

Memorandum

Date: April 23, 2021

To: Hospital Medical Staff and Pharmacists

From: BC COVID-19 Therapeutics Committee

Re: **Therapeutic Anticoagulation for Hospitalized COVID-19 Patients**

In light of surging hospitalizations for COVID-19 in BC and stretched critical care capacity, the BC COVID-19 Therapeutics Committee (CTC) has recently recommended therapeutic anticoagulation for select hospitalized COVID-19 patients. The data for this recommendation have not yet been publically released, but the implications for care were deemed sufficient to warrant a change in practice. The BC CTC provides the following guidance to clinicians to support decision making:

Organ support is defined as the need for high flow nasal cannula, vasopressor/inotropes, ECMO, or invasive or non-invasive ventilation.

A. For patients NOT requiring organ support at initial presentation (Severe Group):

Therapeutic anticoagulation (LMWH preferred) is suggested in patients without high-risk features for serious bleeding. These include: age 75 or greater, eGFR less than 30 mL/min, any coagulopathy, platelet count less than $50 \times 10^9/L$, use of dual antiplatelet therapy, recent history of serious GI bleed or recent intracranial condition (stroke, neurosurgery, aneurysm, cancer), epidural or spinal catheter.

Therapeutic anticoagulation for COVID-19 should start within 72 hours of admission and be continued for 14 days or until hospital discharge, whichever is sooner. Therapeutic anticoagulation should be continued even if there is deterioration requiring organ support during this period.

Possible Benefit = Reduced 21-day mortality and organ support (16% vs 23%), reduced thrombotic events (1.9% vs 3.2%)

Possible Harm = Increase in major bleeding (1.6% vs 0.9%)

B. For patients requiring organ support at initial presentation (Critical Care Group):

Therapeutic anticoagulation IS NOT RECOMMENDED due to lack of benefit and potential for increased harm in terms of mortality and major bleeding. Usual care prophylaxis should be used in this setting.

Evidence used for these recommendations:

The multiplatform RCT (ATTACC, ACTIV-4a & REMAP-CAP) was designed to determine if therapeutic anticoagulation is superior to usual care anticoagulant prophylaxis in treating patients hospitalized for COVID-19. Interim pre-publication data were released on January 28, 2021 (<https://www.attacc.org/presentations>). Results of the critical care group were later released in preprint on March 12, 2021. More recent data of the group not requiring organ support were confidentially shared with the BC CTC on April 16, 2021 but they have not been publically released at this time. A preprint is expected in the next few weeks. The final data are consistent with the interim results.

Therapeutic anticoagulation was **SUPERIOR** to usual care (intermediate or prophylactic intensity anticoagulation) in reducing 21-day mortality and organ-support in hospitalized COVID-19 patients who did not require organ support or critical care at enrollment. This benefit was seen regardless of D-dimer level. Importantly, the BC CTC considers the potential benefit from reducing the requirement for mechanical ventilation or death to exceed the potential harm of major bleeding with therapeutic anticoagulation.

In the critically ill COVID-19 patients (those requiring organ support at enrollment), therapeutic anticoagulation met the pre-defined criteria for **FUTILITY** with respect to 21-day mortality and organ support compared with usual care (aOR 0.87; 95% credible interval (CrI) 0.70-1.08; posterior probability of futility 99.8%). No improvement in hospital survival was seen. Major bleeding was more common with therapeutic anticoagulation (3.1% vs 2.4%; aOR 1.19; 95% CrI 0.57-2.49).

The CTC will continue to update the "Clinical Practice Guidance for Antimicrobial and Immunomodulatory Therapy in Adult Patients with COVID-19" document based on any new studies and relevant data. Please refer to the BCCDC website for the most updated information:

<http://www.bccdc.ca/health-professionals/clinical-resources/covid-19-care/clinical-care/treatments>