

CORRECTIONAL SERVICE CANADA

CHANGING LIVES. PROTECTING CANADIANS.



SERVICE CORRECTIONNEL CANADA

TRANSFORMONS DES VIES. PROTÉGEONS LES CANADIENS.

Date: July 2020
Issue No. 5

COVID-19 Clinical Corner Considerations for Thrombosis

Key Messages: Thrombosis

- *COVID-19 appears to be associated with both venous and arterial thrombosis; the mechanism is not known.*
- *Thrombosis can be life-threatening; it occurs when blood clots block the blood flow in veins and arteries, and by doing so, reduce, if not block, oxygen supply to organs.*
- *The overall prevalence of thrombosis among patients with COVID-19 is not established. Traditional VTE risk factors still apply, e.g., advanced age, gender (male sex), obesity, cancer, history of VTE and critical illness.*
- *When presented with patients with COVID-19 infection with unexplained worsening respiratory status/hypoxia, unexplained hypotension or tachycardia, or signs of DVT, consider pulmonary embolism as part of the differential diagnoses.*
- *Prevention for all risk groups includes exercising (please see examples in Appendix A), quitting smoking, losing weight, and managing other health conditions such as diabetes, high blood pressure, and high cholesterol.*

A number of coagulation abnormalities may be presented in patients with COVID-19. As most of the literature is focused on hospitalized patients who are more likely to have comorbid conditions, the overall incidence of thrombosis among patients with COVID-19 is not yet known. From a clinician's perspective, this raises questions surrounding appropriate evaluations and therapeutic interventions for thrombosis prevention and treatment.

Patients with COVID-19 may be susceptible to venous thromboembolism (VTE) (a blood clot that starts in a vein) due to severe infection and inflammation (1,2). Other possible risk factors include advanced age, gender, obesity, cancer, history of VTE and critical illness.

VTE can present as deep vein thrombosis (DVT) and/or pulmonary embolism (PE) (3). In patients with COVID-19 pneumonia affecting the small air sacs within the lungs, autopsy findings include blood clots throughout the lungs (pulmonary

microvascular thrombosis, a known complication of COVID-19 ARDS), a scenario that is not seen with other types of lung infections (4,5,6). This may explain why blood oxygen levels fall dramatically in patients with severe COVID-19 infection (3).

There are also reports of arterial thrombosis resulting in stroke, acute limb and mesenteric ischemia, and heart attacks (7,8,9,10,11). Risk factors of arterial thrombosis include older age, smoking, diabetes, obesity and family history of arterial thrombosis.

The pathogenesis of COVID-19 hypercoagulability is not well understood at this time. What we do know, however, is that it is associated with increased risk of death (12,13). Current evidence suggests that the mechanisms are likely multifactorial involving a systemic inflammatory response similar to what is seen in sepsis, stasis of blood flow, endothelial injury through direct viral invasion of the endothelial cells along with depletion of angiotensin-converting enzyme 2 (ACE2), and changes in circulating prothrombotic factors (e.g., elevated fibrinogen, hyperviscosity) (7,13,14,15,16).

COVID-19 hematology lab abnormalities observed include elevated D-dimer and fibrinogen levels that are typically seen in patients with COVID-19 due to the profound inflammatory state experienced (13). A markedly elevated D-dimer is considered a poor prognostic indicator and is associated with increased risk of death from COVID-19 infection (12,16). Modest prolongation of the prothrombin time (PT) and activated partial thromboplastin time (aPTT) may be seen (12). Also, lymphopenia and mild thrombocytopenia (100-150 x 10⁹/L) may be seen (12).

Further investigation for VTE is warranted if there is a clinical suspicion of DVT and/or PE (12). Coagulation testing include a baseline CBC, PT, aPTT, fibrinogen and D-dimer (12) and repeated based on patient's clinical status. This information can be used to inform level of care.

"An elevated D-dimer alone does not warrant investigation for VTE unless there is also a high clinical suspicion for DVT and/or PE" (Alberta Health Services).



Please see **CSC's COVID-19 Clinical Guidance Document** for more information with regards to investigations and management of COVID-19 patients.

Although thrombotic events may be observed in patients with COVID-19 not admitted to the hospital, data on its incidence is not known. There is little high-quality evidence available to inform effectiveness and safety of different approaches for thrombosis prevention and treatment in general and in this setting.

Evidence is constantly evolving regarding the benefits/risks of different regimens for prevention and treatment of VTE based on setting (outpatient, inpatient, ICU patients, post-ICU patients). For treatment or prevention of VTE associated with COVID-19, please refer to current treatment guidelines (17, see Resources).

What can we do for our patients?

Variations in the clinical course of COVID-19 associated thrombosis appear to be linked to age and lymphocytopenia as opposed to viral factors. CSC clinicians should help identify their patients' risk factors for thrombosis to help minimize their risk, as a preventive strategy.

About 20-55% of patients admitted to hospital for COVID-19 have laboratory evidence of coagulopathy (18).

Thrombosis prevention for all risk groups includes exercising (please see examples provided in **Appendix A** which could be discussed taking into consideration patient factors), quitting smoking, losing weight, and managing other health conditions such as diabetes, high blood pressure, and high cholesterol.

Staff collaboration is key in determining tailored health interventions to help patients mitigate their risk. Patients may benefit from undergoing a global Cardiovascular Disease (CVD) risk reduction and health education surrounding their CVD risk along with discussion on which risks are modifiable and how they can control them. Discussion surrounding guideline directed medical therapy may be warranted to help reduce patient's overall CVD risk (please see CSC's [Guidance for the Primary Prevention of Cardiovascular Disease](#) and [Guidance for Chronic Cardiovascular Diseases](#)).

Management of patients with COVID-19 should also focus on observation for signs of reduced peripheral circulation as well as asking them about calf pain.

The role of thromboprophylaxis for quarantined patients with mild COVID-19 but significant co-morbidities or for patients without COVID-19 who are less active because of quarantine is uncertain. These patients should be advised to stay active at home [21]. In general, recommendations for therapeutic anticoagulation with known DVT or PE remain the same.

Continue to emphasize personal protection measures to prevent transmitting, spreading, or acquiring COVID-19, specifically (19,20):

- Regular hand hygiene, using alcohol based hand rub or soap and water (dry hands with a single-use towel)
- Observe and maintain physical distancing
- Optimize respiratory hygiene. Cover mouth and nose with tissue when coughing or sneezing or cough into the bend of your arm, discard tissue immediately in a covered bin, and perform hand hygiene
- Avoid touching eyes, nose or mouth as the virus can survive on surfaces.

Continue to emphasize importance of vaccinations including pneumococcal vaccine given the increased risk of secondary bacterial infection with COVID-19 patients.

Stay tuned as more data becomes available.

Please send any other clinical questions related to COVID-19 to [GEN-NHQ Pharmacy](#).

References:

1. Ren B, Yan F, Deng Z et al. Extremely high incidence of lower extremity deep venous thrombosis in 48 patients with severe COVID-19 in Wuhan. *Circulation* 2020. Doi: 10.1161/circulationaha.120.047407. Retrieved from: <https://www.ahajournals.org/doi/pdf/10.1161/CIRCULATIONAHA.120.047407>
2. Wichmann D, Sperhake J-P, Lutgehetmann M et al. Autopsy findings and venous thromboembolism in patients with COVID-19. A prospective cohort study. *Annals of Internal Medicine* 2020. Retrieved from: <https://doi.org/10.7326/M20-2003>.
3. Poggiali E, Bastoni D, Ioannilli E et al. Deep vein thrombosis and pulmonary embolism: Two complications of COVID-19 Pneumonia? *Eur J Case Rep Intern Med* 2020;7(5):001646. Doi: 10.12890/2020_001646.
4. Blood clotting a significant cause of death in patients with COVID-19, *NewsRx Health*, 20, ISSN: 1944-2580, BUTTER® ID: 020607946.
5. Magro C, Mulvey JJ, Berlin D et al. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: a report of five cases. *Transl Res* 2020 Apr 15;S1931-5244(20)30070-0. Doi: 10.1016/j.trsl.2020.04.007.
6. Connors JM, Levy JH. Thromboinflammation and the hypercoagulability of COVID-19. *J Thromb Haemos* 2020 Apr 17. Doi: 10.1111/jth.14849.
7. Hess DC, Eldahshan W, Rutkowski E. Commentary. COVID-19-Related Stroke. *Translational Stroke Research* 2020;11:322-325.

COVID-19 CLINICAL CORNER (ISSUE 5): COVID-19 AND THROMBOSIS

- Doi: 10.1007/s12975-020-00818-9. Retrieved from:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7202903/pdf/12975_2020_Article_818.pdf
8. Oxley TJ, Mocco J, Majidi S et al. Large-vessel stroke as a presenting feature of COVID-19 in the young. *N Engl J Med* 2020;382(20):e60. Doi: 10.1056/NEJMc2009787.
 9. Bellosta R, Luzzani L, Natalini G et al. Acute limb ischemia in patients with COVID-19 pneumonia. *J Vasc Surg* 2020 April 29;S0741-5214(20)31080-6. Doi: 10.1016/j.jvs.2020.04.483.
 10. Klok FA, Kruijff MJHA, van der Meer NJM et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thromb Res* 2020;191:145-147.
<https://reader.elsevier.com/reader/sd/pii/S0049384820301201?token=F979E0C4113327126D0BFBDFFB0EBA56D26F2D033592212EB94A0D1D3C61F7DFA4254BCD0B3730B8DFE244C6FDE3109A>
 11. Kaur P, Qaqa F, Ramahi A et al. Case Report. Acute upper limb ischemia in a patient with COVID-19. 2020. Retrieved from:
<https://reader.elsevier.com/reader/sd/pii/S1658387620300960?token=5C6FA79B11D011257574C31D69E8AEC45144B9AAECF6BBC696AD35A99F29CA607AC0F717CFE7E792111608CECD578778>
 12. Alberta Health Services. Thrombosis and Coagulopathy. Guidance in COVID-19. Retrieved from:
<https://www.albertahealthservices.ca/assets/info/ppih/if-ppih-covid-19-thrombosis-coagulopathy-guidance.pdf>
 13. Levi M, Thachil J, Iba T et al. Comment. Coagulation abnormalities and thrombosis in patients with COVID-19. *The Lancet Haematology* 2020; 7(6):E438-E440. DOI:
[https://doi.org/10.1016/S2352-3026\(20\)30145-9](https://doi.org/10.1016/S2352-3026(20)30145-9).
 14. Brigham Health. Brigham and Women's Hospital. COVID-19 Protocols. Hematology. Retrieved from:
<https://covidprotocols.org/protocols/hematology/#thrombotic-disease>. Last updated: May 7, 2020.
 15. Magro G. Letter to Editors. Cytokine Storm: Is it the only major death factor in COVID-19 patients? Coagulation role. *Medical Hypotheses* 2020;142. Retrieved from:
<https://doi.org/10.1016/j.mehy.2020.109829>.
 16. Becker RC. COVID-19 update: COVID-19-associated coagulopathy. *Journal of Thrombosis and Thrombolysis* 2020; p.1-14. Doi:10.1007/s11239-020-02134-3. Retrieved from:
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7225095/>
 17. Moores LK, Tritschler T, Brosnahan S, Carrier M, Collen JF, DoerschugK, Holley AB, Jimenez D, LeGal G, Rali P, Wells P, Prevention, diagnosis and treatment of venousthromboembolism in patients with COVID-19: CHEST Guideline and Expert Panel Report, *CHEST*(2020), doi: <https://doi.org/10.1016/j.chest.2020.05.559>. Journal Pre-Proof
 18. Lee SG, Fralick M, Sholzberg M. Practice. Five things to know about... Coagulopathy associated with COVID-19. *CMAJ* 2020;192:E583. Doi:10.1503/cmaj.200685, early-released May 1, 2020. Retrieved from:
<https://www.cmaj.ca/content/cmaj/192/21/E583.full.pdf>
 19. World Health Organization. Preparedness, prevention and control of COVID-19 in prisons and other places of detention. Interim guidance March 15, 2020. Copenhagen. WHO Regional office for Europe. Retrieved from:
http://www.euro.who.int/data/assets/pdf_file/0019/434026/Preparedness-prevention-and-control-of-COVID-19-in-prisons.pdf?ua=1
 20. Correctional Services Canada. Clinical Management of Patients with COVID-19. Guidance Document for Healthcare Professionals. Updated May 1, 2020
 21. Blkdeli B et al. JACC State-of-the-Art Review. COVID-19 and thrombotic or thromboembolic disease: Implications for prevention, antithrombotic therapy and follow-up. Retrieved from:
<https://www.sciencedirect.com/science/article/pii/S0735109720350087?via%3Dihub>

Resources:

1. Government of Canada. Clinical management of patients with moderate to severe COVID-19: Interim Guidance. Section 7.3. Prevention of complications. Prevention of VTE. Retrieved from:
<https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/clinical-management-covid-19.html#6> on June 5, 2020.
2. BC Center for Disease Control (BCCDC). Treatments. Specific Therapies. VTE Prophylaxis. Retrieved from:
<http://www.bccdc.ca/health-professionals/clinical-resources/covid-19-care/clinical-care/treatments>. Accessed June 5, 2020
3. Thrombosis Canada. Thrombosis & COVID-19: Canadian Expert Perspectives. COVID coagulopathy: main messages. Retrieved from: https://thrombosiscanada.ca/wp-content/uploads/2020/04/TC-COVID-19_Webinar_10April2020.pdf;
4. Spyropoulos AC et al on behalf of the International Society on Thrombosis and Hematosis (ISTH) Scientific and standardization committee communication: Clinical Guidance on the Diagnosis, Prevention and Treatment of Venous Thromboembolism in Hospitalized Patients with COVID-19. Retrieved from:
<https://onlinelibrary.wiley.com/doi/pdf/10.1111/jth.14929>. Accessed June 5, 2020
5. American Society of Hematology. COVID-19 and VTE/Anticoagulation: Frequently Asked Questions: Version 3.0. Last Updated May 18, 2020. Retrieved from:
<https://www.hematology.org/covid-19/covid-19-and-vte-anticoagulation> on June 5, 2020.

Appendix A: Examples of Exercises to Reduce Thrombosis Risk and Maintain Heart Health

Sitting still for long periods of time can leave your legs feeling numb, and at worst, pose a risk to your health. There are exercises offenders can do to avoid health complications associated with prolonged sitting.

1. Foot pumps

- *Start with your feet on the floor.*
- *Lift your heels up while keeping the balls of your feet on the floor. Hold the pose for a few seconds.*
- *Set your heels to the floor and lift your toes up. Hold for a few seconds.*
- *Repeat the stretch each way a few times.*

2. Ankle circles

- *Lift your feet off the floor.*
- *Trace circles with your toes, from the inside out. Keep this up for a few seconds.*
- *Switch direction and draw circles from the outside inwards for a few seconds.*
- *Repeat both directions a few times.*

3. Leg lifts

- *Lift your foot off the floor, and straighten your leg as much as you can, while keeping your ankles bent and your toes pointed upward.*
- *Relax your leg.*
- *Repeat with the other leg.*
- *Alternate each leg a few times.*

4. Knee pull-ins

- *Bend your leg and hug your knee as close to your chest as you can.*
- *Keep your back straight and hold the pose for a few seconds.*
- *Alternate each side a few times.*

Source: <https://www.finnavia.fi/en/newsroom/2017/easy-flight-exercises-prevent-deep-vein-thrombosis>

Maintaining Heart Health

Cardiovascular exercise will help get your heart rate up, making your blood pump faster. This delivers more oxygen throughout your body, which keeps your heart and lungs healthy. Regular cardio exercise can also help you lose weight, get better sleep, and reduce your risk for chronic disease. Here are some exercises offenders can do to reduce their risk:

- **High knees:** This exercise involves running in place, so you can do it anywhere with minimal space.
- **Jumping jacks:** For a full-body workout, add in jumping jacks; This works your entire body while increasing your heart rate.
- **Standing alternating toe touches:** This exercise works your arms, core, and legs, making it great full-body cardio move.
- **Lunge jumps:** Lunge jumps, which combine jumps and standard lunges, will get your heart pumping.

Source: <https://www.healthline.com/health/cardio-exercises-at-home#beginner>