Lung Imaging and Personalized Care in ARDS

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Disclosures

• Conflicts of interest: none
• Funding:
  – NIH
  – FAER
  – ITMATT
  – Hill-Rom
Overview

- Heterogeneity of the ARDS population and the need for better characterization of lung injury

- Can lung imaging help personalize ARDS care?

- Measuring small scale inflation and the progression of early lung injury
Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries

Giacomo Bellani, MD, PhD; John G. Laffey, MD, MA; Tài Pham, MD; Eddy Fan, MD, PhD; Laurent Brochard, MD, HDR; Andres Esteban, MD, PhD; Luciano Gattinoni, MD, FRCP; Frank van Haren, MD, PhD; Anders Larsson, MD, PhD; Daniel F. McAuley, MD, PhD; Marco Ranieri, MD; Gordon Rubenfeld, MD, MSc; B. Taylor Thompson, MD, PhD; Hermann Wrigge, MD, PhD; Arthur S. Slutsky, MD, MA; Antonio Pesenti, MD; for the LUNG SAFE Investigators and the ESICM Trials Group
How to Improve ARDS Survival
Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries

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A  Cumulative frequency distribution of tidal volume

- All (n = 2255)
- ARDS severity
  - Mild (n = 672)
  - Moderate (n = 1050)
  - Severe (n = 533)

Cumulative Rate vs Tidal Volume, mL/kg of Predicted Body Weight
ARDS Finder

The ARDS Finder identified your patient, JF, in 0983A as having ARDS. Use of the Low Stretch Protocol (SCM) is life-saving & strongly recommended, unless contraindicated.
Comparison of the Berlin Definition for Acute Respiratory Distress Syndrome with Autopsy

Arnaud W. Thille¹,², Andrés Esteban¹, Pilar Fernández-Segoviano², José-Maria Rodríguez², José-Antonio Aramburu², Oscar Peñuelas¹, Irene Cortés-Puch¹, Pablo Cardinal-Fernández¹, José A. Lorente¹, and Fernando Frutos-Vivar¹

356 Autopsies of patients meeting Berlin criteria

AJRCCM 2013
ARDS: progress unlikely with non-biological definition

S. Fröhlich¹,²*, N. Murphy¹,² and J. F. Boylan¹
Outcome heterogeneity is unmasked by standardized ventilator settings

- 41 ARDS pts screened at baseline and with standardized ventilator settings (PEEP 10, FiO2 1.0)
- 24 did not meet ARDS criteria with the new settings

PaO$_2$/FiO$_2$

Oxygenation Response to Positive End-Expiratory Pressure Predicts Mortality in Acute Respiratory Distress Syndrome
A Secondary Analysis of the LOVS and ExPress Trials

Ewan C. Goligher¹,²,³,⁴, Brian P. Kavanagh¹,⁵,⁶, Gordon D. Rubenfeld¹,²,⁷, Noill K. J. Adhikari¹,²,⁷, Ruxandra Pinto⁷, Eddy Fan¹,²,⁴, Laurent J. Brochard¹,²,⁸, John T. Granton¹,²,⁴, Alain Mercat⁹, Jean-Christophe Marie Richard¹⁰, Jean-Marie Chretien¹¹, Graham L. Jones¹², Deborah J. Cook¹²,¹³, Thomas E. Stewart¹,²,⁴, Arthur S. Slutsky¹,²,⁴, Maureen O. Meade¹²,¹³, and Niall D. Ferguson¹,²,³,⁴

ΔPEEP > 0

ΔPEEP ≤ 0

Adjusted probability of death

ΔP/F (mm Hg) following initial PEEP modification

AJRCCM 2014
Acute Respiratory Distress Syndrome Subphenotypes Respond Differently to Randomized Fluid Management Strategy

Katie R. Famous\textsuperscript{1}, Kevin Delucchi\textsuperscript{2}, Lorraine B. Ware\textsuperscript{3,4}, Kirsten N. Kangelaris\textsuperscript{5}, Kathleen D. Liu\textsuperscript{6,7}, B. Taylor Thompson\textsuperscript{8}, and Carolyn S. Calfee\textsuperscript{1,7}; for the ARDS Network

Table 3. Clir

<table>
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<th>60-d mortality</th>
<th>90-d mortality</th>
<th>Ventilator-free</th>
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<td>Definition of ab P value represents</td>
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<tr>
<th>Individual Observed Variables</th>
<th>P Value</th>
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<tr>
<td>Interleukin-6</td>
<td>&lt;0.0001</td>
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<tr>
<td>Interleukin-1</td>
<td>&lt;0.0001</td>
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<td>Angioprotein-2</td>
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<td>Creatinine</td>
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<td>PAI-1</td>
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<td>MMP-9</td>
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<td>HPA</td>
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<td>ICAM-1</td>
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<td>Brain Edema</td>
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<td>Mean Arterial Pressure</td>
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<td>Respiration Rate</td>
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<td>PEEP</td>
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<td>Baseline Temp (Centigrade)</td>
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<td>Apnea</td>
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<td>Hb</td>
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<tr>
<td>Platelets</td>
<td>&lt;0.0001</td>
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<td>Platelet CRP</td>
<td>&lt;0.0001</td>
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<tr>
<td>Platelet CEB</td>
<td>&lt;0.0001</td>
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AJRCCM 2017
ARDS Subtypes

Gas exchange

Imaging
Biomarkers

Lung mechanics
The ‘Baby Lung’

Baby Lung

Consolidation/Atelectasis

Lung Strain

Mechano-signaling

Ventilator Induced Lung Injury (VILI)
Lungs of patients with acute respiratory distress syndrome show diffuse inflammation in normally aerated regions: A [18F]-fluoro-2-deoxy-D-glucose PET/CT study

Giacomo Bellani, MD; Cristina Messa, MD; Luca Guerra, MD; Ester Spagnolli, MD; Giuseppe Foti, MD; Nicolò Patroniti, MD; Roberto Fumagalli, MD; Guido Musch, MD; Ferruccio Fazio, MD; Antonio Pesenti, MD

CCM 2009
One size fits all?
Tidal Hyperinflation during Low Tidal Volume Ventilation in Acute Respiratory Distress Syndrome

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
Driving Pressure and Survival in the Acute Respiratory Distress Syndrome

Unstable Recruitment and Atelectrauma

Courtesy of J. Hermann, D. Kaczka
Mechanisms of atelectrauma

Wellman et al. et al. CCM 2014
“Open up the lung and keep it open!”
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

Hazard ratio, 1.20 (95% CI, 1.01-1.42); P = .041

Days After Randomization

Mortality, %

No. at risk
Lung recruitment and titrated PEEP
Low PEEP
501
509
397
423
340
378
340
343
303
312
276
286
254
264
233
226
225
225

JAMA 2017
Recruit this!
Lung Recruitment in Patients with the Acute Respiratory Distress Syndrome

Luciano Gattinoni, M.D., F.R.C.P., Pietro Caironi, M.D., Massimo Cressoni, M.D., Davide Chiumello, M.D., V. Marco Ranieri, M.D., Michael Quintel, M.D., Ph.D., Sebastiano Russo, M.D., Nicolò Patroniti, M.D., Rodrigo Cornejo, M.D., and Guillermo Bugedo, M.D.

Gattinoni 2006
Lung morphology predicts response to recruitment maneuver in patients with acute respiratory distress syndrome

Jean-Michel Constantin, MD, PhD; Salvatore Grasso, MD, PhD; Gerald Chanques, MD; Sophie Auffort, MD; Emmanuel Futier, MD; Mustapha Sebbane, MD; Boris Jung, MD; Benoît Gallix; Jean Etienne Bazin, MD, PhD; Jean-Jacques Rouby, MD, PhD; Samir Jaber, MD, PhD
Elevated Plasma Levels of sRAGE Are Associated With Nonfocal CT-Based Lung Imaging in Patients With ARDS

Mrozek et al. Chest 2016
‘Baby Lung’: a Binary Model
Lung Inhomogeneity in Patients with Acute Respiratory Distress Syndrome

Massimo Cressoni¹, Paolo Cadrinher¹, Chiara Chiurazzi¹, Martina Amini¹, Elisabetta Gallazzi¹, Antonella Marino¹, Matteo Brioni¹, Eleonora Carlesso¹, Davide Chiumello², Michael Quintel³, Guillermo Bugedo⁴, and Luciano Gattinoni¹,²

AJRCCM 2014
Find the ‘Normal’ Lung’
Interpretation of CT Densities
Sub-Voxel Heterogeneity of Inflation

1 mm
Imaging the Injured Lung

(A)

(B)

(C)

Healthy

Surfactant Depletion

Anesthesiology 2019
Early Inflammation Mainly Affects Normally and Poorly Aerated Lung in Experimental Ventilator-Induced Lung Injury*

João Batista Borges, MD, PhD\textsuperscript{1,2}; Eduardo L. V. Costa, MD, PhD\textsuperscript{2,3};
Fernando Suarez-Sipmann, MD, PhD\textsuperscript{1,4}; Charles Widström, MSc\textsuperscript{5}; Anders Larsson, MD, PhD\textsuperscript{1};
Marcelo Amato, MD, PhD\textsuperscript{2}; Göran Hedenstierna, MD, PhD\textsuperscript{6}
ARDS as a Spatially Evolving Process
Visualizing the Propagation of Acute Lung Injury

Maurizio Cereda, M.D., Yi Xin, M.S., Natalie Meeder, B.A., Johnathan Zeng, B.S.E., YunQing Jiang, M.S.E., Hooman Hamedani, M.S., Harrilla Profka, D.V.M., Stephen Kadlecak, Ph.D., Justin Clapp, Ph.D., Charuhas G. Deshpande, M.D., Jue Wu, Ph.D., James C. Gee, Ph.D., Brian P. Kavanagh, M.B., Rahim R. Rizi, Ph.D.

HCl aspiration
(TV 12 ml/kg)

1 h 2 h 3 h 4 h
A Model of Lung Injury Propagation
Voxel-wise Tracking of Inflation and Injury Progression
Image Registration

End-Inspiratory (EI)  
End-Expiratory (EE)  
Overlaid EI/EE

End-Inspiratory (EI)  
End-Expiratory (EE)  
Warped (deformed)  
End-Expiratory

Align EE to EI  
3D Image Registration
Tidal changes on CT and progression of ARDS

Maurizio Cereda, Yi Xin, Hooman Hamedani, Giacomo Bellani, Stephen Kadlecak, Justin Clapp, Luca Guerra, Natalie Meeder, Jennia Rajaei, Nicholas J Tustison, James C Gee, Brian P Kavanagh, Rahim R Rizi
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![Graphs showing tidal changes on CT and progression of ARDS](image)

- **Severe Injury**
- **Normal Lung**
- **‘High Risk’ Unstable Inflation**

*Thorax 2017*
Tidal changes on CT and progression of ARDS

Maurizio Cereda,¹ Yi Xin,² Hooman Hamedani,² Giacomo Bellani,³ Stephen Kadlecak,² Justin Clapp,¹ Luca Guerra,⁴ Natalie Meeder,¹ Jennia Rajaei,² Nicholas J Tustison,⁵ James C Gee,² Brian P Kavanagh,⁶,⁷ Rahim R Rizi²

Thorax 2017
Unstable Inflation and ARDS Mortality

Thorax 2017
Unstable Inflation Causing Injury
Insight from Prone Position and Paired Computed Tomography Scans

Yi Xin¹*, Maurizio Cereda²*, Hooman Hamedani¹, Mehrdad Pourfathi¹, Sarmad Siddiqui¹, Natalie Meeder², Stephen Kadlecik¹, Ian Duncan¹, Harrilla Profka¹, Jennia Rajaei³, Nicholas J. Tustison⁴, James C. Gee¹, Brian P. Kavanagh⁵,⁶, and Rahim R. Rizi¹

AJRCCM 2018
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AJRCCM 2018
Progression of Lung Injury in Ventilated Pigs

2 hours

26 hours
Conclusions

• Heterogeneity of the ARDS population is a major obstacle to progress in treatment

• The way we understand ARDS and ventilate patients is heavily influenced by lung imaging

• Small-scale heterogeneity and instability of lung inflation may promote ARDS progression

• Imaging research may provide the tools to predict outcomes and guide therapy
• In an autopsy study in patients meeting Berlin ARDS criteria, the fraction of patients who also had disseminated alveolar damage (DAD) was:
  – 90%
  – 45%
  – 25%
• A diffuse vs. focal pattern of CT infiltrates in ARDS is associated with the following:
  – Alveolar recruitment by positive pressure
  – Serum markers of epithelial injury
  – Worse mortality
  – All of the above
• PET imaging studies in human ARDS showed high metabolic activity in ventilated lung tissue.
  – True
  – False
## Acknowledgements

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Lung Injury Propagation in a Large Animal Model
Unstable Recruitment and Atelectrauma

INSPIRATION

EXPIRATION