COVID-19 and SIC (!)

Ilja Nevzorov, PhD, Riikka Tulamo, MD, PhD, Anders Albäck, MD, PhD, Riitta Lassila, MD, PhD

PII: S0741-5214(20)31303-3

DOI: https://doi.org/10.1016/j.jvs.2020.05.047

Reference: YMVA 11368

To appear in: *Journal of Vascular Surgery*

Received Date: 14 April 2020

Accepted Date: 22 May 2020

Please cite this article as: Nevzorov I, Tulamo R, Albäck A, Lassila R, COVID-19 and SIC (!), *Journal of Vascular Surgery* (2020), doi: https://doi.org/10.1016/j.jvs.2020.05.047.

COVID-19 and SIC (!)

Ilja Nevzorov, PhD[1], Riikka Tulamo, MD, PhD[2], Anders Albäck, MD, PhD[2] and Riitta Lassila, MD, PhD[3,*].

[1] Faculty of Medicine, University of Helsinki, Helsinki, Finland.

[2] Department of Vascular Surgery, Helsinki University Hospital, University of Helsinki, Helsinki, Finland.

[3] Coagulation Disorders Unit, University of Helsinki, Departments of Haematology and Clinical Chemistry (HUSLAB Laboratory Services), Comprehensive Cancer Center, Helsinki University Hospital and Research Program in Systems Oncology, Faculty of Medicine, University of Helsinki, Helsinki, Finland; Helsinki University, Faculty of Medicine, Research Program in Oncology, Helsinki, Finland; Aplagon Oy, Helsinki, Finland.

* Corresponding Author: riitta.lassila@hus.fi

To the Editor,

Accurate risk stratification tools are paramount for optimal disease management. Patients with cardiovascular conditions, diabetes and cancer are most susceptible to COVID-19 complications leading to poor outcome[1]. These systemic diseases relate to enhanced fibrin formation and thromboinflammation. Indeed, severity of peripheral occlusive arterial disease correlates with the levels of both fibrinogen and its turnover measure D-dimer[2]. In severe COVID-19-infection, elevation of D-dimer and sepsis-induced coagulopathy (SIC), predicts poor prognosis. The incidence of venous thromboembolism (VTE) in patients with severe COVID-19 pneumonia is 25% (!)[3]. Furthermore, endothelial injury inherent to vascular procedures may predispose to coagulopathy in COVID-19. The benefit of low-molecular-weight heparin therapy is protection of critically ill patients against VTE, as well as its putative anti-inflammatory properties. Pulmonary

embolism (PE), triggered by severe infection, may be masked by the symptoms and signs of hypoxia in COVID-19. We advocate these considerations for vascular specialists.

A large retrospective Chinese cohort study[1] demonstrated that the fibrin turnover-measure D-dimer exceeding 1 µg/mL on admission was associated with an increased risk of in-hospital death (OR 20, 95% CI 6.5-61.56, P < .0001) in COVID-19 patients. Another retrospective study[4] assessed the benefits of anticoagulation on 28-day mortality, which does not appear to differ between heparin users (22%) and nonusers (mortality rates 30.3% vs 29.7%, respectively). However, patients with 6-fold D-dimer levels (3 µg/mL) to normal clearly benefited from anticoagulation, translating to lower mortality (32.8% vs 52.4%, P = .017). Therefore, D-dimer levels on admission are particularly useful for risk stratification in COVID-19 patients (Fig. 1).

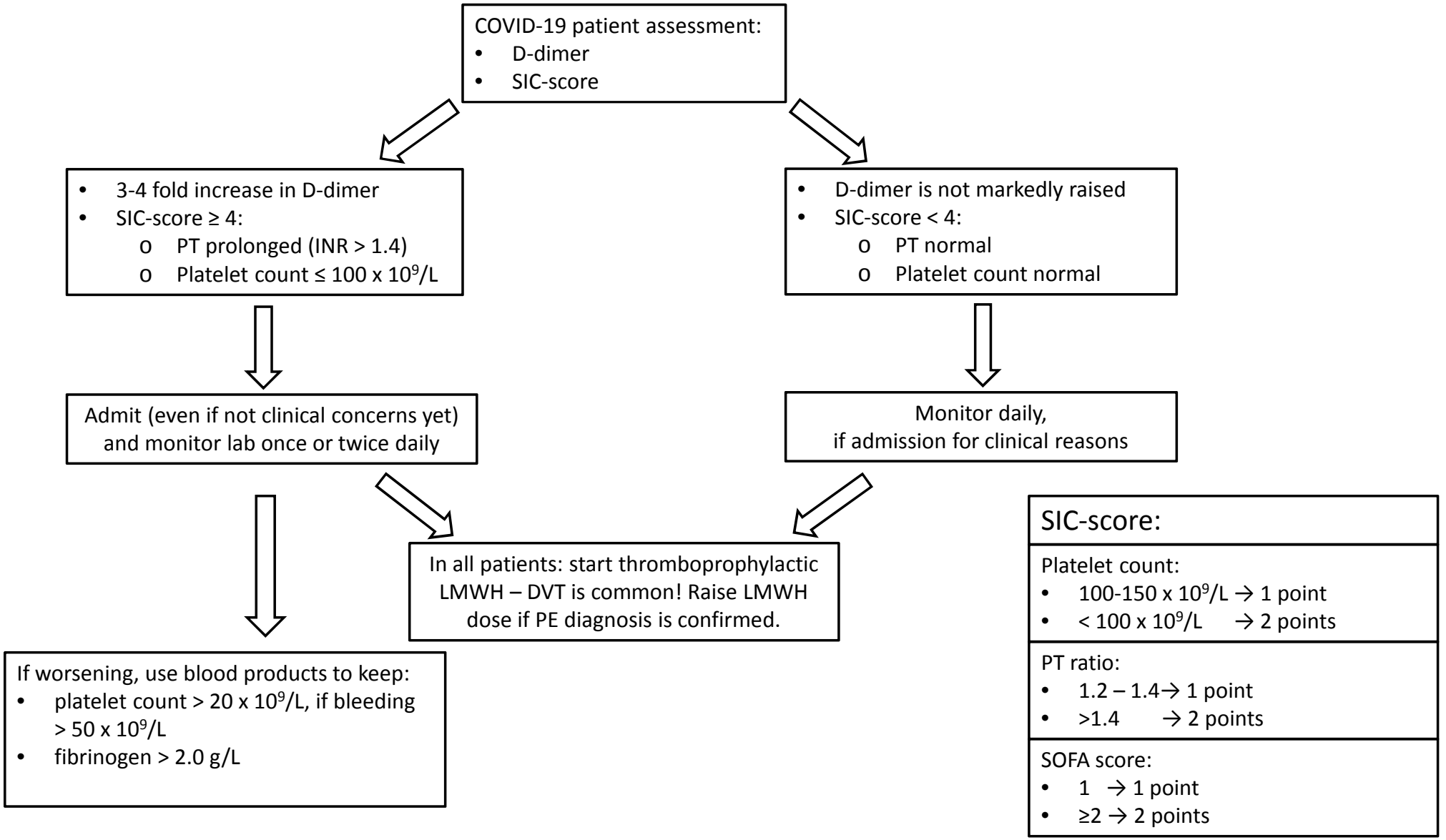
Another important predictor of mortality is the International Society of Thrombosis and Haemostasis (ISTH) SIC-score[5], which includes prothrombin time (ratio >1.5), platelet count (<100 $x10^9$/l) and sequential organ function assessment (SOFA-score). In the above-mentioned study[3], patients with ISTH SIC-score of ≥4 treated with anticoagulation showed again lower 28-day mortality rates than the untreated ones (40% vs 64%; P=.029).

To guarantee the best outcomes for patients we suggest that all medical professionals, including vascular specialists, adhere to ISTH guidelines on recognition and management of coagulopathy in COVID-19 based on D-dimer and SIC-scores as major prognostic factors[6] (Fig. 1).

References:

1. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet.* 2020;395:1054-62.
2. Lassila R, Peltonen S, Lepäntalo M, Saarinen O, Kauhanen P, Manninen V. Severity of peripheral atherosclerosis is associated with fibrinogen and degradation of cross-linked fibrin. *Arterioscler Thromb Vasc Biol.* 1993;13:1738-1742.
3. Cui S, Chen S, Li X, Liu S, Wang F. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. *J Thromb Haemost*. 2020;00:1-4.Epub 2020 Apr 9.
4. Tang N, Bai H, Chen X, Gong J, Li D, Sun Z. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. *J Thromb Haemost*. 2020 May;18(5):1094-1099. Epub 2020 March 27.
5. Iba T, Nisio MD, Levy JH, Kitamura N, Thachil J. New criteria for sepsis-induced coagulopathy (SIC) following the revised sepsis definition: a retrospective analysis of a nationwide survey. *BMJ Open*. 2017;7(9):e017046.
6. Thachil J, Tang N, Gando S, Falanga A, Cattaneo M, Levi M, et al. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. *J Thromb Haemost*. 2020 May;18(5):1023-1026. Epub 2020 March 25.

Figure 1. Outline of the algorithm for the management of coagulopathy in COVID-19 based on D-dimer and SIC-score. DVT – deep vein thrombosis, PE – pulmonary embolism, LMWH – low molecular weight heparin, SIC – sepsis-induced coagulopathy.


COVID-19 patient assessment:
• D-dimer
• SIC-score
• 3-4 fold increase in D-dimer
• SIC-score ≥ 4:
o PT prolonged (INR > 1.4)
o Platelet count ≤ 100 x 10^9/L
• D-dimer is not markedly raised
• SIC-score < 4:
o PT normal
o Platelet count normal
Admit (even if not clinical concerns yet) and monitor lab once or twice daily
Monitor daily, if admission for clinical reasons
In all patients: start thromboprophylactic LMWH – DVT is common! Raise LMWH dose if PE diagnosis is confirmed.
If worsening, use blood products to keep:
• platelet count > 20 x 10^9/L, if bleeding > 50 x 10^9/L
• fibrinogen > 2.0 g/L
SIC-score:
Platelet count:
• 100-150 x 10^9/L → 1 point
• < 100 x 10^9/L → 2 points
PT ratio:
• 1.2 – 1.4→ 1 point
• >1.4 → 2 points
SOFA score:
• 1 → 1 point
• ≥2 → 2 points