.40 and PEEP less than or equal to 10 cm H<sub>2</sub>O.





Intensive Care Med (2010) 36:585–599 DOI 10.1007/s00134-009-1748-1

#### REVIEW

Sachin Sud Jan O. Friedrich Paolo Taccone Federico Polli Neill K. J. Adhikari **Roberto Latini** Antonio Pesenti Claude Guérin Jordi Mancebo Martha A. Q. Curley **Rafael Fernandez Ming-Cheng Chan** Pascal Beuret **Gregor Voggenreiter** Maneesh Sud **Gianni Tognoni** Luciano Gattinoni

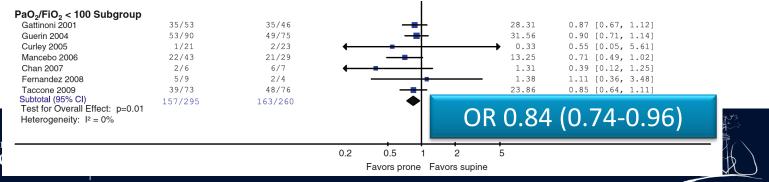
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 $\mathbf{OR}$ 

Prone ventilation reduces mortality in patients with acute respiratory failure and severe hypoxemia: systematic review and meta-analysis

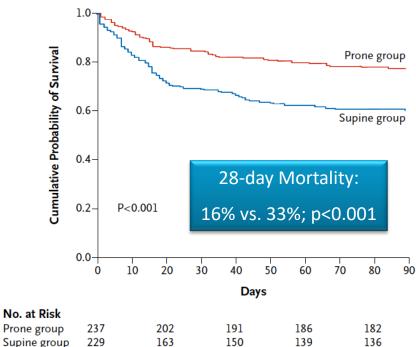
Prone vs. Supine Position

• ARDS with P/F < 100



## Prone Positioning in Severe Acute Respiratory Distress Syndrome

ORIGINAL ARTICLE	
Prone Positioning in Severe Acute Respiratory Distress Syndrome	
Cases Golde, M.D., R.D., Japes Rights K. L.D., R.D., Japas Charlow, H. K. Mark, M. U., A.D., And M. K. M. K. Mark, M. K. M. K. Mark, M. K.	
ABSTRACT	
Panolose trials involving partness with the same supprisely disease updatess (UEEG) have fielded to show a beneficial effect of prene positioning design enclusies of were titleory support on outcomes. We enclused the effect of early application of prene positioning on manemess in partness with severe ALGs. <b>VETTOOI</b> In this multiconter, prospective, randomized, controlled trial, we randomly as-	Appendix Address exploit regards to Gablie at Service du Resisterie M aub Highlich K-Cole Resear, 120 Ger Bare de la Cacle Resear, 1990 fui Fonce, es d'aude garring-blu-bre "The Desting Server ADS Paris (PRODUC), shalp investigation are in the Servering Server and Servering Server 1990 for Servering Servering 1990 for Servering Servering and International Servering Servering 1990 for Servering Servering Servering 1990 for Servering Servering Servering 1990 for Servering Servering Servering 1990 for Servering 1990 f
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N Engl J Med 2013. DOI: 10.1056/NEJMoa1214103





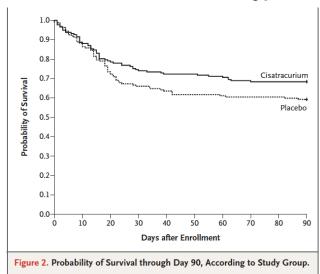
#### Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome

Laurent Papazian, M.D., Ph.D., Jean-Marie Forel, M.D., Arnaud Gacouin, M.D., Christine Penot-Ragon, Pharm.D., Gilles Perrin, M.D., Anderson Loundou, Ph.D., Samir Jaber, M.D., Ph.D., Jean-Michel Arnal, M.D., Didier Perez, M.D., Jean-Marie Seghboyan, M.D., Jean-Michel Constantin, M.D., Ph.D., Pierre Courant, M.D., Jean-Yves Lefrant, M.D., Ph.D., Claude Guérin, M.D., Ph.D., Gwenaël Prat, M.D., Sophie Morange, M.D., and Antoine Roch, M.D., Ph.D.,

for the ACURASYS Study Investigators\*

N Engl J Med 2010;363:1107-16









# **Spontaneous Ventilation in ARDS**

ROSE Trial Results

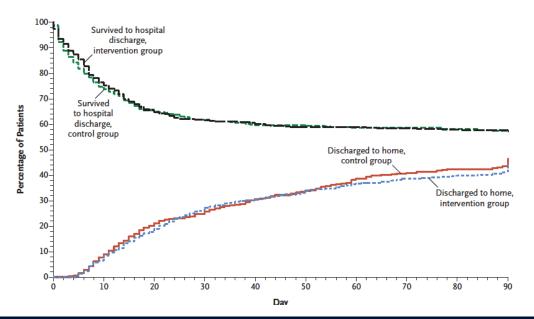




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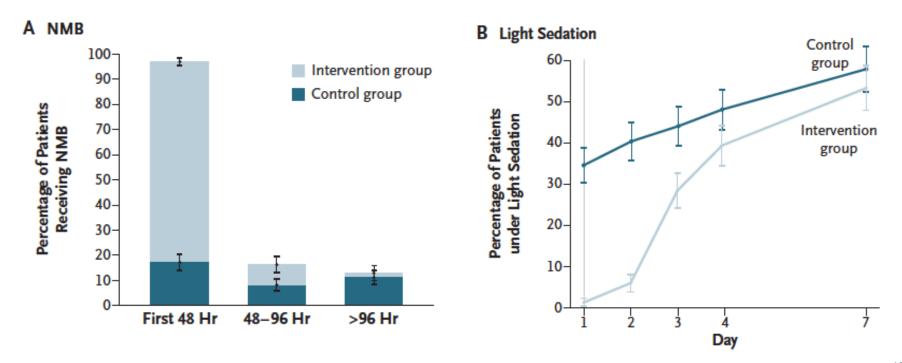
The National Heart, Lung, and Blood Institute PETAL Clinical Trials Network\*

- 1006 early ARDS P/F < 150
- 48h cisatricurium & deep sedation *vs.* lighter sedation
- Higher PEEP in both groups
- 15% prone in both groups
- Primary: 90-day mortality
- Stopped for futility





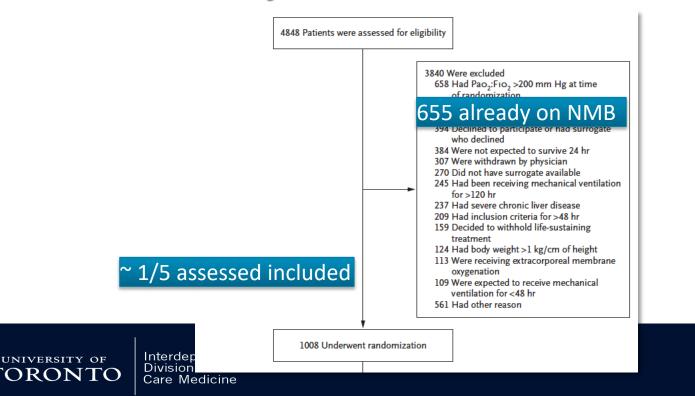
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The National Heart, Lung, and Blood Institute PETAL Clinical Trials Network\*



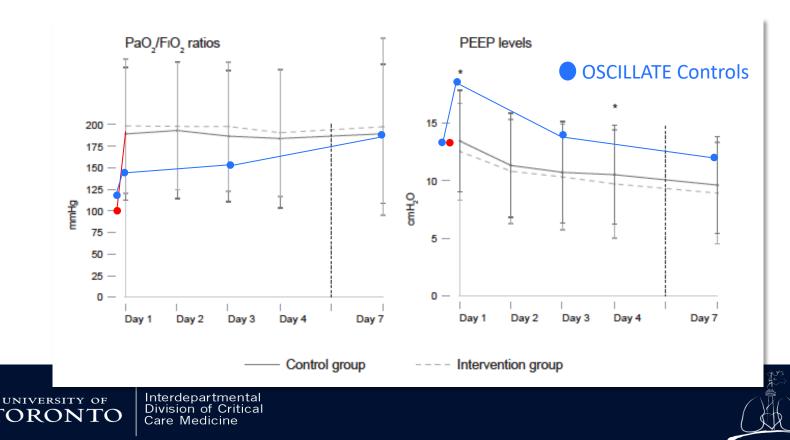
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Table 1. Baseline Characteristics of the Patients.*							
Characteristic	Intervention Group (N=501)	Control Group (N=505)					
Age — yr	56.6±14.7	55.1±15.9					
Female sex — no. (%)†	210 (41.9)	236 (46.7)					
White race — no. (%)†	361 (72.1)	344 (68.1)					
Shock at baseline — no. (%)	276 (55.1)	309 (61.2)					
Median time from enrollment to randomization (IQR) — hr	8.2 (4.0–16.4)	6.8 (3.3–14.5)					
Assessments and measurements							
APACHE III score‡	103.9±30.1	104.9±30.1					
Total SOFA score§	8.7±3.6	8.8±3.6					
Tidal volume — ml/kg of predicted body weight¶	6.3±0.9	6.3±0.9					
FI02	0.8±0.2	0.8±0.2					
Inspiratory plateau pressure — cm of water**	25.5±6.0	25.7±6.1					
PEEP — cm of water††	12.6±3.6	12.5±3.6					
Pao2:Fio2 — mm Hg‡‡	98.7±27.9	99.5±27.9					
Imputed Pao <sub>2</sub> :Fio <sub>2</sub> — mm Hg§§	94.8±26.7	93.2±28.9					





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

#### Why are ROSE and ACURASYS results different?

- Higher PEEP?
- Lighter sedation comparator?
- Lower use of proning (15% vs. ~50%)
- Less sick patients





# **Spontaneous Ventilation in ARDS**

- Rose Trial Results
- Spontaneous is not always better





#### **Evolution of Mortality Over Time in Patients Receiving Mechanical Ventilation** A Esteban, F Frutos Vivar, A Muriel, ND Ferguson, et al. Am J Respir Crit Care Med 2013 2010 Day of mechanical ventilation 45 90.00.00 Patients Assist-control SIMV SIMV-PSV PS -PCV PRVC BIPAP/APRV Other Non invasive ventilation Proportion of patients in each mode of ventilation 8000 40 35 7000 30 6000 No. of patients 25 20 3000 15 10 2000 1000 0 22 28 23 25 26 27 Day of mechanical ventilation

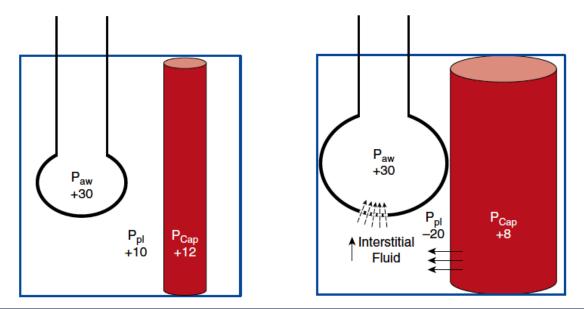
UNIVERSITY OF TORONTO



#### FIFTY YEARS OF RESEARCH IN ARDS Spontaneous Breathing during Mechanical Ventilation Risks, Mechanisms, and Management

Am J Respir Crit Care Med Vol 195, Iss 8, pp 985-992, Apr 15, 2017

Takeshi Yoshida<sup>1,2,3,4</sup>, Yuji Fujino<sup>4</sup>, Marcelo B. P. Amato<sup>5</sup>, and Brian P. Kavanagh<sup>1,2,3</sup>



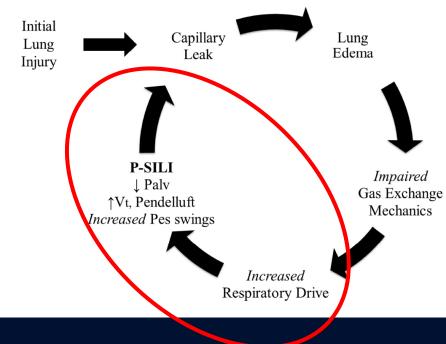




#### MECHANICAL VENTILATION TO MINIMIZE PROGRESSION OF LUNG INJURY IN ACUTE

RESPIRATORY FAILURE AJRCCM Articles in Press. Published on 14-September-2016 as 10.1164/rccm.201605-1081CP

Laurent Brochard<sup>1,2</sup>, Arthur Slutsky<sup>1,2</sup>, Antonio Pesenti<sup>3,4</sup>



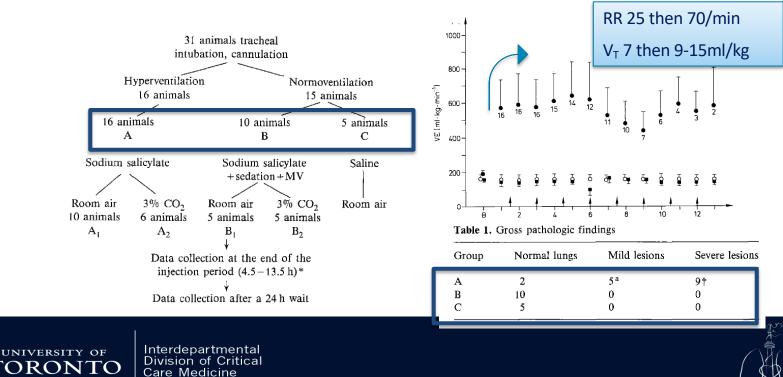




#### Original articles

# Acute respiratory failure following pharmacologically induce hyperventilation: an experimental animal study

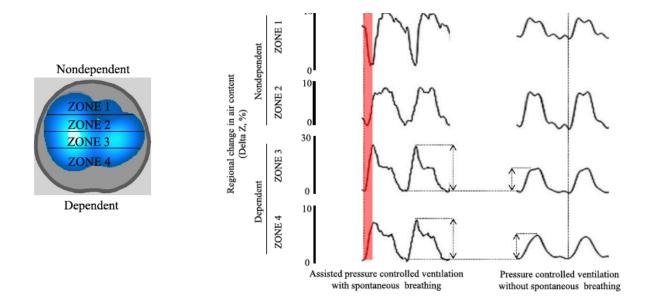
D. Mascheroni\*, T. Kolobow, R. Fumagalli\*, M. P. Moretti\*\*, V. Chen and D. Buckhold



Intensive Care Medicine © Springer-Verlag 1988

#### Spontaneous Effort Causes Occult Pendelluft during Mechanical Ventilation Am J Respir Crit Care Med Vol 188, Iss. 12, pp 1420-1427, Dec 15, 2013

Takeshi Yoshida<sup>1,2</sup>, Vinicius Torsani<sup>1</sup>, Susimeire Gomes<sup>1</sup>, Roberta R. De Santis<sup>1</sup>, Marcelo A. Beraldo<sup>1</sup>, Eduardo L. V. Costa<sup>1</sup>, Mauro R. Tucci<sup>1</sup>, Walter A. Zin<sup>3</sup>, Brian P. Kavanagh<sup>4,5</sup>, and Marcelo B. P. Amato<sup>1</sup>



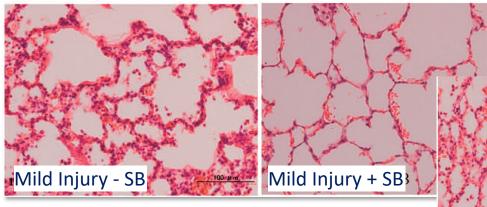




# The Comparison of Spontaneous Breathing and Muscle Paralysis in Two Different Severities of Experimental Lung Injury\* Crit Care Med 2013; 41:536–545

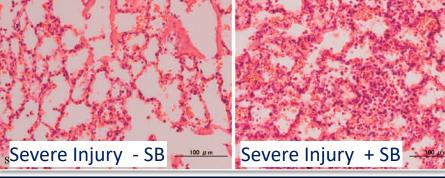
Takeshi Yoshida, MD<sup>1,2</sup>; Akinori Uchiyama, MD, PhD<sup>2</sup>; Nariaki Matsuura, MD, PhD<sup>3</sup>;

Takashi Mashimo, MD, PhD<sup>2</sup>; Yuji Fujino, MD, PhD<sup>2</sup>



Rabbits with mild (saline lavage) or

severe (saline lavage + VILI) lung injury

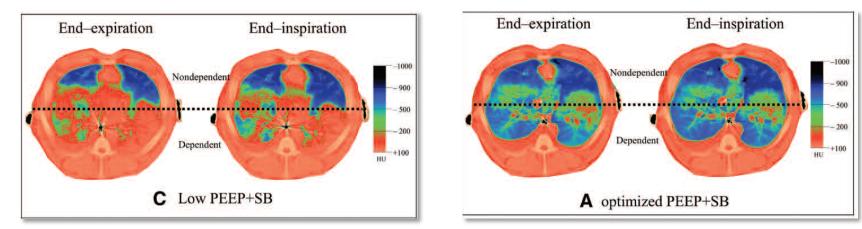






## Spontaneous Effort During Mechanical Ventilation: Maximal Injury With Less Positive End-Expiratory Pressure\* Crit Care Med 2016; 44:e678–e688

Takeshi Yoshida, MD, PhD<sup>1,2</sup>; Rollin Roldan, MD<sup>1,3</sup>; Marcelo A. Beraldo, PhD<sup>1,4</sup>; Vinicius Torsani, PhD<sup>1</sup>; Susimeire Gomes, PhD<sup>1</sup>; Roberta R. De Santis, MD<sup>1</sup>; Eduardo L. V. Costa, MD<sup>1,5</sup>; Mauro R. Tucci, MD<sup>1</sup>; Raul G. Lima, PhD<sup>6</sup>; Brian P. Kavanagh, MD<sup>7</sup>; Marcelo B. P. Amato, MD, PhD<sup>1</sup>







# **Spontaneous Breathing in ARDS**

When to allow any?

How much to allow?

Consider maintaining normal effort levels – implies measuring effort





# **Spontaneous Breathing in ARDS**

- PRO
  - Prevent diaphragm atrophy (overassist myotrauma)
  - Improved hemodynamics
  - Less sedation and associated adverse effects
  - Progress patients towards liberation

- CONs
  - Direct overdistention injury
  - Pendelluft injury
  - Increased lung perfusion
  - Dyssynchrony double-trigger
  - Expiratory muscle activation leading to decreased EELV

#### Effect Modifiers:

ARDS Severity; Smaller Baby Lung; High Drive; Injurious Settings





#### REVIEW



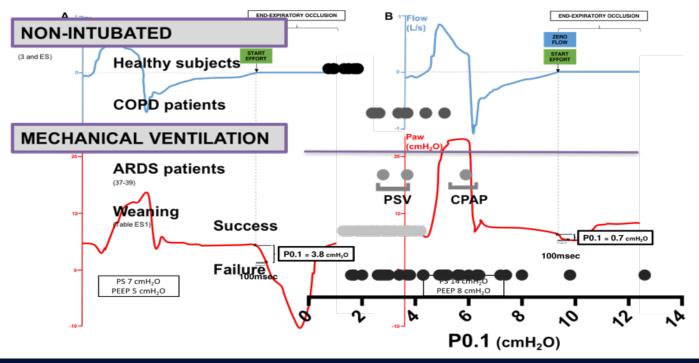
# Esophageal and transpulmonary pressure in the clinical setting: meaning, usefulness and perspectives







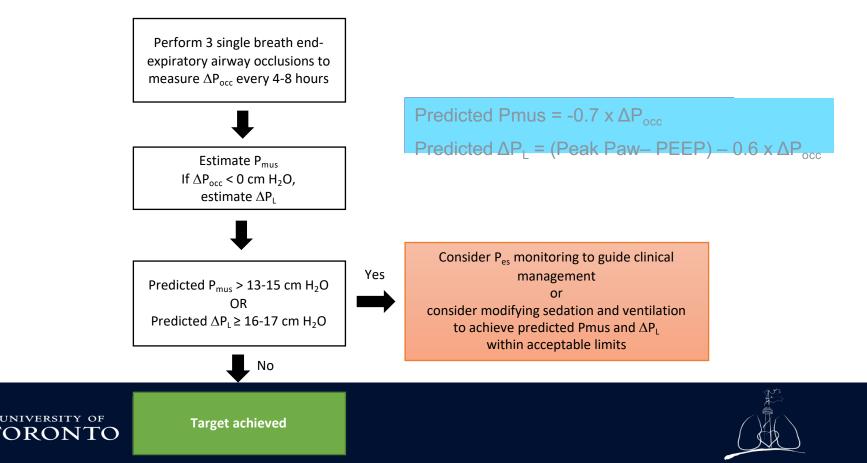
# **Airway Occlusion Pressure – P0.1**







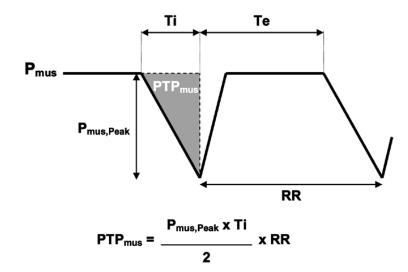
# **End-Expiratory Exclusion Manoeuvre**

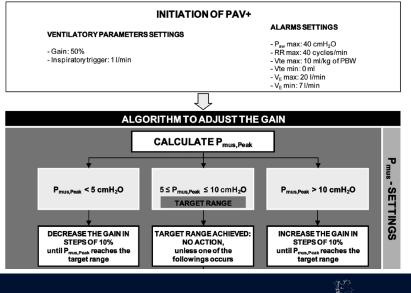


#### Bedside Adjustment of Proportional Assist Ventilation to Target a Predefined Range of Respiratory Effort\*

Guillaume Carteaux, MD<sup>1,2</sup>; Jordi Mancebo, MD, PhD<sup>3</sup>; Alain Mercat, MD, PhD<sup>4</sup>; Jean Dellamonica, MD, PhD<sup>5,6</sup>; Jean-Christophe M. Richard, MD, PhD<sup>7,8</sup>; Hernan Aguirre-Bermeo, MD<sup>3</sup>; Achille Kouatchet, MD<sup>4</sup>; Gaetan Beduneau, MD<sup>7,9</sup>; Arnaud W. Thille, MD, PhD<sup>8</sup>; Laurent Brochard, MD<sup>10,11</sup>

Crit Care Med 2013;41:2125-2132



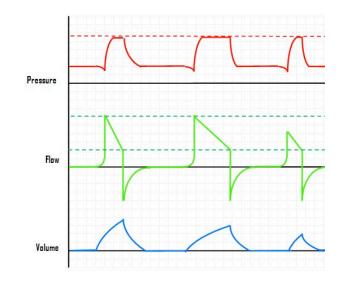




# **Pressure Support Ventilation**

Ventilator's mission is to regulate pressure

- Set PS level;  $C_{RS}$ ; AND Patient Effort determine  $V_T$ 



PS 8; PEEP 5  $V_T = 750 \text{ mL}$ How do control  $V_T$  in this patient???





# **Decreasing spontaneous effort levels**

- Increase inspiratory assist but be careful with  $V_T$ Increase PEEP Consider NMB – but trade Under for Over-assist Consider partial NMB
- Consider ECLS





Intensive Care Med (2006) 32:1515–1522 DOI 10.1007/s00134-006-0301-8

ORIGINAL

Arnaud W. Thille Pablo Rodriguez Belen Cabello François Lellouche Laurent Brochard

# Patient-ventilator asynchrony during assisted mechanical ventilation

	Asynchrony index $< 10\%$ ( $n = 47$ )	Asynchrony index $\ge 10\%$ ( <i>n</i> = 15)	р
Duration of mechanical ventilation (days; IQR) Duration of mechanical ventilation $\geq$ 7 days Tracheostomy Mortality	7 (3–20)	25 (9-42)	0.005
	23 (49%)	13 (87%)	0.01
	2 (4%) 15 (32%)	5 (33%) 7 (47%)	0.007 0.36

#### 25% of patients showed significant asynchrony





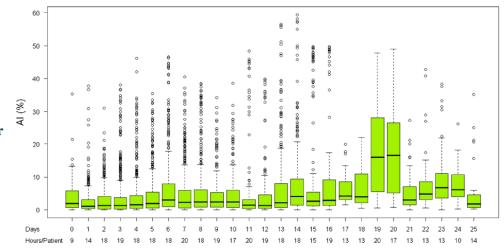
Intensive Care Med DOI 10.1007/s00134-015-3692-6

#### ORIGINAL

Lluís Blanch Ana Villagra Bernat Sales Jaume Montanya **Umberto Lucangelo** Manel Luján **Oscar García-Esquirol** Encarna Chacón Anna Estruga Joan C. Oliva Alberto Hernández-Abadia Guillermo M. Albaiceta Enrique Fernández-Mondejar Rafael Fernández Josefina Lopez-Aguilar Jesús Villar Gastón Murias **Robert M. Kacmarek** 

UNIVERSITY ORON

## Asynchronies during mechanical ventilation are associated with mortality



	AI $\leq 10 \% (n = 44)$	AI > 10 % $(n = 6)$	p value
Length of MV (days)	6 [5.0; 15.0]	16 [9.7; 20.0]	0.061
Reintubation	9 (20 %)	0 (0 %)	0.57
Tracheostomy	14 (32 %)	2 (33 %)	0.999
ICU mortality	6 (14 %)	4 (67 %)	0.011*
Hospital mortality	10 (23 %)	4 (67 %)	0.044*



## **Types of Asynchrony**

Ineffective Efforts / Delayed Triggering

- Trigger too insensitive / weak efforts
- Auto PEEP
- Cycle-off Asynchrony (prolonged inspiration)
- Cycle-off Asynchrony
- Prolonged inspiration
- Premature termination
- Double Triggering
- High respiratory drive
- Short set inspiratory time
- Auto Triggering
- Cardiac oscillations
- Trigger too sensitive

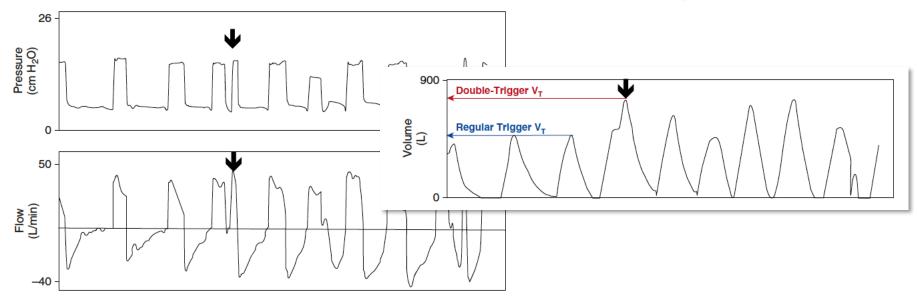




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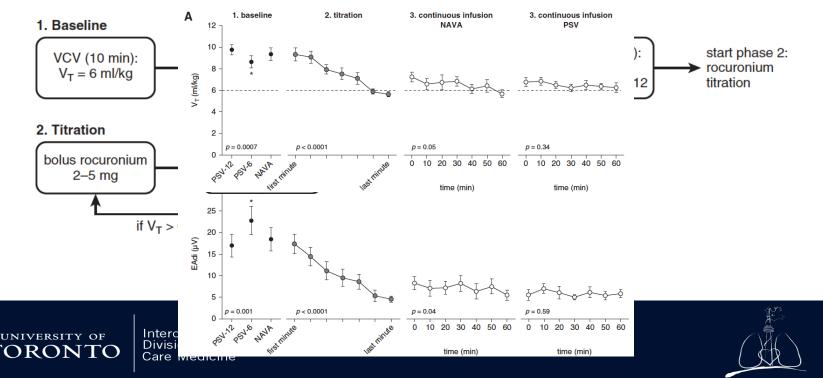




# Partial Neuromuscular Blockade during Partial Ventilatory Support in Sedated Patients with High Tidal Volumes

Jonne Doorduin<sup>1</sup>, Joeke L. Nollet<sup>1</sup>, Lisanne H. Roesthuis<sup>1</sup>, Hieronymus W. H. van Hees<sup>2</sup>, Laurent J. Brochard<sup>3,4</sup>, Christer A. Sinderby<sup>3,4</sup>, Johannes G. van der Hoeven<sup>1</sup>, and Leo M. A. Heunks<sup>1</sup>

Am J Respir Crit Care Med Vol 195, Iss 8, pp 1033-1042, Apr 15, 2017

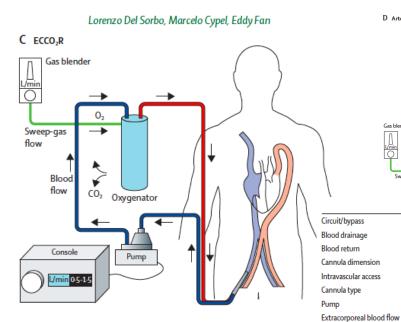


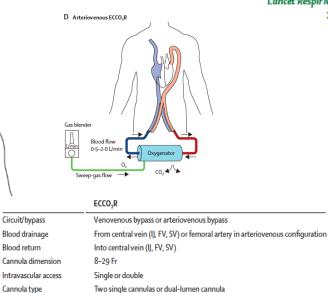
# Extracorporeal life support for adults with severe acute respiratory failure

CO<sub>2</sub> clearance

Oxygen delivery capacity

Anticoagulation target





0.2-2.0 L/min

Not significant

Centrifugal or peristaltic (absent in arteriovenous configuration)

10-100% VCO2, dependent mainly on sweep-gas flow

ACT 1.5 times normal, aPTT 1.5 times normal

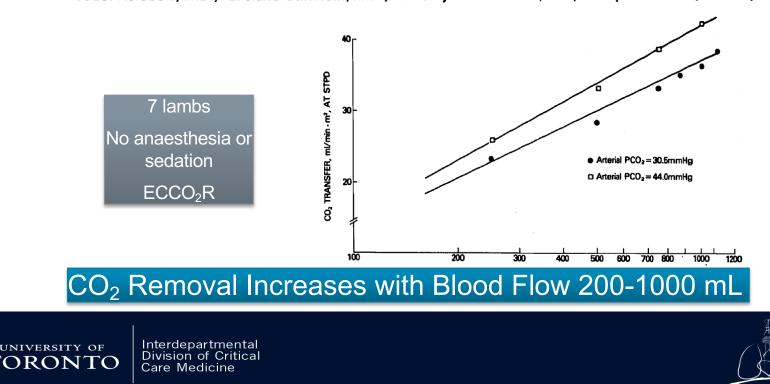
Lancet Respir Med 2014; 2: 154-64

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*	UNIVERSITY OF	
	TORONTO	



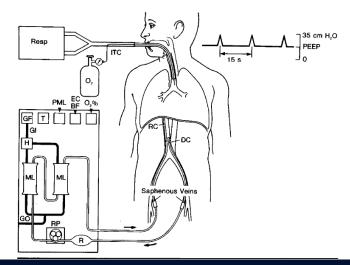
#### **Laboratory Report**

Control of Breathing Using an Extracorporeal Membrane Lung Theodor Kolobow, M.D.,\* Luciano Gattinoni, M.D.,\* Timothy A. Tomlinson, B.S.,\* Joseph E. Pierce, D.V.M.†

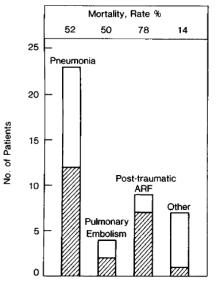


### Low-Frequency Positive-Pressure Ventilation With Extracorporeal CO<sub>2</sub> Removal in Severe Acute Respiratory Failure (JAMA 1986;256:881-886)

Luciano Gattinoni, MD; Antonio Pesenti, MD; Daniele Mascheroni, MD; Roberto Marcolin, MD; Roberto Fumagalli, MD; Francesca Rossi, MD; Gaetano Iapichino, MD; Giuliano Romagnoli, MD: Ljii Uziel, MD; Angelo Agostoni, MD; Theodor Kolobow, MD; Giorgio Damia, MD



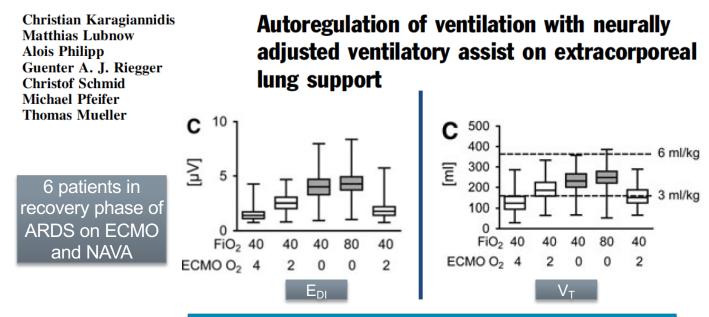








#### ORIGINAL



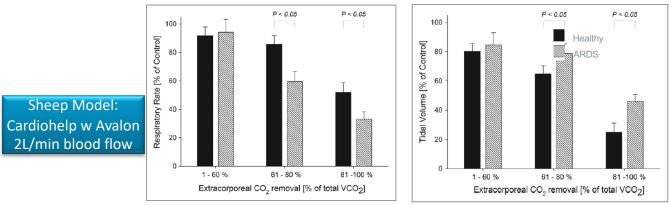
ECMO can Modulate Respiratory Drive





### Extracorporeal Gas Exchange and Spontaneous Breathing for the Treatment of Acute Respiratory Distress Syndrome: An Alternative to Mechanical Ventilation?\*

Thomas Langer, MD<sup>1,2,3</sup>; Vittoria Vecchi, MD<sup>1,3,4</sup>; Slava M. Belenkiy, MD<sup>1</sup>; Jeremy W. Cannon, MD<sup>1,5</sup>; Kevin K. Chung, MD<sup>1,6</sup>; Leopoldo C. Cancio, MD<sup>1</sup>; Luciano Gattinoni, MD<sup>2,7</sup>; Andriy I. Batchinsky, MD<sup>1</sup>



-  $\Delta P_{es}$  6 vs. 35 cmH<sub>2</sub>O (baseline)

- V<sub>T</sub> and P<sub>es</sub> variations only reduced when >80% of VCO<sub>2</sub> removed (ARDS)



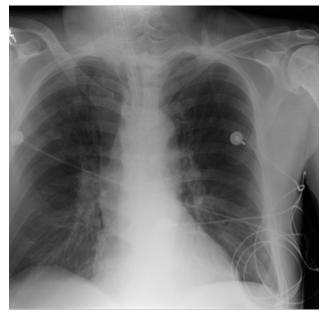


## **Opinion Based Medicine...**

 $Set \ V_T \mbox{=} 6 \ ml/kg \ (or \ lower) \\ Control \ breath \ size \ if \ mod-severe \ ARDS$ 



Set  $V_T$ =6-8 ml/kg Tolerate larger spontaneous breaths Consider check for pendeluft







## **Take Home Points**

Impact of spontaneous breathing during ARDS depends on timing and severity

Measuring patient effort is important

When allowing spontaneous breathing – consider normalizing efforts to protect both lung and diaphragm

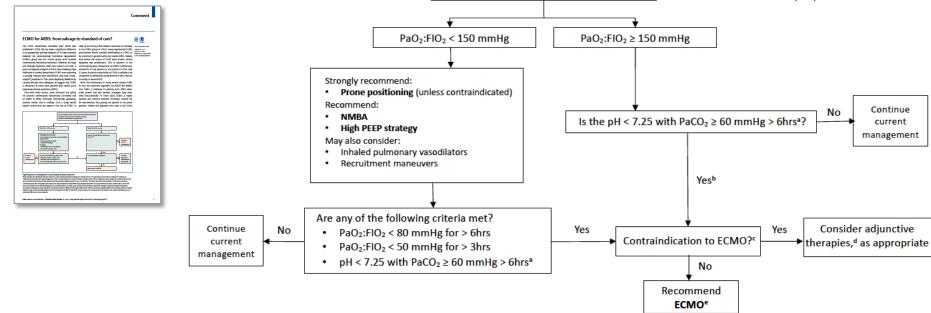




### ECMO for ARDS: from salvage to standard of care?

#### Lancet Respir Med 2019

Darryl Abrams, Niall D Ferguson, Laurent Brochard, Eddy Fan, Alain Mercat, Alain Combes, Vin Pellegrino, Matthieu Schmidt, Arthur S Slutsky, \*Daniel Brodie Published **Online** January 11, 2019 http://dx.doi.org/10.1016/ S2213-2600(18)30506-X



Treat underlying cause of ARDS

Standard lung-protective ventilation strategy Diuresis or resuscitation as appropriate





### University of Toronto Critical Care Medicine International Fellowship Programme n.ferguson@utoronto.ca www.criticalcaretoronto.com







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Interdepartmental Division of Critical Care Medicine

n.ferguson@utoronto.ca

@nialldferguson

