

Suggestions for thromboprophylaxis and monitoring for in-hospital patients with COVID-19

Growing evidence from multiple retrospective cohorts indicates that hospitalised COVID-19 patients often could suffer from an excessive coagulation activation leading to an increased risk of venous and arterial thrombosis (including small calibre vessels) and a poor evolution¹. Notably, D-dimer level at the time of hospital admission is a predictor of the risk of ARDS development², the risk of intensive care admission and the risk of death³. An observational study among COVID-19 patients with elevated D-dimer at baseline showed that the 28-day mortality was lower in those receiving heparin than in those who did not⁴.

Based on the available literature and published recommendations from the International Society of Thrombosis and Hemostasis (<https://www.isth.org>), from the American Society of Haematology (<https://www.hematology.org/covid-19>) and from the Society for Thrombosis and Haemostasis Research (<http://gth-online.org>), the Working Party of Hemostasis (Swiss Society of Hematology) proposes the following on pharmacological thromboprophylaxis in COVID-19 patients in the acute setting. Suggestions will be regularly updated:

- All in-hospital COVID-19 patients should receive a pharmacological thromboprophylaxis according to a risk stratification score, unless contraindicated.
- In patients with CrCl > 30 mL/min, low molecular weight heparin (LMWH) should be administered according to license. An increased dose should be considered in overweight patients (>100Kg).
- In patients with CrCl < 30 ml/min, unfractionated heparin (UHF) SC b.i.d or t.i.d or UHF IV should be administered according to license. An increased dose should be considered in overweight patients (>100Kg).
- Anti-Xa activity should be monitored when indicated (e.g. evidence of renal dysfunction).
- Antithrombin should not be monitored but could be considered on an individual basis in case of disseminated intravascular coagulation or sepsis-induced coagulopathy
- We suggest to regularly monitor PT, D-dimers, fibrinogen, the platelet count, LDH, creatinine and ALT (daily or at least 2-3x a week).
- In patients in intensive care with large increase of D-dimer or strong inflammation or sign of hepatic or renal organ dysfunction or imminent respiratory failure, intermediate or therapeutic posology LMWH or UHF should be considered, according to the bleeding risk.
- Heparin-induced thrombocytopenia (HIT) should be considered in patients with fluctuations in platelet counts or signs of heparin resistance.

- In patients under ECMO treatment we suggest maintaining UFH in the therapeutic anti-Xa activity range.
- There are no data on the use of direct oral anticoagulants.

Working Party of Hemostasis: Lorenzo Alberio, Anne Angelillo-Scherrer, Alessandro Casini, Pierre Fontana, Bernhard Gerber, Lukas Graf, Inga Hegemann, Wolfgang Korte, Johanna Kremer Hovinga, Asmis Lars, Thomas Lecompte, Maria Martinez, Michael Nagler, Jan-Dirk Studt, Dimitrios Tsakiris, Walter Wuillemin.

1. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J Thromb Haemost.* 2020;18(4):844-847.
2. Wu C, Chen X, Cai Y, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Intern Med.* 2020.
3. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* 2020;395(10223):497-506.
4. Zhou F, Yu T, Du R, 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(10229):1054-1062.