COVID, ECMO, and lymphopenia: a word of caution

Extracorporeal membrane oxygenation (ECMO) can serve as life-saving rescue therapy for refractory respiratory failure in the setting of acute respiratory distress syndrome, such as that induced by coronavirus disease 2019 (COVID-19). In the study by Yang and colleagues, who compared clinical characteristics and outcomes in patients with severe COVID-19, five (83%) of six patients receiving ECMO died. Although this sample was small, and specific baseline characteristics and disease courses were almost unknown, it raises concerns about potential harms of ECMO therapy for COVID-19.

Lymphocyte count has been associated with increased disease severity in COVID-19. Patients who died from COVID-19 are reported to have had significantly lower lymphocyte counts than survivors. As such, we need to consider the potential compounding immunological insults involved with initiation of an extracorporeal circuit in these patients. During ECMO, substantial decreases in the number and function of some populations of lymphocytes is commonplace. As it might be hypothesized that depletion of lymphocytes could be key to recovery from COVID-19, lymphocyte count should be closely monitored in these patients receiving ECMO.

Ruan and colleagues also showed that interleukin-6 (IL-6) concentrations differed significantly between survivors and non-survivors of COVID-19, with non-survivors having up to 3.2-times higher values. During ECMO, IL-6 concentrations are consistently elevated and inversely correlated with survival in children and adults. Those that survived ECMO were able to normalise their IL-6 concentrations, whereas those that died had persistently elevated values. Moreover, elevated IL-6 concentrations in lung induced by initiation of ECMO have been convincingly shown to be associated with parenchymal damage in animal models of veno-venous ECMO.

While not to discourage the use of ECMO, based on the abovementioned observations, the immunological status of patients should be considered when selecting candidates for ECMO. More reports are needed to understand the potential benefits or harms of extracorporeal life support in severe COVID-19 and future authors should be encouraged to provide more data for this subset of patients. Lastly, clinicians should consider tracking both lymphocyte count and IL-6 during ECMO to monitor patient status and prognosis.

SARS Cov 2: inflammation +++
- IL6 provokes lung injury, ARDS
- Non survivors
  - increased IL6
  - low Lymphocytes

ECMO provokes inflammation
- increase IL6 level
- Parenchymal damage (animal)
- ECMO will make patients worse

G. Lebreton – COVID & ECMO: Paris experience
COVID & ECMO... It will not work!

About Chinese experience...

Letter to the Editor

Poor survival with extracorporeal membrane oxygenation in acute respiratory distress syndrome (ARDS) due to coronavirus disease 2019 (COVID-19): Pooled analysis of early reports

Brandon Michael Henry
Cardiac Intensive Care Unit, The Heart Institute, Cincinnati Children’s Hospital Medical Center, OH, USA

<table>
<thead>
<tr>
<th>Authors</th>
<th>Age (yrs): a</th>
<th># of patients: n = (# ARDS patients)</th>
<th>Conventional ARDS Therapy: n=</th>
<th>Conventional ARDS Therapy Survivors: n (%)</th>
<th>ECMO: n=</th>
<th>ECMO - Survivors: n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ruan Q et al. 2020</td>
<td>Survivors: 67 (15-81) Non-Survivors: 50 (44-81)</td>
<td>150 (62)</td>
<td>55</td>
<td>7 (12.7%)</td>
<td>7</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Wu et al. 2020</td>
<td>51 (43-60)</td>
<td>210 (84)</td>
<td>83</td>
<td>40 (46.2)</td>
<td>1</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Yang X et al. 2020</td>
<td>59.7 (13.3)</td>
<td>52 (35)</td>
<td>29</td>
<td>9 (31.0%)</td>
<td>6</td>
<td>1 (16.6%)</td>
</tr>
<tr>
<td>Zhou F et al. 2020</td>
<td>56.0 (46.0-67.0)</td>
<td>191 (59)</td>
<td>56</td>
<td>9 (16.1%)</td>
<td>3</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Data presented as mean (SD) or median (IQR). ARDS – Acute Respiratory Distress Syndrome.
COVID & ECMO... in Paris

Regional network & Centralization

Expert group

Hotline COVID ECMO
- Indications
- Bed management
- Mobile unit

ECMO Pooling
- Pumps, circuits,…

Continuous follow-up
- Results assessment
- Adjustment of (contra-)indications
- Stock management…

G. Lebreton – COVID & ECMO: Paris experience
COVID & ECMO... in Paris

Indications & network

Prone positionning is mandatory

Strict EOLIA criteria

Contra-indications

- Age > 65yrs
- Severe Comorbidities
- Advanced COPD, cardiac failure, Cirrhosis (Child B/C), home O2...
- Severe immunocompromised status
- Hematological cancer, advanced cancer...
- Cardiac arrest
- Except witnessed, with bystander CPR, low-flow <15 minutes
- MV duration > 10 days
- Multiple organ failure
- Except isolated AKI...
- BMI>35 kg/m2

Lancet Resp Med, 2019

G. Lebreton – COVID & ECMO: Paris experience
COVID & ECMO... *in Paris*

*Regional network & Centralization*

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G. Lebreton – COVID & ECMO: Paris experience
COVID & ECMO... in Paris
Mobile Unit & ECMO implantation

<table>
<thead>
<tr>
<th>VV ECMO</th>
<th>Drainage</th>
<th>Reinjection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoro-jugular</td>
<td>Venous Canula</td>
<td>Arterial canula</td>
</tr>
<tr>
<td></td>
<td>21-23 Fr</td>
<td>19 Fr</td>
</tr>
<tr>
<td>Femoro-femoral</td>
<td>25-29 Fr, 55 cm</td>
<td>Venous Canula Distal reinjection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>19 Fr, 60 cm</td>
</tr>
</tbody>
</table>
COVID & ECMO... in Paris

ECMO Implantations

Paris Area – 21% COVID: ICU
ICU: 1200 beds increased to 2600
15 ECMO centers (CTS centers)

<table>
<thead>
<tr>
<th>Feb 25th – Apr 21st</th>
<th>279 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>20.3%</td>
</tr>
<tr>
<td>Age</td>
<td>51 ± 9.2</td>
</tr>
<tr>
<td>BMI</td>
<td>29.9 ± 4.8</td>
</tr>
<tr>
<td>Mec. Vent.</td>
<td>5.5 [3-7] days</td>
</tr>
<tr>
<td>pH</td>
<td>7.3 [7.26 - 7.36]</td>
</tr>
<tr>
<td>PaO2</td>
<td>61 [55-70]</td>
</tr>
<tr>
<td>PaCO2</td>
<td>60 [50.7-69.7]</td>
</tr>
<tr>
<td>P/F</td>
<td>60 [55.2-69]</td>
</tr>
<tr>
<td>PEEP</td>
<td>12 [10-14]</td>
</tr>
<tr>
<td>Plat P</td>
<td>30 [30-32]</td>
</tr>
<tr>
<td>Vt</td>
<td>400 [360-430]</td>
</tr>
<tr>
<td>RR</td>
<td>30 [28-32]</td>
</tr>
</tbody>
</table>

Courtesy A Combes

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COVID & ECMO... in Paris

Stock management

ECMO shortage

Continuous follow-up

ECMO Pooling
- Pump
- Circuits
- Cannula

Few new pumps
- Companies
- France (little affected regions)...
- Germany/Austria

G. Lebreton – COVID & ECMO: Paris experience
COVID & ECMO... *in Paris*

Regional network & Centralization

**Expert group**

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- Bed management
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**ECMO Pooling**
- *Pumps, circuits,*...

**Continuous follow-up**
- Results assessment
- Adjustment of (contra-)indications
- Stock management...

G. Lebreton – COVID & ECMO: Paris experience
COVID & ECMO... in Paris
Preliminary Results

Still on-going...

Different centers...

... different results

April 21st 2020
Total ECMO 279
On-going: 127 45.5%
Death: 76 27.2%
Weaning: 76 27.2%

Greater Paris
n = 279

ICU #1
n = 45

ICU #2
n = 41

G. Lebreton – COVID & ECMO: Paris experience
COVID: Thromboembolism & coagulopathy

Pulmonary embolism +++

*In one ICU (A. Combes), about 51 patients:*
- 3 PE with cardiogenic shock
- 4 PE under ECMO support !!!
- 1 died before ECMO: autopsy = PE

Sars Cov 2:
- D-dimeres
- FDPs, PT
- Platelets

VV ECMO COVID
- Ratio TCA = 2-2.5
- antiXa = 0.3 UI/mL
- IV Unfractionned Heparin +++

G. Lebreton – COVID & ECMO: Paris experience
COVID & ECMO... in Paris

Take home messages

NOT ALL PATIENTS DIE ON ECMO !!!
Most patients stabilized while on ECMO

SARS Cov 2 & ARDS
- VERY severe lung disease
- Good Anticoagulation is mandatory +++
- Expert centers +++

TOO EARLY TO DRAW ANY CONCLUSIONS
We need time to evaluate our results
- Some patients weaned <10 days of ECMO
- Few patients extubated & ICU discharged
- Others may require weeks of support

Matthias 28 y
ECMO 13 – 30/3
Discharge 20/4

ECMO doesn’t kill patients,
it should even save them...

G. Lebreton – COVID & ECMO: Paris experience