ECCO$_2$R for ARDS Patients

Alain Combes, MD, PhD
Cardiology Institute, Hôpital Pitié-Salpêtrière, AP-HP
Inserm UMRS 1166, iCAN, Institute of Cardiometabolism and Nutrition
Sorbonne Pierre et Marie Curie University, Paris, France

www.paris-tcsecmo.org
alain.combes@aphp.fr
Conflict of interest

• Principal Investigator: EOLIA trial
  • VV ECMO in ARDS
  • NCT01470703
  • Sponsored by MAQUET, Getinge Group

• Received honoraria from
  • MAQUET, XENIOS, GAMBRO, ALUNG
The rationale...
For ARDS patients...
The goods and the bads of MV in patients with ARDS…

• **MV harms the respiratory system**
  - Ventilator-Induced Lung Injury
    - *Pressure*
    - *Volume*
    - *Resp Rate*
  - Inactivity of the diaphragm

• **MV promotes VAP**

• **MV requires patients sedation/paralysis**
Changes in the ultrastructural appearance of the alveolar-capillary barrier after MV

Detachment of the thin part of the endothelial cell from the basement membrane

Diffuse alveolar damage resulting from very severe changes in the alveolar-capillary barrier

Rat model
MV at 45 cm H₂O peak airway pressure

The ARDS Network trial – MV with lower versus traditional tidal volumes

Randomised controlled trial in patients with acute lung injury (n = 861)

PBW, predicted body weight; $V_T$, tidal volume

Probability of survival

- Lower $V_T$ (6 mL/kg PBW)
- Traditional $V_T$ (12 mL/kg PBW)

Mortality rate 31.0%
Mortality rate 39.8%
p = 0.007

Lung protective MV and two-year survival in patients with ALI

Adjusted HR of 1.18 (95% CI 1.07–1.31) indicated an 18% relative increase in mortality for each 1 mL/kg predicted body weight.


p-value shown for non-linear terms in cubic spline model
Prospective cohort study (n = 485)
ALI, acute lung injury
Hyperrinflation 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

Am J Respir Crit Care Med 2007;175:160-166.
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

Am J Respir Crit Care Med 2007;175:160-166.

Relationship between amount of tidal hyperinflation and plateau pressure

Relationship between amount of tidal hyperinflation and plateau pressure

Hyperinflation
Overdistension

R² = 0.795
p = 0.001

Tidal hyperinflation (% total tidal inflation-related change in CT lung volume)

Pplat (cm H₂O)

More protected (n = 20)
Less protected (n = 10)
Relationship between mortality and Day 1 plateau pressure

Robust locally weighted regression and smoothing (Lowess) plot (bandwidth, 0.4) of mortality and Day 1 plateau pressure among patients enrolled in the ARDS Network study (n = 787)


Bivariate regression analysis: Lower $V_T$ strategy was associated with lower mortality vs higher $V_T$ strategy ($p = 0.02$)
Driving Pressure and Survival in the Acute Respiratory Distress Syndrome
Probability of hospital survival by driving pressure

Driving pressure, cm H₂O
- ≤14
- >14

Log-rank P = .02
Potentially modifiable factors contributing to outcome from acute respiratory distress syndrome: the LUNG SAFE study

Laffey, Intensive Care Med 2016
Targeting Resp Rate?...
Factors associated with hospital mortality in invasively ventilated patients \((n = 2377)\)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Multivariate model ((n = 2091))</th>
<th>(p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95 % CI)</td>
<td></td>
</tr>
<tr>
<td><strong>Demographic factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.03 (1.019–1.032)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Risk factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active neoplasm</td>
<td>1.83 (1.31–2.57)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>1.42 (1.04–1.93)</td>
<td>0.027</td>
</tr>
<tr>
<td><strong>Hematologic neoplasm</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (ref. no)</td>
<td>4.77 (2.82–8.04)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Chronic liver failure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (ref. no)</td>
<td>3.28 (1.99–5.40)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Illness severity factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(pH)</td>
<td>0.12 (0.05–0.29)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(\text{PaO}_2/\text{FiO}_2) ratio (mmHg)</td>
<td>0.998 (0.997–1.000)</td>
<td>0.025</td>
</tr>
<tr>
<td>Non-pulmonary SOFA score adjusted</td>
<td>1.12 (1.09–1.15)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Management factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RR total (breaths/min)</td>
<td>1.03 (1.01–1.04)</td>
<td>0.003</td>
</tr>
<tr>
<td>PEEP (cm(H_2)O)</td>
<td>0.95 (0.92–0.98)</td>
<td>0.001</td>
</tr>
<tr>
<td>Peak inspiratory pressure (cm(H_2)O)</td>
<td>1.02 (1.01–1.04)</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>ICU organizational factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of beds</td>
<td>0.99 (0.99–1.00)</td>
<td>0.035</td>
</tr>
</tbody>
</table>
Low Respiratory Rate Plus Minimally Invasive Extracorporeal CO₂ Removal Decreases Systemic and Pulmonary Inflammatory Mediators in Experimental Acute Respiratory Distress Syndrome

Grasso, Crit Care Med, 2014

Objective: The Acute Respiratory Distress Syndrome Network protocol recommends limiting tidal volume and plateau pressure; it also recommends increasing respiratory rate to prevent hypercapnia. We tested a strategy that combines the low tidal volume with lower respiratory rates and minimally invasive CO₂ removal.

Subjects: Ten lung-damaged pigs (instilled hydrochloride).

Interventions: Two conditions randomly applied in a crossover fashion: the Acute Respiratory Distress Syndrome Network protocol and the Acute Respiratory Distress Syndrome Network protocol plus lower respiratory rate plus minimally invasive CO₂ removal. A similar arterial CO₂ partial pressure was targeted in the two conditions.
Low Respiratory Rate Plus Minimally Invasive Extracorporeal CO₂ Removal Decreases Systemic and Pulmonary Inflammatory Mediators in Experimental Acute Respiratory Distress Syndrome

Grasso, Crit Care Med, 2014

<table>
<thead>
<tr>
<th>Variable</th>
<th>ARDS Net</th>
<th>Low RR ECCO₂R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tidal volume (mL)</td>
<td>345±79</td>
<td>342±73</td>
</tr>
<tr>
<td>Respiratory rate (breaths/min)</td>
<td>30.5±3.8</td>
<td>14.2±3.5*</td>
</tr>
<tr>
<td>Minute volume (L/min)</td>
<td>10.4±1.6</td>
<td>4.9±1.7*</td>
</tr>
<tr>
<td>Inspiratory time (s)</td>
<td>0.68±0.1</td>
<td>1.53±0.5*</td>
</tr>
<tr>
<td>Inspiratory flow (mL/s)</td>
<td>509±97</td>
<td>243±83*</td>
</tr>
<tr>
<td>$P_{A\theta,PLAT}$ (cm H₂O)</td>
<td>23.3±3.6</td>
<td>23.2±3.2</td>
</tr>
<tr>
<td>$P_{A\theta,MEAN}$ (cm H₂O)</td>
<td>15.4±3.3</td>
<td>14.8±2.7</td>
</tr>
<tr>
<td>Total positive end-expiratory pressure (cm H₂O)</td>
<td>10.5±2.9</td>
<td>10.4±2.6</td>
</tr>
<tr>
<td>Stress index</td>
<td>1.034±0.023</td>
<td>1.028±0.026</td>
</tr>
<tr>
<td>Static respiratory system elastance (cm H₂O/L)</td>
<td>41.6±10.6</td>
<td>38.9±11.7</td>
</tr>
<tr>
<td>Static lung elastance (cm H₂O/L)</td>
<td>34.3±10.9</td>
<td>31.9±11.7</td>
</tr>
<tr>
<td>Static chest wall elastance (cm H₂O/L)</td>
<td>7.5±2.1</td>
<td>6.9±2.8</td>
</tr>
<tr>
<td>$P_{A\theta}/Fio₂$ (cm H₂O/L)</td>
<td>252±75</td>
<td>231±86</td>
</tr>
<tr>
<td>$P_{A\theta}$ (mm Hg)</td>
<td>61.8±11.6</td>
<td>61.9±9.7</td>
</tr>
<tr>
<td>pH</td>
<td>7.381±0.041</td>
<td>7.375±0.054</td>
</tr>
<tr>
<td>Base excess</td>
<td>4.5±1.5</td>
<td>4.8±1.9</td>
</tr>
</tbody>
</table>
Low Respiratory Rate Plus Minimally Invasive Extracorporeal CO₂ Removal Decreases Systemic and Pulmonary Inflammatory Mediators in Experimental Acute Respiratory Distress Syndrome

Grasso, Crit Care Med, 2014

Less pro-inflammatory Cytokines in Blood and BAL with Low RR
The evolving paradigm...

• ARDSnet strategy might not protect against tidal hyperinflation
  • When Pplat remains >28-30 cm H₂O

• Further decrease of Vt to reduce VILI
  • From 6 to 5, 4 or 3 ml/kg IBW
  • To decrease Pplat <25 cm H₂O
  • With sufficient PEEP to prevent lung derecruitment
  • Resulting in a significant **decrease in ΔP**

• Induced Hypercapnia controlled by ECCO₂ removal
  • “CO₂ dialysis”
  • Low-flow devices
Trials of ECCO2R for ARDS Patients
Randomised clinical trial of pressure-controlled inverse ratio ventilation and ECCO$_2$R for ARDS

**Study design**
- Randomised controlled clinical trial
- 40 patients with severe ARDS
- ECCO$_2$R versus MV
  - Low-flow veno-venous ECCO$_2$R$_2$ device

**Results**
- No significant difference in survival at 30 days ($p = 0.08$):
  - 42% in the MV group ($n = 19$)
  - 33% in the ECCO$_2$R patients ($n = 21$)
  - All deaths occurred within 30 days of randomization
- Study stopped for futility
- $>30\%$ patients with severe haemorrhage

Lower tidal volume strategy (≈ 3 ml/kg) combined with extracorporeal CO₂ removal versus ‘conventional’ protective ventilation (6 ml/kg) in severe ARDS

The prospective randomized Xtravent-study
Novalung, ILA pumpless AV shunt
Lower tidal volume strategy ($\approx 3$ ml/kg) combined with extracorporeal CO$_2$ removal versus ‘conventional’ protective ventilation (6 ml/kg) in severe ARDS

The prospective randomized Xtravent-study

- Screening $\rightarrow$ 305 patients: acute respiratory failure $\text{PaO}_2/\text{FI}O_2 \leq 200$

  - Stabilization over 24 hrs:
    - $V_T$ 6 ml/kg/IBW
    - ARDSNet „high-PEEP“
    - CVP 10 – 16 mmHg
    - MAP $\geq$ 70 mmHg
    - echocardiography

  - 103 patients: no inclusion criteria fulfilled

  - 64 patients: no inclusion due to improvement $\text{PaO}_2/\text{FI}O_2 > 200$

  - 50 patients: no inclusion due to deterioration $\text{PaO}_2/\text{FI}O_2 < 70 \rightarrow$ vvECMO

  - 4 patients: no inclusion due to death

  - 5 patients: no informed consent

- Randomization $\rightarrow$ 79 patients

  - 40 patients $\rightarrow$ avECCO$_2$-R
    - $V_T$ 3 ml/kg/IBW
    - ARDSNet „high-PEEP“

  - Ventilation target:
    - $\text{PaO}_2 \geq 60$ mmHg
    - art. pH $\geq 7.2$

  - 39 patients $\rightarrow$ control
    - $V_T$ 6 ml/kg/IBW
    - ARDSNet „high-PEEP“
Lower tidal volume strategy (≈ 3 ml/kg) combined with extracorporeal CO₂ removal versus ‘conventional’ protective ventilation (6 ml/kg) in severe ARDS

The prospective randomized Xtravent-study

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>avECCO₂-R</td>
</tr>
<tr>
<td>Ventilator-free-days-28</td>
<td>10.0 ± 8</td>
</tr>
<tr>
<td>Ventilator-free-days-60</td>
<td>33.2 ± 20</td>
</tr>
<tr>
<td>Non-pulmonary organ failure free days-60</td>
<td>21.0 ± 14</td>
</tr>
<tr>
<td>Lung injury score on day 10</td>
<td>2.2 ± 0.6</td>
</tr>
<tr>
<td>Length of stay in hospital (days)</td>
<td>46.7 ± 33</td>
</tr>
<tr>
<td>Length of stay in ICU (days)</td>
<td>31.3 ± 23</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>7/40 (17.5 %)</td>
</tr>
</tbody>
</table>

Thomas Bein
Steffen Weber-Carstens
Anton Goldmann

Intensive Care Med
Lower tidal volume strategy (≈ 3 ml/kg) combined with extracorporeal CO₂ removal versus ‘conventional’ protective ventilation (6 ml/kg) in severe ARDS

The prospective randomized Xtravent-study

<table>
<thead>
<tr>
<th>Subgroup: PaO₂/FIO₂ &lt;150</th>
<th>avECCO₂-R</th>
<th>Control</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilator-free-days-28</td>
<td>11.3 ± 7.5</td>
<td>5.0 ± 6.3</td>
<td>0.033</td>
</tr>
<tr>
<td>Ventilator-free-days-60</td>
<td>40.9 ± 12.8</td>
<td>28.2 ± 16.4</td>
<td>0.033</td>
</tr>
<tr>
<td>Non-pulmonary organ failure free days-60</td>
<td>24.1 ± 7.5</td>
<td>29.0 ± 17.7</td>
<td>0.428</td>
</tr>
<tr>
<td>Lung injury score on day 10</td>
<td>2.3 ± 0.8</td>
<td>2.2 ± 0.5</td>
<td>0.601</td>
</tr>
<tr>
<td>Length of stay in hospital (days)</td>
<td>42.0 ± 16.6</td>
<td>40.3 ± 15.7</td>
<td>0.815</td>
</tr>
<tr>
<td>Length of stay in ICU (days)</td>
<td>25.9 ± 13.1</td>
<td>31.0 ± 12.7</td>
<td>0.258</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>1/21 (4.8 %)</td>
<td>1/10 (10 %)</td>
<td>0.563</td>
</tr>
</tbody>
</table>
Hemodec DECAP
Tidal Volume Lower than 6 ml/kg Enhances Lung Protection

Role of Extracorporeal Carbon Dioxide Removal

Anesthesiology 2009; 111:826-35

Pier Paolo Terragni, M.D.,* Lorenzo Del Sorbo, M.D.,† Luciana Mascia, M.D., Ph.D.,* Rosario Urbino, M.D.,* Erica L. Martin, Ph.D.,* Alberto Birocco, M.D.,† Chiara Faggiano, M.D.,† Michael Quintel, M.D.,† Luciano Gattinoni, M.D.,§ V. Marco Ranieri, M.D.,∥

**DIAGNOSIS of ARDS**
*"ARDSNet" strategy for 72 hrs*

N = 32

- 25 < P_{PLAT} < 28 cmH$_2$O
  - N = 22
  - BAL and CT scan

- 28 ≤ P_{PLAT} ≤ 30 cmH$_2$O
  - N = 10
  - BAL and CT scan

**LOWER "ARDSNet"/CARBON DIOXIDE REMOVAL:**

- "ARDSNet" strategy for 72 hrs
  - N = 22

- BAL (N=15) and CT scan (N=12)

- BAL and CT scan
  - N=10

- Reduce V$_t$ to achieve 25<P_{PLAT}<28 cmH$_2$O
- PEEP-Fio$_2$ combination set according to the higher PEEP arm of the ALVEOLI study
- Increase respiratory rate up to 40 b/min
- Bicarbonate infusion up to 20 mEq/h

If pH < 7.25 apply CARBON DIOXIDE REMOVAL for at least 72 hrs
- N = 10
Tidal Volume Lower than 6 ml/kg Enhances Lung Protection

Role of Extracorporeal Carbon Dioxide Removal

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Erica L. Martin, Ph.D.,* Alberto Birocco, M.D.,† Chiara Faggiano, M.D.,† Michael Quintel, M.D.,‡ Luciano Gattinoni, M.D.,§
V. Marco Ranieri, M.D.||

Individual and average (horizontal bar) respiratory variables before and after initiating CO₂ removal

- $V_T$ (mL/kg PBW)
- $P_{plat}$ (cm H₂O)
- PEEP (cm H₂O)
- $\text{PaO}_2 / \text{FiO}_2$
Tidal Volume Lower than 6 ml/kg Enhances Lung Protection

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V. Marco Ranieri, M.D.||

Table 4. Total Number of Mechanical Complications Occurring during the 144 (84, 168)* Hours of Treatment

<table>
<thead>
<tr>
<th>Frequency (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pump malfunction</td>
</tr>
<tr>
<td>Membrane lung/hemofilter clotting</td>
</tr>
<tr>
<td>Catheter displacement</td>
</tr>
<tr>
<td>Cannula problems, i.e. need for two cannulas instead of a single double-lumen</td>
</tr>
</tbody>
</table>
Techniques of the 2010’s...
iLA ACTIVVE®

**iLA activve® Console**

**iLA Membrane Ventilator®**

**iLA activve® Pump / Mini-console**

Trolley

NOVALUNG

La Pitié Paris Cardiology Institute  alain.combes@aphp.fr  www.paris-tcsecmo.org
A novel pump-driven veno-venous gas exchange system during extracorporeal CO₂-removal


- iLA activve, Novalung, ILA membrane
- 22 French double lumen cannula
- Ten patients hypercapnic respiratory failure
- Step 1:
  - Sweep gas flow increased from 1 to 14 L/min
  - At constant blood flow
- Step 2:
  - Blood flow gradually increased at constant sweep gas flow
- At each step measurement of
  - Arterial blood gas AND
  - Membrane gas transfer
A novel pump-driven veno-venous gas exchange system during extracorporeal CO₂-removal

A novel pump-driven veno-venous gas exchange system during extracorporeal CO₂-removal

Respiratory dialysis: Reduction in dependence on mechanical ventilation by venovenous extracorporeal CO₂ removal*

Andriy I. Batchinsky, MD; Bryan S. Jordan, RN, MSN; Dara Regn, MD; Corina Necsoiu, MD; William J. Federspiel, PhD; Michael J. Morris, MD; Leopoldo C. Cancio, MD

Crit Care Med 2011; 39:1382–1387

Hemolung, Alung Technologies
Feasibility and safety of low-flow extracorporeal carbon dioxide removal to facilitate ultra-protective ventilation in patients with moderate ARDS

Vito Fanelli1*, Marco V. Ranieri2, Jordi Mancebo3, Onnen Moerer4, Michael Quintel4, Scott Morley5, Indalecio Moran3, Francisco Parrilla3, Andrea Costamagna1, Marco Gaudiosi1 and Alain Combes6

Critical Care (2016) 20:36

Methods: In fifteen patients with moderate ARDS, VT was reduced from baseline to 4 mL/kg PBW while PEEP was increased to target a plateau pressure – (Pplat) between 23 and 25 cmH2O. Low-flow ECCO2R was initiated when respiratory acidosis developed (pH < 7.25, PaCO2 > 60 mmHg). Ventilation parameters (VT, respiratory rate, PEEP), respiratory compliance (CRS), driving pressure (DeltaP = VT/CRS), arterial blood gases, and ECCO2R system operational characteristics were collected during the period of ultra-protective ventilation. Patients were weaned from ECCO2R when PaO2/FiO2 was higher than 200 and could tolerate conventional ventilation settings. Complications, mortality at day 28, need for prone positioning and extracorporeal membrane oxygenation, and data on weaning from both MV and ECCO2R were also collected.

Table 2 Time course of ventilation variables during the run-in phase

<table>
<thead>
<tr>
<th>Variables</th>
<th>Baseline</th>
<th>VT 5 mL/kg</th>
<th>VT 4.5 mL/kg</th>
<th>VT 4 mL/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>VT (mL/kg)</td>
<td>6.2 ± 0.7</td>
<td>5.02 ± 0.1*</td>
<td>4.48 ± 0.1*</td>
<td>3.96 ± 0.1*</td>
</tr>
<tr>
<td>Respiratory rate (beats/minute)</td>
<td>28 ± 7</td>
<td>29 ± 4</td>
<td>30 ± 4*</td>
<td>30 ± 5*</td>
</tr>
<tr>
<td>Positive end-expiratory pressure (cmH2O)</td>
<td>12 ± 3</td>
<td>13.8 ± 3</td>
<td>13.6 ± 4</td>
<td>13.0 ± 4</td>
</tr>
<tr>
<td>Plateau pressure (cmH2O)</td>
<td>27.7 ± 1.6</td>
<td>25.2 ± 1.6*</td>
<td>23.6 ± 1.3*</td>
<td>22.7 ± 1.8*</td>
</tr>
<tr>
<td>Patients who reached the pH threshold for ECCO2R, n</td>
<td>0</td>
<td>2</td>
<td>15</td>
<td></td>
</tr>
</tbody>
</table>
Feasibility and safety of low-flow extracorporeal carbon dioxide removal to facilitate ultra-protective ventilation in patients with moderate ARDS

Vito Fanelli¹, Marco V. Ranieri², Jordi Mancebo³, Onnen Moerler⁴, Michael Quintel⁴, Scott Morley⁵, Indalecio Moran³, Francisco Parrilla³, Andrea Costamagna¹, Marco Gaudiosi¹ and Alain Combes⁶

Critical Care (2016) 20:36

Time course of $C_{RS}$

Time course of driving pressure
Feasibility and safety of low-flow extracorporeal carbon dioxide removal to facilitate ultra-protective ventilation in patients with moderate ARDS

Results: During the 2 h run in phase, $V_T$ reduction from baseline (6.2 mL/kg PBW) to approximately 4 mL/kg PBW caused respiratory acidosis (pH < 7.25) in all fifteen patients. At steady state, ECCO$_2$R with an average blood flow of 435 mL/min and sweep gas flow of 10 L/min was effective at correcting pH and PaCO$_2$ to within 10% of baseline values. PEEP values tended to increase at $V_T$ of 4 mL/kg from 12.2 to 14.5 cmH$_2$O, but this change was not statistically significant. Driving pressure was significantly reduced during the first two days compared to baseline (from 13.9 to 11.6 cmH$_2$O; p < 0.05) and there were no significant differences in the values of respiratory system compliance. Rescue therapies for life threatening hypoxemia such as prone position and ECMO were necessary in four and two patients, respectively. Only two study-related adverse events were observed (intravascular hemolysis and femoral catheter kinking).

Conclusions: The low-flow ECCO$_2$R system safely facilitates a low volume, low pressure ultra-protective mechanical ventilation strategy in patients with moderate ARDS.
PALP, MAQUET®
PrismaLung Baxter, Amplya, Bellco...
Novel CO$_2$ removal device driven by a renal-replacement system without hemofilter. A first step experimental validation

Thomas Godet $^a$, Alain Combes $^b$, Elie Zogheib $^c$, Matthieu Jabaudon $^{a,d}$, Emmanuel Futier $^{a,d}$, Arthur S. Slutsky $^e$, Jean-Michel Constantin $^{a,d,*}$

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**Mean CO$_2$ removal rates at $F_O_2$ 1**

Preclinical study in 5 adult hypercapnic pigs to investigate the performance of the PrismaLung system with different flow rates (blood flow/ sweep gas flow)
More to come...
A new paradigm...
Acute Respiratory Distress Syndrome
The Berlin Definition

The ARDS Definition Taskforce. JAMA 2012;307:2526-2533.
Acute Respiratory Distress Syndrome

The Berlin Definition

Increasing Intensity of Intervention

Mild ARDS
Moderate ARDS
Severe ARDS

0 50 100 150 200 250 300
PaO$_2$/FiO$_2$

Low Tidal Volume Ventilation
Low-Moderate PEEP
Higher PEEP
Prone Positioning
Neuromuscular Blockade
Inhaled NO
ECMO

The ARDS Definition Taskforce. JAMA 2012;307:2526-2533.
“In God we trust; all others must bring data...”

W. Edwards Deming
(1900-1993)
A Strategy of Ultra Protective lung ventilation
With Extracorporeal CO₂ Removal for New-Onset moderate to seVere ARDS

The SUPERNova trial
Pilot trial, RCT

• PILOT trial
  • Feasibility and safety
  • 100 patients
  • 3 devices (MAQUET, NOVALUNG, ALUNG)
  • Start: October 2015
  • ESICM trial group

• RCT
  • Will randomize up to 1500 patients
  • Adaptive design
  • Protocol will be finalized according to the results of the Pilot trial
  • ESICM trial group
Study objectives

• **ECCO$_2$R**
  - PALP, MAQUET; ILA, NOVALUNG; Hemolung, ALung

• To allow **V$_T$/Pplat/ΔP reduction**
  - in patients with moderate ARDS
  - P/F: 200-100 mmHg, with PEEP > 5 cmH$_2$O

• This study will **assess changes in**
  - pH/ PaO$_2$/PaCO$_2$, Respiratory Rate and device CO$_2$ clearance
  - In the first 24 hours of ECCO$_2$R following V$_T$ and plateau pressure reduction
  - In patients with moderate ARDS

• Safety variables will also be analyzed
Conclusion

• ExtraCorporeal CO$_2$ Removal
  • “Respiratory dialysis”
  • Not for refractory hypoxemia: VV-ECMO

• Potential for use for moderate to severe ARDS
  • To allow further reduction of Vt/Pplat/ΔP, to limit VILI,

• Before large diffusion, should be (re)test in large clinical trials…