COVID-19 and thrombosis

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CANVECTOR

Thrombosis in COVID-19 infection

- COVID-19 infection → high incidence of venous thromboembolism (VTE) and arterial thrombosis (stroke, heart attack), despite standard use of thromboprophylaxis (i.e. low dose anticoagulant)

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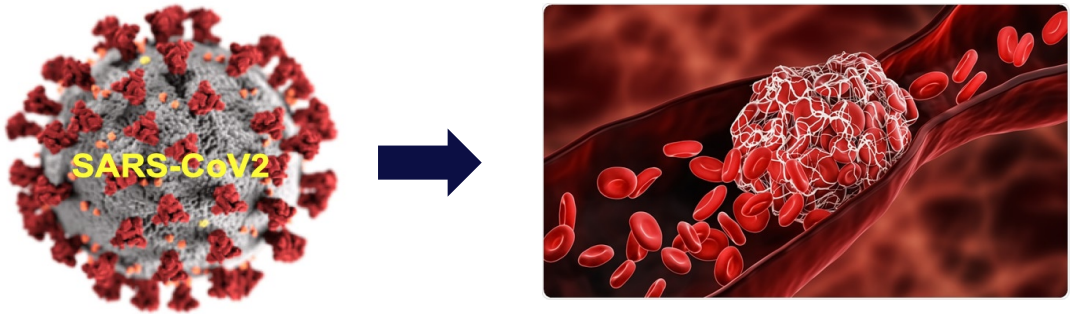
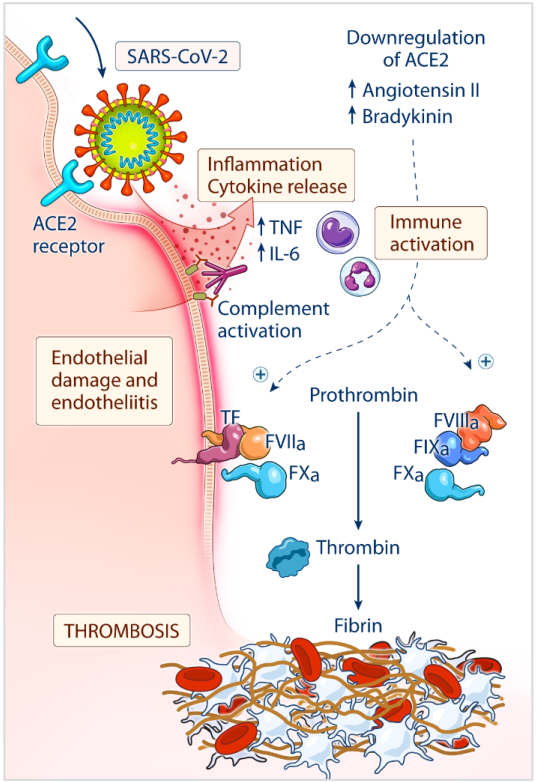


Tritschler T et al, JTH 2020

Mechanisms of Thrombosis in COVID-19

- Endothelial injury / tissue factor expression
- Inflammation and immune activation
- ACE-2 down regulation
- NETs/NETosis
- Platelet and macrophage activation
- Complement activation
- Increased fibrinogen; reduced fibrinolysis
- Reduced natural anticoagulants
- ? antiphospholipid antibodies



Godoy F, Goligher EC, Lawler P, Slutsky A, Zarychanski R. CMAJ. 2020

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Rationale for anticoagulation as an intervention in COVID-19

Several lines of evidence support **potential efficacy** of therapeutic parenteral anticoagulation with heparin for the treatment of COVID-19:

1) **COVID-19 associated with a hypercoagulable state**
   - Many patients experience significant cardiac and pulmonary macro- and micro-vascular thrombotic complications contributing to clinical deterioration
   - COVID-19 is associated with an unusually high incidence of venous thromboembolic events

2) **Heparin induces conformational changes in the SARS-CoV-2 receptor spike protein**
   - may limit cellular invasion into the pulmonary epithelium, myocardium, and vascular endothelium, improve acute lung injury

3) **Heparin has direct anti-inflammatory effects**
   - may reduce severity of organ injury and hemodynamic collapse.

4) **Easy scalability**
   - given ubiquitous availability, heparin may be rapidly translatable to clinical care globally if found to be effective, at a time when immediately implementable solutions are urgently needed.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

N Engl J Med. 2021 Aug 26;385(9):790-802.

Therapeutic Anticoagulation with Heparin in Noncritically Ill Patients with Covid-19

The ATTACC, ACTIV-4a, and REMAP-CAP Investigators*

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Recent metaanalysis of trials to date →

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DOI: 10.1002/rth2.12638

BRIEF REPORT

Randomized trials of therapeutic heparin for COVID-19: A meta-analysis

Michelle Sholzberg MDCM, MSc, FRCPC[1,2] | Bruno R. da Costa PhD[3,4] | et al

Bottom line (results so far)

Hospitalized non-ICU patients with COVID-19

- Therapeutic dose AC better than sub-therapeutic (prophylactic or intermediate) dose AC

Hospitalized ICU patients with COVID-19

- No benefit of therapeutic dose AC vs. sub-therapeutic (prophylactic or intermediate) dose AC, and may be harm
- No benefit of intermediate dose AC vs. prophylactic dose
- So: prophylactic dose seems best

Vaccine-Induced Thrombosis with Thrombocytopenia (VITT)

- Rare but serious complication of AstraZeneca and J&J COVID vaccines (but not Pfizer and Moderna vaccines)
- A prior history of thrombosis or having thrombosis risk factors does not increase the risk of this rare complication

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