Can we Still Justify and Open Lung Approach?

Alexandre Biasi Cavalcanti
Director - HCor Research Institute – São Paulo
HCor ICU
BRICNet – Brazilian Intensive Care Network
Conflicts of Interest Declaration

My institution receives support for clinical trials from Baxter (donation of IV fluids), Fisher & Paykel (equipment and supplies) and Bactiguard (funding and catheters).
Background

- Functional lung size is decreased in ARDS
- VILI – overdistention and atelectrauma
Open Lung Approach – use of transiently high transpulmonary pressures to reopen lung units followed by sufficient PEEP to maintain them opened
Reversibility of Lung Collapse and Hypoxemia in Early ARDS

Mean: 13±11%
## Background

### 1.6.2 Lower Risk of Bias

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>ARM Events</th>
<th>Control Events</th>
<th>Risk Ratio M-H, Random, 95% CI Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meade 2008</td>
<td>173</td>
<td>475</td>
<td>0.90 [0.77, 1.06] 2008</td>
</tr>
<tr>
<td>Hodgson 2011</td>
<td>3</td>
<td>1</td>
<td>1.50 [0.32, 7.14] 2011</td>
</tr>
<tr>
<td>Kacmarek 2014</td>
<td>29</td>
<td>99</td>
<td>0.85 [0.56, 1.27] 2014</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>584</strong></td>
<td><strong>649</strong></td>
<td>0.90 [0.78, 1.04]</td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td><strong>205</strong></td>
<td><strong>242</strong></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 0.50, df = 2 (P = 0.78); I² = 0%
Test for overall effect: Z = 1.42 (P = 0.16)

### 1.6.3 Higher Risk of Bias

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>ARM Events</th>
<th>Control Events</th>
<th>Risk Ratio M-H, Random, 95% CI Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lim 2003</td>
<td>10</td>
<td>20</td>
<td>0.57 [0.34, 0.95] 2003</td>
</tr>
<tr>
<td>Park 2003</td>
<td>4</td>
<td>11</td>
<td>0.55 [0.21, 1.43] 2003</td>
</tr>
<tr>
<td>Long 2006</td>
<td>5</td>
<td>16</td>
<td>0.55 [0.23, 1.29] 2006</td>
</tr>
<tr>
<td>Wang 2007</td>
<td>6</td>
<td>14</td>
<td>0.66 [0.39, 1.11] 2007</td>
</tr>
<tr>
<td>Huh 2009</td>
<td>14</td>
<td>30</td>
<td>0.84 [0.50, 1.40] 2009</td>
</tr>
<tr>
<td>Xi 2010</td>
<td>23</td>
<td>55</td>
<td>0.74 [0.50, 1.09] 2010</td>
</tr>
<tr>
<td>Liu 2011</td>
<td>14</td>
<td>50</td>
<td>0.82 [0.46, 1.48] 2011</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>196</strong></td>
<td><strong>174</strong></td>
<td>0.72 [0.58, 0.89]</td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td><strong>76</strong></td>
<td><strong>89</strong></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 2.31, df = 6 (P = 0.89); I² = 0%
Test for overall effect: Z = 3.01 (P = 0.003)

**Total (95% CI)** | **780** | **793** | 100.0% | 0.84 [0.74, 0.95] |

**Total events** | **281** | **331** |                     |

Heterogeneity: Tau² = 0.00; Chi² = 5.71, df = 9 (P = 0.77); I² = 0%
Test for overall effect: Z = 2.86 (P = 0.004)
Test for subgroup differences: Chi² = 2.87, df = 1 (P = 0.09), I² = 65.2%

---

Intensive Care Med 2014;40:1227–1240
Flow of patients

2077 Patients assessed for eligibility

- 863 Were ineligible
- 147 Eligible but were not enrolled
- 54 Excluded due to unknown reason

1013 Randomized

- 501 Allocated to receive lung recruitment maneuver and titrated PEEP
  - 480 Received assigned treatment
  - 21 Did not receive lung recruitment
    - 14 Hypotension
    - 3 Pneumothorax
    - 4 Other reasons

- 512 Allocated to the low-PEEP
  - 512 Received assigned treatment

- 0 Were lost to 28-day follow-up

501 Included in primary outcome analysis

509 Included in primary outcome analysis

3 Withdrew consent and were excluded from analysis
Lung recruitment and PEEP titration – after protocol changes

Except for lung RM and titrated PEEP all other MV settings equal between groups
## Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Lung recruitment maneuver with PEEP titration group (n=501)</th>
<th>Low-PEEP group (n=509)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>51.3 ± 17.4</td>
<td>50.6 ± 17.4</td>
</tr>
<tr>
<td>Female sex, %</td>
<td>37.5</td>
<td>37.5</td>
</tr>
<tr>
<td>SAPS3 score</td>
<td>63.5 ± 18.1</td>
<td>62.7 ± 18.1</td>
</tr>
<tr>
<td>No. of non-pulmonary organ failures</td>
<td>2.4 ± 1.2</td>
<td>2.4 ± 1.2</td>
</tr>
<tr>
<td>Septic shock, %</td>
<td>67.1</td>
<td>65.0</td>
</tr>
<tr>
<td>Cause of ARDS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary, %</td>
<td>62.5</td>
<td>61.5</td>
</tr>
<tr>
<td>Extrapulmonary, %</td>
<td>37.5</td>
<td>38.5</td>
</tr>
<tr>
<td>Prone position, %</td>
<td>10.2</td>
<td>9.9</td>
</tr>
<tr>
<td>Time since onset of ARDS</td>
<td>22.5 ± 19.1</td>
<td>22.0 ± 18.6</td>
</tr>
</tbody>
</table>
Primary Outcome:
28-Day Mortality

Hazard ratio, 1.20 (95% CI, 1.01 to 1.42); P=0.041
## Secondary and Exploratory Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Lung Recruitment and Titrated PEEP (n=501)</th>
<th>Low-PEEP (n=509)</th>
<th>Absolute Difference (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumothorax requiring drainage within 7 days, %</td>
<td>3.2</td>
<td>1.2</td>
<td>2.0 (0.0 to 4.0)</td>
<td>0.03</td>
</tr>
<tr>
<td>Barotrauma within 7 days, %</td>
<td>5.6</td>
<td>1.6</td>
<td>4.0 (1.5 to 6.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>No. of ventilator-free days from day 1 to day 28, d</td>
<td>5.3 ± 8.0</td>
<td>6.4 ± 8.6</td>
<td>-1.1 (-2.1 to -0.1)</td>
<td>0.03</td>
</tr>
<tr>
<td>Length of hospital stay, d</td>
<td>25.5 ± 32.3</td>
<td>26.2 ± 31.7</td>
<td>-0.7 (-4.6 to 3.3)</td>
<td>0.74</td>
</tr>
<tr>
<td>Commencement/increase of vasopressors or hypotension within 1 hour, %</td>
<td>34.8</td>
<td>28.3</td>
<td>6.5 (0.5 to 12.4)</td>
<td>0.03</td>
</tr>
</tbody>
</table>
Implementation

• Training
  • Multiprofessional ICU team of all sites trained in loco before enrolling the first patient (except for Malaysia trained with web conference).
  • Training visit repeated when requested by sites

• Investigators’ meetings

• Formal teleconferences 3 times per year

• Whatsapp communication with sites after every patient randomized

• Bedside manual of operations

• Phone line available 24/7 for support
For patients randomized to the:

**ART Group**

<table>
<thead>
<tr>
<th>Patient name</th>
<th>Height</th>
</tr>
</thead>
</table>

Write down the target tidal volume adjusted to the predicted body weight (check Manual of Operations):

**Tidal Volume 6ml/Kg predicted body weight**

Attention: Start with 6ml/kg of predicted body weight, but if plateau pressure >30cmH₂O, reduce the tidal volume.

<table>
<thead>
<tr>
<th>Tidal volume 5ml/Kg of predicted body weight</th>
<th>Tidal volume 4ml/Kg of predicted body weight</th>
</tr>
</thead>
</table>

Mechanical ventilation settings before Maximum Alveolar Recruitment Maneuver:

- Controlled Pressure mode (PCV)
- PEEP of 15cmH₂O
- Respiratory rate of 15/min
- I:E ratio of 1:1 (Inspiratory time = 2 seconds)
- FiO₂ 100%

**Steps for Maximum Alveolar Recruitment Maneuver:**

**Step 1**
- Start with PEEP of 25cmH₂O
  - Peak pressure of 35cmH₂O
- Keep it for 1 minute (15 respiratory cycles)

**Step 2**
- Increase PEEP to 30cmH₂O
  - Peak pressure of 40cmH₂O
- Keep it for 1 minute (15 respiratory cycles)

**Step 3**
- Increase PEEP to 35cmH₂O
  - Peak pressure of 50cmH₂O
- Keep it for 1 minute (15 respiratory cycles)

After completing the maximum alveolar recruitment maneuver, IMMEDIATELY start PEEP titration as described in the section "ART STRATEGY - PEEP TITRATION".

**KEEP PLATEAU PRESSURE ≤ 30 cmH₂O**

**KEEP SpO₂ BETWEEN 90% AND 95%**
Tidal volume

Tidal volume (ml/kg)

Lung recruitment and titrated PEEP

Low-PEEP
Prof Gordon Guyatt
Dr Niall Ferguson
Dr Stephen Walter
STUDY PROTOCOL

Rationale, study design, and analysis plan of the Alveolar Recruitment for ARDS Trial (ART): Study protocol for a randomized controlled trial

The ART Investigators

Abstract

Background: Acute respiratory distress syndrome (ARDS) is associated with high in-hospital mortality. Alveolar recruitment followed by ventilation at optimalpreset PEEP may reduce ventilation-induced lung injury and improve organ function in patients with ARDS, but the effects on mortality and other clinical outcomes remain unknown. This article reports the rationale, study design, and analysis plan of the Alveolar Recruitment for ARDS Trial (ART).

Methods/Design: ART is a pragmatic, multicenter, randomized (concealed), controlled trial, which aims to determine if maximum inspiratory alveolar recruitment associated with PEEP titration is able to increase 28-day survival in patients with ARDS compared to conventional treatment (ART/control strategy). We will enroll adult patients with ARDS of at least 72-hour duration. The intervention group will receive an alveolar recruitment maneuver, with stepwise increases of PEEP achieving 45 cm H\(_2\)O and peak inspiratory pressure of 30 cm H\(_2\)O, followed by ventilation with optimal PEEP titration according to the static compliance of the respiratory system. In the control group, mechanical ventilation will follow a conventional protocol (ARDSNet). In both groups, we will use a controlled volume mode with low tidal volumes (<6 ml/kg of predicted body weight) and targeting p0.5 fraction of inspired oxygen (FIO\(_2\) ≤ 0.5). The primary outcome is 28-day survival, and the secondary outcomes are length of ICU stay (days), length of hospital stay, post-ICU survival, and 6-month survival. ART is an event-guided trial planned to last until 725 events (should within 28 days are observed. These events allow detection of a hazard ratio of 0.75, with 80% power and two-sided alpha of 0.05. All analyses will follow the intention-to-treat principle.

Discussion: If the ART strategy with maximum recruitment and PEEP titration improves 28-day survival, this will represent a notable advance in the care of ARDS patients. Conversely, if the ART strategy is similar or inferior to the current evidence-based strategy (ARDSNet), this should alter current practice as many institutions routinely employ recruitment maneuvers and set PEEP levels according to some trial method.

Trial registrations: ClinicalTrials.gov identifier: NCT013174322

Keywords: Acute respiratory distress syndrome, Alveolar recruitment, PEEP, Mechanical ventilation, Clinical trials, Randomized

Statistical analysis plan for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART): A randomized controlled trial

Plano de análise estatística para o Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART): Ensai controleado randomizado

ABSTRACT

Backgrounds: The Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART) is an international multicenter randomized pragmatic controlled trial with enrollment consent involving 139 new care units in Brazil, Argentina, Colombia, Italy, Poland, Portugal, Malaysia, Spain, and Uruguay. The primary objective of ART is to determine whether maximum inspiratory alveolar recruitment associated with PEEP titration, adjusted according to the static compliance of the respiratory system (ART strategy), is able to increase 28-day survival in patients with acute respiratory distress syndrome compared to conventional treatment (ARDSNet strategy).

Objective: To describe the data management process and statistical analysis plan.

Methods: The statistical analysis plan was designed by the trial executive committee and reviewed and approved by the trial steering committee. We provide an overview of the trial design with a special focus on describing the primary (28-day survival) and secondary outcomes. We describe our data management process, data monitoring, statistical analysis, and sample size calculation. We describe our planned analysis plans for primary and secondary outcomes as well as pre-specified subgroup analysis. We also provide details for presenting results, including stack tables for baseline characteristics, adherence to the protocol and effect on clinical outcomes.

Conclusion: According to best practice, we report our statistical analysis plan and data management plan prior to locking the database and beginning analysis. We anticipate that this document will prevent analysis bias and enhance the utility of the reported results.

Trial registration: ClinicalTrials.gov number: NCT013174322

Keywords: Acute respiratory distress syndrome; Positive-pressure ventilation; Clinically ill

INTRODUCTION

Alveolar collapse with reduction of functional lung zones ("baby lung") is a hallmark of acute respiratory distress syndrome (ARDS).[1] Although mechanical ventilation is needed to support life in patients with moderate-severe ARDS, it may damage lungs via two mechanisms: (1) respiration-induced lung injury (VILI);[2][3] (2) cyclic opening and closing of small airways and alveoli (atelectrauma).[4][5] Mechanical ventilation with low tidal volumes and low positive end-expiratory pressures (PEEP) decreases these but does not eliminate ventilation-induced lung injury (VILI).[6][7] Cyclic opening and closing of lung units worsens this
Why the open lung approach did not help ARDS patients?

- Incomplete physiological basis:
  - Very high PEEP s needed to prevent alveolar cycling
  - Biotrauma with RM

- Initial clinical evidence was unreliable
  - Lung recruitability is low (on average)
  - High risk of bias of clinical trials suggesting beneficial effect on mortality
  - Adverse effects: hemodynamic impact; lung injury

- Best recruitment maneuver?
- Best PEEP titration method?
- Heterogeneity of treatment effects
Does high PEEP prevent alveolar cycling?

Why the open lung approach did not help ARDS patients?

- Incomplete physiological basis:
  - Very high PEEPs needed to prevent alveolar cycling
  - Biotrauma with RM

- Initial clinical evidence was unreliable
  - Lung recruitability is low (on average)
  - High risk of bias of clinical trials suggesting beneficial effect on mortality
  - Adverse effects: hemodynamic impact; lung injury

- Best recruitment maneuver?
- Best PEEP titration method?
- Heterogeneity of treatment effects
Recruitment maneuver leads to increased expression of pro-inflammatory cytokines in acute respiratory distress syndrome

ARDS model in 18 pigs (removal of surfactant with 5% tweens)
Why the open lung approach did not help ARDS patients?

• Incomplete physiological basis:
  • Very high PEEPs needed to prevent alveolar cycling
  • Biotrauma with RM

• Initial clinical evidence was unreliable
  • Lung recruitability is low (on average)
  • High risk of bias of clinical trials suggesting beneficial effect on mortality
  • Adverse effects: hemodynamic impact; lung injury

• Best recruitment maneuver?
• Best PEEP titration method?
• Heterogeneity of treatment effects
Driving Pressure

Low-PEEP

2 cmH2O

Lung recruitment and titrated PEEP
Average Lung Weight, 59±51 g
Average Lung Weight, 374±236 g

Lower

Higher

No. of Patients

Patients with acute lung injury without ARDS
Patients with ARDS

Mean: 13±11%

Amount of Potentially Recruitable Lung (% total lung weight)
Why the open lung approach did not help ARDS patients?

- Incomplete physiological basis:
  - Very high PEEP needed to prevent alveolar cycling
  - Biotrauma with RM

- Initial clinical evidence was unreliable
  - Lung recruitability is low (on average)
  - High risk of bias of clinical trials suggesting beneficial effect on mortality
  - Adverse effects: hemodynamic impact; lung injury

- Best recruitment maneuver?
- Best PEEP titration method?
- Heterogeneity of treatment effects
PHARLAP - Maximal Recruitment Open Lung Ventilation in Acute Respiratory Distress Syndrome: A Phase II, Multicenter, Randomized, Controlled Trial

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Intervention Group</th>
<th>Control Group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total No.</strong></td>
<td>No. (%)</td>
<td>No. (%)</td>
<td></td>
</tr>
<tr>
<td>Primary outcome:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VFDs to day 28, median (IQR), days</td>
<td>57</td>
<td>56</td>
<td>0.95</td>
</tr>
<tr>
<td>Death in ICU</td>
<td>57</td>
<td>56</td>
<td>0.79</td>
</tr>
<tr>
<td>Death in hospital</td>
<td>57</td>
<td>56</td>
<td>0.49</td>
</tr>
<tr>
<td>Mortality at day 28</td>
<td>57</td>
<td>56</td>
<td>0.79</td>
</tr>
<tr>
<td>Mortality at day 90</td>
<td>57</td>
<td>56</td>
<td>0.49</td>
</tr>
<tr>
<td>Mortality at 6 months</td>
<td>57</td>
<td>56</td>
<td>0.49</td>
</tr>
<tr>
<td>Ventilation duration, median (IQR), hours</td>
<td>57</td>
<td>56</td>
<td>0.41</td>
</tr>
<tr>
<td>ICU length of stay, median (IQR), days</td>
<td>57</td>
<td>56</td>
<td>0.69</td>
</tr>
<tr>
<td>Hospital length of stay, median (IQR), days</td>
<td>57</td>
<td>56</td>
<td>0.8</td>
</tr>
<tr>
<td><strong>Safety outcomes – Days 1 to 28</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New cardiac arrhythmia®</td>
<td>58</td>
<td>56</td>
<td>0.03</td>
</tr>
<tr>
<td>Bradycardia (&lt;40bpm)®</td>
<td>58</td>
<td>56</td>
<td>0.99</td>
</tr>
<tr>
<td>Severe hypotension</td>
<td>58</td>
<td>56</td>
<td>0.12</td>
</tr>
<tr>
<td>New inhaled nitric oxide cases</td>
<td>58</td>
<td>56</td>
<td>0.03</td>
</tr>
<tr>
<td>New prone positioning cases</td>
<td>58</td>
<td>56</td>
<td>0.02</td>
</tr>
<tr>
<td>New ECMO cases</td>
<td>58</td>
<td>56</td>
<td>0.03</td>
</tr>
<tr>
<td>New neuromuscular blocking drugs</td>
<td>58</td>
<td>56</td>
<td>0.47</td>
</tr>
<tr>
<td>Refractory acidosis</td>
<td>58</td>
<td>56</td>
<td>0.16</td>
</tr>
<tr>
<td>Barotrauma</td>
<td>58</td>
<td>56</td>
<td>0.32</td>
</tr>
<tr>
<td>Pneumothorax requiring a chest drain</td>
<td>58</td>
<td>56</td>
<td>0.99</td>
</tr>
<tr>
<td><strong>Exploratory outcomes,</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumothorax requiring drainage ≤7 days</td>
<td>58</td>
<td>56</td>
<td>0.99</td>
</tr>
<tr>
<td>Barotrauma ≤7 days</td>
<td>58</td>
<td>56</td>
<td>0.99</td>
</tr>
</tbody>
</table>

N = 113
Why the open lung approach did not help ARDS patients?

• Incomplete physiological basis:
  • Very high PEEPs needed to prevent alveolar cycling
  • Biotrauma with RM

• Initial clinical evidence was unreliable
  • Lung recruitability is low (on average)
  • High risk of bias of clinical trials suggesting beneficial effect on mortality
    • Adverse effects: hemodynamic impact; lung injury

• Best recruitment maneuver?
• Best PEEP titration method?
• Heterogeneity of treatment effects
Why the open lung approach did not help ARDS patients?

- Incomplete physiological basis:
  - Very high PEEPs needed to prevent alveolar cycling
  - Biotrauma with RM

- Initial clinical evidence was unreliable
  - Lung recruitability is low (on average)
  - High risk of bias of clinical trials suggesting beneficial effect on mortality
  - Adverse effects: hemodynamic impact; lung injury

- Best recruitment maneuver?
- Best PEEP titration method?
- Heterogeneity of treatment effects
How to titrate PEEP?

• Oxygenation goals
  – PEEP and FiO\textsubscript{2} table: ARDNet low and high, LOVS
  – Best SpO\textsubscript{2}: PHARLAP

• Mechanics
  – Plateau pressure: EXPRESS
  – Best static compliance: ART, OLA
  – Zero to positive transpulmonary end-expiratory pressure: EPVENT

• CT

• Electrical impedance tomography
EPVent - 2

![Graph showing survival probability over time with comparisons between P_{ES}-guided PEEP, Empirical PEEP, and PEEP-Fio_{2}](image-url)

Log-rank P = .90
Why the open lung approach did not help ARDS patients?

• Incomplete physiological basis:
  • Very high PEEPs needed to prevent alveolar cycling
  • Biotrauma with RM

• Initial clinical evidence was unreliable
  • Lung recruitability is low (on average)
  • High risk of bias of clinical trials suggesting beneficial effect on mortality
  • Adverse effects: hemodynamic impact; lung injury

• Best recruitment maneuver?
  • Heterogeneity of treatment effects
Comparison of the Berlin Definition for Acute Respiratory Distress Syndrome with Autopsy

Total = 45% DAD

- Pneumonia (n = 97, 49%)
- Pulmonary abscess (n = 6, 3%)
- Tuberculosis (n = 3, 1.5%)
- Cancer infiltration (n = 11, 5.5%)
- Pulmonary embolism (n = 9, 4.5%)
- Acute pulmonary edema (n = 9, 4.5%)
- Pulmonary hemorrhage (n = 12, 6%)
- Interstitial pneumonia/fibrosis (n = 9, 4.5%)
- Severe emphysema (n = 14, 7%)

Thille et al. Am J Respir Crit Care Med 2013;187:761–767
Heterogeneous effects of alveolar recruitment in acute respiratory distress syndrome: a machine learning reanalysis of the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patient characteristics identified by unsupervised cluster analysis. Data are presented as mean (standard deviation) or n (%).</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cluster 1</td>
</tr>
<tr>
<td>Number of patients</td>
<td>475</td>
</tr>
<tr>
<td>Vasopressor use at admission, n (%)</td>
<td>475 (100.0)</td>
</tr>
<tr>
<td>ARDS cause, n (%)</td>
<td></td>
</tr>
<tr>
<td>Unspecified shock</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Gastric aspiration</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Sepsis, not pulmonary</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>475 (100.0)</td>
</tr>
<tr>
<td>Orthopaedic surgery</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Abdominal surgery</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Cardiac surgery</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Aortic surgery</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Traumatic brain injury</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Smoke inhalation</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Near drowning</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Lung contusion</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Trauma</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Multiple transfusions</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Drug overdose</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Barotrauma, n (%)</td>
<td>22 (4.6)</td>
</tr>
<tr>
<td>Pneumothorax, n (%)</td>
<td>12 (2.5)</td>
</tr>
<tr>
<td>Mortality, n (%)</td>
<td>280 (58.9)</td>
</tr>
</tbody>
</table>

Heterogeneous effects of alveolar recruitment in acute respiratory distress syndrome: a machine learning reanalysis of the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial

ARDS is heterogeneous and so are treatment effects!

Personalised mechanical ventilation tailored to lung morphology versus low PEEP for patients with ARDS (the LIVE study): a multicentre, single-blind, RCT

Moderate-to-severe ARDS for less than 12 h

Focal ARDS: $V_t = 8\text{mL/kg PBW}$ and low PEEP; Prone position encouraged

Diffuse ARDS: $V_t=6\text{mL PBW}$, recruitment maneuvers (CPAP 35cmH$_2$O or sigh) and high PEEP (to reach $P_{plat}$ 30cmH$_2$O)

$V_t = 6\text{mL/kg PBW}$ and low PEEP (ARDSNet); Prone position encouraged
Personalised mechanical ventilation tailored to lung morphology versus low PEEP for patients with ARDS (the LIVE study): a multicentre, single-blind, RCT
Personalised mechanical ventilation tailored to lung morphology versus low PEEP for patients with ARDS (the LIVE study): a multicentre, single-blind, RCT

OLA:
Non-focal ARDS: HR 0.63; 0.39–1.02; p=0.06
Focal ARDS: HR 3.45; 1.4–8.5; p=0.02
Conclusions

• The effect of open lung approaches (OLA) on clinical outcomes is heterogeneous.

• OLA do not improve mortality and may cause harm, particularly to patients with focal ARDS

• RM plus titrated PEEP should not be used routinely in patients with moderate to severe ARDS
  – RM may be useful for patients with refractory hypoxemia

• There is still room for research assessing the effect of OLA on subphenotypes of ARDS (e.g. non-focal)
Alexandre Biasi Cavalcanti

abiasi@hcor.com.br