SARS-CoV-2 viral sepsis: from bedside to bench

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### Survivors

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Days</th>
<th>Days</th>
<th>Days</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>1d</td>
<td>2d</td>
<td>3d</td>
<td>4d</td>
</tr>
<tr>
<td>Cough</td>
<td>5d</td>
<td>6d</td>
<td>7d</td>
<td>8d</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>9d</td>
<td>10d</td>
<td>11d</td>
<td>12d</td>
</tr>
<tr>
<td>ICU admission</td>
<td>13d</td>
<td>14d</td>
<td>15d</td>
<td>16d</td>
</tr>
<tr>
<td>Systemic steroid</td>
<td>17d</td>
<td>18d</td>
<td>19d</td>
<td>20d</td>
</tr>
<tr>
<td>SARS-CoV-2 RNA positive</td>
<td>21d</td>
<td>22d</td>
<td>23d</td>
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</table>

### Non-Survivors

<table>
<thead>
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<th>Symptom</th>
<th>Days</th>
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<th>Days</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>1d</td>
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<td>3d</td>
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</tr>
<tr>
<td>Cough</td>
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<td>7d</td>
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</tr>
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<td>Dyspnea</td>
<td>9d</td>
<td>10d</td>
<td>11d</td>
<td>12d</td>
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<tr>
<td>ICU admission</td>
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<td>15d</td>
<td>16d</td>
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<tr>
<td>Invasive ventilation</td>
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<td>Systemic steroid</td>
<td>21d</td>
<td>22d</td>
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<td>SARS-CoV-2 RNA positive</td>
<td>21d</td>
<td>22d</td>
<td>23d</td>
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**ARTICLES**

- Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study
  - Zhou et al.

**ARTICLES**

- Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China
  - Huang et al.
Clinical findings of severe or critical COVID-19

Viral infection

Multi-organ dysfunction

- Pneumonia, Respiratory failure, ARDS
- Metabolic acidosis and internal environment disorders
- AKI
- Acute cardiac injury
- ...........

——Viral sepsis

SARS-CoV-2 viral sepsis——Our hypothesis

Hui Li, et al. 2020; unpublished, under peer review
Virus attack may directly contribute to COVID-19 pathogenesis in multiple organs

- Virus RNA was detected in respiratory specimen, blood, feces and urine
- Viral particles were observed in the bronchial and type 2 alveolar epithelial cells by electron microscopy
- Pulmonary pathology showed diffuse alveolar damage with the formation of hyaline membranes.

Effective antiviral therapy is essential to improve outcome

Antiviral interventions

- So far, no specific antiviral against SARS-CoV-2 has been proved.
- Clinically evaluated drugs:
  - Lopinavir/ritonavir monotherapy (LOTUS China, ChiCTR2000029308): *completed, unpublished, under peer review*
    - Promising results
  - CAP China Remdesivir 1 (mild-moderate pneumonia, NCT04252664): *ongoing*
  - CAP China Remdesivir 2 (severe-critical pneumonia, NCT04257656): *ongoing*

*Emmie de Wit et al. Nature Reviews Microbiology 2016; 14, 523–534*
*Timothy P Sheahan; Nat Commun 2020; 11 (1), 222*
*Yeming wang, et al. Trial, 2020, under peer review*
Dysregulated host immune response characterized by cytokine storm and lymphopenia


- IL-1β, IL-6, G-SCF, IP-10, and MCP1 were significantly elevated
- Peripheral lymphocyte counts, mainly T cells were substantially reduced in severe COVID-19 patients

---Host-directed therapies might be an option---

- Corticosteroid
- Convalescent plasma
- tocilizumab
Abnormal coagulation is present in severe COVID-19 patients

- Significantly increased D-dimer and FDP were associated with poor prognosis
- Thrombosis in pulmonary interstitial vessels were seen on autopsy
- Vascular endothelial cells express high levels of ACE2

Anticoagulation therapy should be initiated for severe COVID-19 patients if otherwise contraindicated.

Take Home Message

- Invasion of SARS-CoV-2 into the lung is an explosive fusion of multi-organ dysfunction in severe or critical COVID-19 patients. More intensive surveillance or individually tailored therapeutic approaches is needed for severe patients with COVID-19.

- Effective antiviral therapy and measures to restore the adaptive immune response, as well as supportive care, are important to improve the outcome of the patients.
Acknowledgements

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Frederick G Hayden

Oxford University
Peter W Horby

HuaZhong University
Liang Liu

Cooperators:

<table>
<thead>
<tr>
<th>Wuhan Jinyintan Hospital</th>
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<tr>
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<td>The Central Hospital of Wuhan</td>
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<td>Zhongnan Hospital of Wuhan University</td>
<td>Renmin Hospital of Wuhan University</td>
</tr>
<tr>
<td>Union Hospital</td>
<td>Wuhan First hospital</td>
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<tr>
<td>Wuhan Third hospital</td>
<td>Wuhan Fourth hospital</td>
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All health-care workers involved in the diagnosis and treatment of patients in Wuhan