ISTH ACADEMY WEBINAR

THROMBOSIS, THROMBOPROPHYLAXIS AND COAGULOPATHY IN COVID-19 INFECTIONS

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Prof Beverley Hunt
M.D., O.B.E.
King's College London (U.K.)

Prof Marcel Levi
M.D., Ph.D.
University College Hospital (U.K.)

Simon Stanworth
Ph.D.
John Radcliffe Hospital (U.K.)
Coagulopathy of COVID-19

Marcel Levi
University College London, UK
Clinical Characteristics of Coronavirus Disease 2019 in China


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# Clinical Characteristics of Coronavirus Disease 2019 in China

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Patients (N = 1099)</th>
<th>Disease Severity</th>
<th>Presence of Composite Primary End Point</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Nonsevere (N = 926)</td>
<td>Severe (N = 173)</td>
</tr>
<tr>
<td><strong>Platelet count</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR) — per mm³</td>
<td>168,000 (132,000–207,000)</td>
<td>172,000 (139,000–212,000)</td>
<td>137,500 (99,000–179,500)</td>
</tr>
<tr>
<td><strong>Distribution — no./total no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;150,000 per mm³</td>
<td>315/869 (36.2)</td>
<td>225/713 (31.6)</td>
<td>90/156 (57.7)</td>
</tr>
<tr>
<td>Median hemoglobin (IQR) — g/dL</td>
<td>13.4 (11.9–14.8)</td>
<td>13.5 (12.0–14.8)</td>
<td>12.8 (11.2–14.1)</td>
</tr>
<tr>
<td><strong>d-dimer ≥0.5 mg/liter</strong></td>
<td>260/560 (46.4)</td>
<td>195/451 (43.2)</td>
<td>65/109 (59.6)</td>
</tr>
</tbody>
</table>
Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study

<table>
<thead>
<tr>
<th></th>
<th>Non survivor (n=54)</th>
<th>Survivor (n=137)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphocytes &lt; 0.8x10^9/L</td>
<td>41 976%</td>
<td>36 (26%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Platelet count &lt;100x10^9/L</td>
<td>1 (20%)</td>
<td>2 (1%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LDH (IU)</td>
<td>521 (98%)</td>
<td>253 (54%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Troponin I (&gt; 28 pg/ml)</td>
<td>46%</td>
<td>1%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Prothrombin time (&gt;16s)</td>
<td>13%</td>
<td>3%</td>
<td>-</td>
</tr>
<tr>
<td>Serum ferritin ug/L</td>
<td>1435 (96%)</td>
<td>503 (71%)</td>
<td>0.00008</td>
</tr>
<tr>
<td>IL-6 pg/ml</td>
<td>11 (7-14.5)</td>
<td>6.3 (5.0-7.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>D Dimer &gt;1 ug/ml</td>
<td>81%</td>
<td>24%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia

Ning Tang\(^1\) | Dengju Li\(^2\) | Xiong Wang\(^1\) | Ziyong Sun\(^1\)

<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>On admission</td>
<td></td>
<td></td>
<td></td>
<td></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>
COVID-19 coagulopathy: summary

• Signs of coagulation activation mimicking DIC, but different from ‘usual’ sepsis-related DIC
  – Less prominent thrombocytopenia
  – Less consumption of coagulation proteins

• Clinical and pathological signs of thrombotic microangiopathy
  – vWF multimers and ADAMTS13 ?

• Prominent increase in D-dimer with predictive value for adverse outcome
Tissue damage

SARS-CoV-2

DAMPs

Phosphatidyl serine

Tissue factor +VIIa

XIa

XIIa

Cell-free-DNA

Cytokines release

Platelet aggregation

Thrombin

Fibrinogen

Fibrin

Thrombus formation

Antithrombin

Glycocalyx

Neutrophil

Mediator release

Heparan sulfate

Anticoagulants

Healthy endothelial cell

Damaged endothelial cell

Iba T, et al, 2020
Plasminogen activator-driven pathways determine activation of the plasminogen-plasmin system and are an important factor in lethality.
Fig. 2

SARS-CoV-2

Macrophage
Lymphocyte
Neutrophil
Alveolar effusion

Cytokines release

Neutrophil extracellular traps

Endothelial cell
Red cell

D-dimer
Platelet
Microthrombus

Iba T, et al, 2020
Acute pulmonary embolism and COVID-19 pneumonia: a random association?

Gian Battista Danzi ID 1*, Marco Loffi ID 1, Gianluca Galeazzi ID 1, and Elisa Gherbesi ID 2

1Division of Cardiology, Ospedale di Cremona, Cremona, Italy; and 2 Università degli Studi di Milano, Milano, Italy

* Corresponding author. Division of Cardiology, Ospedale di Cremona, Viale Concordia 1, 26100 Cremona, Italy. Tel: +39 0372405333, Email: gbdanzi@tin.it

In a 75-year-old Covid-19-positive woman hospitalized for severe bilateral pneumonia, CT scan documented bilateral pulmonary embolism associated with extensive ground-glass opacifications involving both the lung parenchymas.

Acute infections are associated with a transient increased risk of venous thromboembolic events. A COVID-19-positive 75-year-old woman, with severe bilateral pneumonia and concomitant acute pulmonary embolism, was hospitalized after 10 days of fever and a recent onset of dyspnoea. She was haemodynamically stable and without strong predisposing risk factors for venous thromboembolism.
Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy

Ning Tang, Huan Bai, Xing Chen, Jiale Gong, Dengju Li, Ziyong Sun

First published: 27 March 2020 | https://doi.org/10.1111/jth.14817
1786 consecutive patients with COVID-19 entering Tongji hospital

1261 classified as mild and moderate COVID-19

76 met the exclusion criteria

449 classified as severe COVID-19

99 with heparin treat for 7 days or longer

30 died within 28-day

350 without heparin treat or treating less than 7 days

104 died within 28-day
Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy

<table>
<thead>
<tr>
<th>Patients with</th>
<th>28-day mortality</th>
<th>Univariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Treating with Heparin</td>
<td>Non-treated with Heparin</td>
</tr>
<tr>
<td>SIC score ≥4 (n=97)</td>
<td>40.0%</td>
<td>64.2%</td>
</tr>
<tr>
<td>SIC score ≤4 (n=352)</td>
<td>29.0%</td>
<td>22.6%</td>
</tr>
</tbody>
</table>
Conclusion

• Severe COVID-19 infection is associated with a coagulopathy with features of both DIC and thrombotic microangiopathy

• Coagulopathy is at least a marker of adverse outcome

• Severe COVID-19 seems to result in a pro-hemostatic state with possible consequences for the incidence of venous thromboembolism