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Hypercoagulable State of COVID-19

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Introduction

From the end of 2019 until present and into the foreseeable future, SARS-CoV-2, or Coronavirus disease 2019 (COVID-19), has been in the forefront of our concerns. Having a novel virus at the root of a pandemic, limited information is available, especially initially, on the scope of the signs and symptoms, effective treatment, and the extent of the lasting effects, as well as the many other aspects involved with this illness. As time has passed, it has been realized that the virus leaves many in a hypercoagulable state (Abou-Ismail et al., 2020).

To effectively treat those afflicted with this specific symptom of COVID-19, an understanding of the pathophysiology of the virus must be established to effectively treat and potentially prevent coagulopathy and the thrombotic events that can ensue. Gaining more insight into this will allow for standardized plan of care that includes appropriate predicative labs and effective prophylactic medications to be utilized in outpatient or inpatient settings to prevent a hypercoagulable state from occurring or minimize the medical effects of a thrombotic event.

Underlying Pathophysiology

There are a several coagulation abnormalities that have been revealed in individuals diagnosed with COVID-19. As with many infections or inflammatory responses, a hypercoagulable state can emerge. These are familiarly classified under **Virchow's Triad:**

1. Injury to vessel endothelium – research shows that the virus directly attacks endothelial cells. Endothelialitis is a significant contributor to thrombosis formation.
2. Abnormalities of Blood Flow, or Stasis – for most patients with COVID-19, this is in direct response to decreased mobility in light of the extenuating symptoms of the virus, especially with hospitalized individuals.
3. Hypercoagulability of the Blood – this is caused by the inflammatory state of the virus or infection.

Significance of Pathophysiology

"The novel SARS-CoV-2 appears to generate a profoundly prothrombotic milieu as evidenced by a surge in global reports of arterial, venous and catheter-related thrombosis *(Abou-Ismail et al., 2020).* While there are similarities shared with other viruses and responses, there are several points of distinction with the hypercoagulable state seen with COVID-19.:

- Venous Thromnoembolism - Pulmonary embolism (PE) is the most common expression. Post-mortem examinations have consistently revealed PE's and microthrombi in alveolar capillaries. . *(Abou-Ismail et al., 2020)* Deep Vein Thrombosis (DVT) are commonly seen as well and have been found to impact the bilateral lower extremities.
- Stroke – Ischemic strokes have been seen as the typical manifestation, along with limb ischemia, both of which are more noted in large vessels.
- The spike protein found on SARS-CoV-2 has been linked to activating a dysregulated alternative complement pathway, causing a cytokine storm.
- The spike protein found on SARS-CoV-2 has been linked to a derangement in the Renin-Angiotensin-Aldosterone pathway, which contributes to the hypercogulable state.

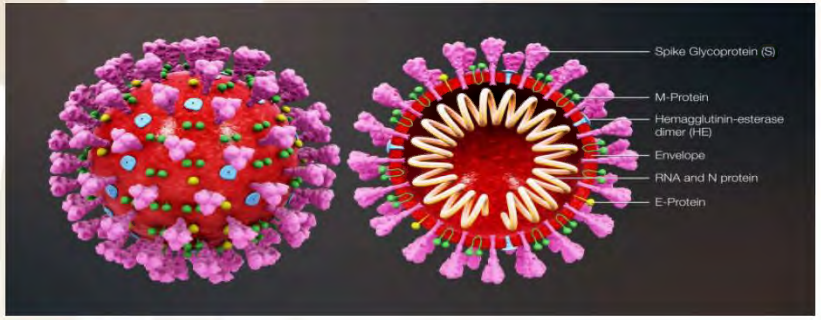

Figure A. (Sars-cov-2 (2019-ncov) proteins 2020)

Pathophysiological Processes

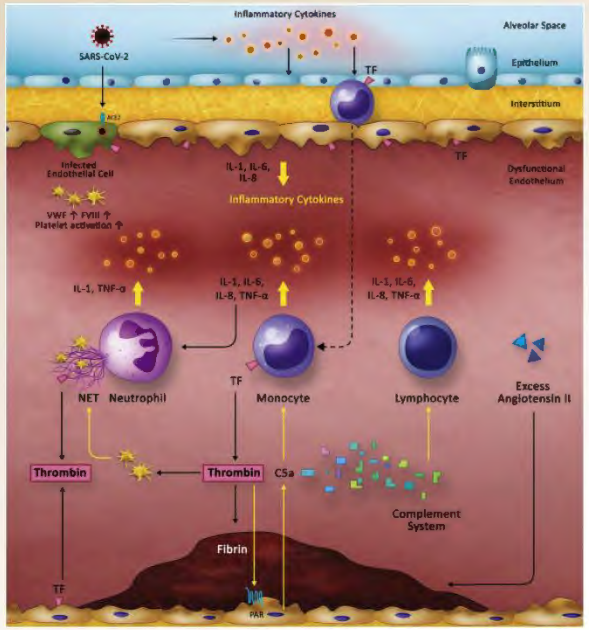

Figure B. Pathophysiology of the Hypercoagulable State in COVID-19. The current understanding of the pathophysiology of COVID-19 induced coagulopathy centers around the bidirectional cross-talk between inflammation (yellow arrows) and thrombosis (black arrows). COVID-19 leads to a severe inflammatory response that originates in the alveoli. Release of inflammatory cytokines leads to activation of epithelial cells, monocytes and macrophages. Direct infection of the endothelial cells through the ACE2 receptor also leads to endothelial activation and dysfunction,, all of which contribute to thrombin generation and fibrin clot formation. Thrombin, in turn, causes inflammation through its effect on platelets which promote NET formation in neutrophils. It also activates endothelium through the PAR receptor, which leads to release of C5A that further activates monocytes. These mechanisms are currently hypothetical based on existing findings in COVID-19 and previous understanding of the cross-talk between inflammation and thrombosis. ACE2: Angiotensin-converting enzyme 2. FVIII: Factor VIII. IL: Interleukin. NET: Neutrophil extracellular trap. TF: Tissue factor. TNF: Tumor necrosis factor. VWF: von Willebrand factor. (Abou-Ismail et al., 2020)

Implications for Nursing Care

Monitoring cogualation abnormalities via serum laboratory testing has been a key indicator in determining hypercoagulable diagnoses. The standard set of test to offer the most insight are:

- Abnormal or slightly prolonged Prothrombin Time AND aPTT
- Platelet counts normal or slightly increased.
- Fibrinogen increased
- D-Dimer increased.

Along with any of these abnormalities, in order to definitely detect and diagnoses a hypercoagulable manifestation, ultrasound imaging has been found to offer the most insight in locating the impacted area of a DVT, while a CT is used to confirm a PE.

Once a confirmation of a thrombotic event has been made, there are several courses of treatment that can be administered to effectively mitigate the situation. The most common and most effective are:

- Low-Molecular Weight Heparin at a moderate to full-dose
- Tissue Plasminogen Activator in cases of a massive and/or obstructive PE, Central-line associated thrombosis, limb-threatening DVT or acute stroke.

Conclusions

Though the research is technically incomplete at this time due to the novelty of the virus, there is reliable and valuable information available to be extracted, applied and utilized in the clinical setting to mitigate the mortality risk of patients diagnosed with COVID-19.

Understanding the causative factors in the pathophysiological process of the hypercoagulable state allows for more strategic management of patients' conditions. Insight is given into serum laboratory tests to monitor, imaging to perform and therapeutic medicinal management to implement. These interventional strategies allow clinicians an opportunity to prevent further complications of the virus for their patients.

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