An assessment of aerosolization via membranous oxygenator and coagulopathy in COVID-19

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1. Can COVID-19 cross the membrane of ECMO?

2. What is known about the coagulopathy in COVID-19
Agenda

1. Can COVID-19 cross the membrane of ECMO?

2. What is known about the coagulopathy in COVID-19
Types of artificial membrane

- Porous Membrane:
  - Blood
  - Gas
  - $O_2$
  - $CO_2$

- Composite Membrane:
  - Blood
  - Gas
  - $O_2$
  - $CO_2$

- Asymmetric Membrane:
  - Blood
  - Gas
  - $O_2$
  - $CO_2$

- Homogenous Membrane:
  - Blood
  - Gas
  - $O_2$
  - $CO_2$

Figures provided from MERA
Comparability of diameters

Blood

Gas

O₂

CO₂

0.04~0.10µm

0.06~0.14µm

COVID-19
Permeability of COVID-19

the risk of crossing membrane is lower than respiratory tract with endotracheal tube and mechanical ventilation
What should bear in mind

※ When the membrane become deteriorated along with long ECMO run.


Plasma Leak → Aerosolization
Plasma leak is major risk

COVID-19 might go through the membrane

Wider than COVID-19
Experiences in Japan

Our Hospital –
10-days long-run membrane without plasma leak
(composite membrane, EXCELAN, MERA, Japan)

Other hospital got positive PCR from exhalation port during plasma leak

→Positive

Exhalation port →Negative
Approach on this topic

1. Lower the threshold of changing artificial lung

2. Prevent spread of aerosol from the exhalation port, especially during transport.
Agenda

1. Can COVID-19 cross the membrane of ECMO?

2. What is known about the coagulopathy in COVID-19
# Coagulopathy in COVID-19

## Table 1: Coagulation parameters of NCP patients on admission

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Normal range</th>
<th>Total (n = 183)</th>
<th>Survivors (n = 162)</th>
<th>Non-survivors (n = 21)</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54.1 ± 16.2</td>
<td>52.4 ± 15.6</td>
<td>64.0 ± 20.7</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>98/85</td>
<td>82/80</td>
<td>16/5</td>
<td>.035</td>
<td></td>
</tr>
<tr>
<td>With underlying diseases</td>
<td>75 (41.0%)</td>
<td>63 (38.9%)</td>
<td>12 (57.1%)</td>
<td>.156</td>
<td></td>
</tr>
<tr>
<td>PT (sec)</td>
<td>11.5-14.5</td>
<td>13.7 (13.1-14.6)</td>
<td>13.6 (13.0-14.3)</td>
<td>15.5 (14.4-16.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>APTT (sec)</td>
<td>29.0-42.0</td>
<td>41.6 (36.9-44.5)</td>
<td>41.2 (36.9-44.0)</td>
<td>44.8 (40.2-51.0)</td>
<td>.096</td>
</tr>
<tr>
<td>Fibrinogen (g/L)</td>
<td>2.0-4.0</td>
<td>4.55 (3.66-5.17)</td>
<td>4.51 (3.65-5.09)</td>
<td>5.16 (3.74-5.69)</td>
<td>.149</td>
</tr>
<tr>
<td>D-dimer (µg/mL)</td>
<td>&lt;0.50</td>
<td>0.66 (0.38-1.50)</td>
<td>0.61 (0.35-1.29)</td>
<td>2.12 (0.77-5.27)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>FDP (µg/mL)</td>
<td>&lt;5.0</td>
<td>4.0 (4.0-4.9)</td>
<td>4.0 (4.0-4.3)</td>
<td>7.6 (4.0-23.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>AT (%)</td>
<td>80-120</td>
<td>91 (83-97)</td>
<td>91 (84-97)</td>
<td>84 (78-90)</td>
<td>.096</td>
</tr>
</tbody>
</table>

Abbreviations: APTT, activated partial thromboplastin time; AT, antithrombin activity; FDP, fibrin degradation product; NCP, novel coronavirus pneumonia; PT, prothrombin time (PT).

(J Thromb Haemost. 2020. Feb 19)
COVID-19 could show DIC

71.4% of the non-survivors matched the International Society on Thrombosis and Haemostasis (ISTH) diagnostic criteria
Coagulopathy is associated with the severity

<table>
<thead>
<tr>
<th></th>
<th>All patients (n=41)</th>
<th>ICU care (n=13)</th>
<th>No ICU care (n=28)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet count, x 10^9 per L</td>
<td>164.5 (131.5-263.0)</td>
<td>196.0 (165.0-263.0)</td>
<td>149.0 (131.0-263.0)</td>
<td>0.45</td>
</tr>
<tr>
<td>&lt;100</td>
<td>2/40 (5%)</td>
<td>1/13 (8%)</td>
<td>1/27 (4%)</td>
<td>0.45</td>
</tr>
<tr>
<td>≥100</td>
<td>38/40 (95%)</td>
<td>12/13 (92%)</td>
<td>26/27 (96%)</td>
<td></td>
</tr>
<tr>
<td>Prothrombin time, s</td>
<td>11.1 (10.1-12.4)</td>
<td>12.2 (11.2-13.4)</td>
<td>10.7 (9.8-12.1)</td>
<td>0.012</td>
</tr>
<tr>
<td>Activated partial thromboplastin time, s</td>
<td>27.0 (24.2-34.1)</td>
<td>26.2 (22.5-33.9)</td>
<td>27.7 (24.8-34.1)</td>
<td>0.57</td>
</tr>
<tr>
<td>D-dimer, mg/L</td>
<td>0.5 (0.3-1.3)</td>
<td>2.4 (0.6-14.4)</td>
<td>0.5 (0.3-0.8)</td>
<td>0.0042</td>
</tr>
</tbody>
</table>

(JAMA Internal Med. 2020. Mar 13)

**Table 4. Bivariate Cox Regression of Factors Associated With ARDS Development or Progression From ARDS to Death**

<table>
<thead>
<tr>
<th>Patient characteristics and findings</th>
<th>ARDS</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>P value</td>
</tr>
<tr>
<td>Coagulation function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PT, s</td>
<td>1.56 (1.32-1.83)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>APTT, s</td>
<td>0.97 (0.94-1.01)</td>
<td>.13</td>
</tr>
<tr>
<td>D-dimer, µg/mL</td>
<td>1.03 (1.01-1.04)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

(Lancet 2020; 395: 497-506)
Underlining mechanism

1. Cytokine storm?  
   (Lancet 2020. March 13.)

2. Elevated ferritin and IL-6 suggesting that mortality might be due to virally driven hyperinflammation?  
   (Intensive Care Med 2020. March 3.)

The severe cases of COVID-19 might be classified into hyperinflammatory ARDS phenotype.
Experiences in Japan

1. Some cases had severe bleeding complications (intracranial hemorrhage, hemothorax, etc).

2. The complication of bleeding is more frequent than that of thrombosis.

3. Some cases showed DIC with hyperfibrinolysis.
Approach on this topic

1. Coagulopathy is one of the indicators whether the patients become worse or not (Clin Chem Lab Med. 2020 Mar 16.)

2. Coagulopathy and Cytokine storm might be target to be treated.

3. More data on complication of bleedings and thrombosis is needed.
Take home messages

1. Virus might cross membrane during the plasma leak

2. Coagulopathy is associated with the severity of COVID-19 and death.

3. Coagulopathy might be an indicator of disease progression and a target to be treated.
Thank you for kind attention

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