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# Post-Acute-COVID-19-Illness Hematological Sequelae

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A 2.5 % cumulative incidence of thrombosis, including ischemic stroke, intracardiac thrombus, segmental pulmonary embolism, and thrombosed arteriovenous fistula at 30 days (median duration of 23 days post-discharge) and a 3.7 % cumulative incidence of bleeding, mostly associated with mechanical falls at 30 days after hospital discharge were reported in 163 post-acute-COVID-19-illness patients from the US without post-hospital-discharge thromboprophylaxis **[**1**]**. Several previous retrospective studies in the UK revealed similar rates of venous thromboembolism (VTE) **[**2, 3**]**. A previous prospective study in Belgium in 102 post-acute-COVID-19-illness patients at 6 weeks post-hospital-discharge follow-up by assessing D-dimer levels and venous ultrasonography revealed that only one asymptomatic VTE event occurred among 8 % of subjects who received post-hospital-discharge **[**4**]**. Hypercoagulable state and hyper inflammation were consistent in COVID-19-related coagulopathy **[**5, 6**]**, contributing to the disproportionately high rates of 20 %-30 % of thromboembolic events rather than bleeding events in the acute COVID-19 phase **[**7**]**. The severity and duration of a hyperinflammatory state with unknown persistence are probably associated with the risk of thromboembolic events in the

post-acute-COVID-19-illness phase [8]. Release of pro-inflammatory cytokines [9], disruption of normal coagulation pathway [10], complement activation [11-13], neutrophil extracellular traps [12, 14, 15], endothelial injury [16, 17-19], platelet-leukocyte interactions and platelet activation [20-22], and hypoxia [23] are the proposed mechanisms of the thrombo-inflammation. These mechanisms are similar to the pathophysiology that are present in thrombotic microangiopathy syndromes [24]. CORE-19, CISCO-19, and CORONA-VTE are the larger ongoing studies that will assist in establishing thromboembolic complications in the post-acute-COVID-19-illness phase [ 25, 26]. Due to lacking the need to frequently monitor the therapeutic levels and the lower risk of drug-drug interactions, low-molecular-weight heparin and direct oral anticoagulants are preferred anticoagulation drugs over vitamin K antagonists [27, 28]. Similar to provoked VTE, for patients with imaging-confirmed VTE, at least 3 months of therapeutic anticoagulation is recommended [29, 30]. In addition to comorbidities, such as immobility and cancer, the elevation of D-dimer levels (higher than two times the upper limit of the normal value) may be a benefit to risk-stratify cases at the highest risk of post-acute-COVID-19-illness thrombosis [25, 27, 28, 31]. Aspirin, an alternative antiplatelet agent for COVID-19 or post-acute-COVID-19-illness thromboprophylaxis has not yet been defined and is presently studied in cases managed as outpatients [9]. In hospital-discharge-COVID-19 patients with outpatient management, extended post-hospital discharge, up to 6 weeks and prolonged primary thromboprophylaxis, up to 45 days may provide a more favorable risk-benefit ratio in COVID-19 with an increase in thrombotic events during the acute COVID-19 phase, and this is currently being studied [32, 33].

In conclusion, in addition to post-acute-COVID-19-illness primary thromboprophylaxis, when appropriate, ambulation and physical activity should be recommended to all patients.

## References

1.Patell R, et al. “Post-discharge thrombosis and hemorrhage in patients with COVID-19”. Blood 2020; 136 : 1342-1346.

2.Robert LN, et al. “Post-discharge venous thromboembolism following hospital admission with COVID-19”. Blood 2020; 136 : 1347-1350.

3.Salisbury R, et al. “Incidence of symptomatic, image-confirmed venous thromboembolism following hospitalization for COVID-19 with 90-day follow-up”. Blood Adv 2020; 4 : 6230-6239.

4.Engelen M, et al. “Incidence of venous thromboembolism in patients discharged after COVID-19 hospitalization”. Res Pract Thromb Haemost 2021. Available at :

https://abstracts.isth.org/abstract/incidence-of-venous-thromboembolism-in-p[atients-discharged-after-covid-19-hospitalisation/ (accessed on May 28, 2021).

5.Pavoni V, et al. “Evaluation of coagulation function by rotation thromboelastometry in critically ill patients with severe COVID-19 pneumonia”. J Thromb Thrombolysis 2020; 50 : 281-286.

6.Chaudhary R, Kreutz RP, Bliden KP, Tantry US, Gurbel PA. “Personalizing antithrombotic therapy in COVID-19 : role of thromboelastography and thromboelastometry”. Thromb Haemost 2020; 120 : 1594-1596.

7.Connors JM, Levy JH. “COVID-19 and its implications for thrombosis and anticoagulation”. Blood 2020; 135 : 2033-2040.

8.Nalbandian A, Sehgal K, Gupta K, Madhavan MV, McGroder C, Stevens JS, et al. “Post-acute COVID-19 syndrome”. Nature Medicine 2021; 27 (April) : 601-615.

9.Bikdeli B, et al. “Pharmacological agents targeting thromboinflammation in COVID-19 : review and implications for future research”. Thromb Haemost 2020; 120 : 1004-1024.

10.Nougier C, et al. “Hypofibrinolytic state and high thrombin generation may play a major role in SARS-CoV-2 associated thrombosis”. J Thromb Haemost 2020; 18 : 2215-2219.

11.Ramlall V, et al. “Immune complement and coagulation dysfunction in adverse outcomes of SARS-CoV-2 infection”. Nat Med 2020; 26 : 1609-1615.

12.Skendros P, et al. “Complement and tissue factor-enriched neutrophil extracellular traps are key drivers in COVID-19 imunothrombosis”. J Clin Invest 2020; 130 : 6151-6157.

13.Cugno M, et al. “Complement activation in patients with COVID-19 : a novel therapeutic target”. J Allergy Clin Immunol 2020; 146 : 215-217.

14.Middleton EA, et al. “Neutrophil extracellular traps (NETS) contribute to immunothrombosis in COVID-19 acute respiratory distress syndrome”. Blood 2020; 136 : 1169-1179.

15.Zuo Y, et al. “Neutrophil extracellular traps in COVID-19”. JCI Insight 2020; 5 : e138999.

16.Ackermann M, Verleden SE, Kuehnel M, Haverich A, Welte T, Laenger F, et al. “Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in COVID-19”. N Engl J Med 2020; 383 : 120-128.

17.Varga Z, et al. “Endothelial cell infection and endotheliitis in COVID-19”. Lancet 2020; 395 : 1417-1418.

18.Goshuo G, et al. “Endotheliopathy in COVID-19-associated coagulopathy evidence from a single-center, cross-sectional study”. Lancet Haematol 2020; 7 : e575-e582.

19.Libby P, Lüscher T. “COVID-19 is in the end, an endothelial disease”. Eur Heart J 2020; 41 : 3038-3044.

20.Hottz ED, et al. “Platelet activation and platelet-monocyte aggregates formation trigger tissue factor expression in severe COVID-19 patients”. Blood 2020; 136 : 1330-1341.

21.Manne BK, et al. “Platelet gene expression and function in COVID-19 patients”. Blood 2020; 136 : 1317-1329.

22.Barret TJ, et al. “Platelet and vascular biomarkers associate with thrombosis and death in coronavirus disease”. Circ Res 2020. DOI : https://doi.org/10.1161/CIRCRESAHA.120.317803

23.Thachil J. “Hypoxia-an overlooked trigger for thrombosis in COVID-19 and other critically ill patients”. J Thromb Haemost 2020; 18 : 3109-3110.

24.Merrill JT, Erkan D, Winakur J, James JA. “Emerging evidence of a COVID-19 thrombotic syndrome has treatment implications”. Nat Rev Rheumatol 2020; 16 : 581-589.

25.Spyropoulos AC, et al. “Scientific and Standardization Committee communication : clinical guidance on the diagnosis, prevention, and treatment of venous thromboembolism in hospitalized patients with COVID-19”. J Thromb Haemost 2020; 18 : 1859-1865.

26.Mangion K, et al. “The Chief Scientist Office Cardiovascular and Pulmonary Imaging in SARS Coronavirus Disease-19 (CISCO-19) study”. Cardiovasc Res 2020; 2185-2196.

27.Bikdeli B, et al. “COVID-19 and thrombotic or thromboembolic disease : implications for prevention, antithrombotic therapy, and follow-up : JACC state-of-the-art review”. J Am Coll Cardiol 2020; 75 : 2950-2973.

28.Barnes GD, et al. “Thromboembolism and anticoagulant therapy during the COVID-19 pandemic : interim clinical guidance from the anticoagulation forum”. J Thromb Thrombolysis 2020; 50 : 72-81.

29.Bai C, et al. “Updated guidance on the management of COVID-19 : from an American Thoracic Society”/European Respiratory Society coordinated International Force (July 29, 2020). Eur Respir Rev 2020; 200287.

30.Moores LK, et al. “Prevention, diagnosis, and treatment of VTE in patients with coronavirus disease 2019 : CHEST Guidelines and Expert Panel report”. Chest 2020; 158 : 1143-1163.

31.COVID-19 and VTE/Anticoagulation : Frequent Asked Questions (American Society of Hematology, 2020). Available at : https://www.hematology.org/covid-19/covid-19-and-vte-anticoagulation (accessed on May 28, 2021).

32.Bajaj NS, et al. “Extended prophylaxis for venous thromboembolism after hospitalization for medical illness : a trial sequential and cumulative meta-analysis”. PLoS 2019; 16 : e1002797.

33.Chiasakul T, et al. “Extended vs standard-duration thromboprophylaxis in acutely ill medical patients : a systematic review and meta-analysis”. Thromb Res 2019; 184 : 58-61.