Proposals for thromboprophylaxis and monitoring in hospitalized patients with COVID-19 (1. update, 14.5.2020)

Growing evidence indicates that hospitalised COVID-19 patients may suffer from excessive coagulation activation, with an increased risk of venous and arterial thrombosis (including small calibre vessels) and a poor evolution [1]. Notably, D-dimer level at the time of hospital admission is a predictor of the risk of ARDS development [2], of intensive care admission, and of death [3]. An observational study among COVID-19 patients with elevated D-dimers upon hospital admission showed that the 28-day mortality was lower in those receiving heparin than in those who did not [4]. Another recent observational study indicates that anticoagulation might be associated with improved outcomes among hospitalized COVID-19 patients [5].

Based on the available literature and published recommendations from the International Society on Thrombosis and Haemostasis (www.isth.org), the American Society of Hematology (www.hematology.org/covid-19), and the Society for Thrombosis and Haemostasis Research (www.gth-online.org), the Working Party Hemostasis of the Swiss Society of Hematology presents the following proposals on the pharmacological thromboprophylaxis in COVID-19 patients in the acute setting.

- All hospitalized COVID-19 patients should receive pharmacological thromboprophylaxis unless contraindicated. Low molecular weight-heparin (LMWH) should be used as a standard, taking into account bleeding risk and renal function. An increased dose should be considered in overweight patients (>100 kg).
- In patients with additional prothrombotic risk factors (such as intensive care treatment, rapid increase of D-dimers while on thromboprophylaxis, severe inflammation, past history of thromboembolism, signs of hepatic or renal dysfunction or imminent respiratory failure) an intensification of the pharmacological thromboprophylaxis should be considered, e.g. LMWH at an intermediate dose (as a single dose of 100 U/kg body weight, or as a prophylactic dose twice daily if a more homogenous anti-Xa activity is desired) taking into account bleeding risk and renal function.
- A therapeutic dose of anticoagulation is recommended in patients with acute thromboembolism or treated with extracorporeal membrane oxygenation (ECMO). In ECMO or hemodialysis patients, UFH should be maintained in the therapeutic range of anti-Xa activity.We discourage monitoring of UFH by aPTT because it may be altered by high FVIII levels.

- At present, there is no solid evidence supporting pharmacological thromboprophylaxis in all COVID-19 outpatients. We suggest considering an extended pharmacological thromboprophylaxis for at least 10 days after hospital discharge in patients with additional prothrombotic risk factors (such as past history of thromboembolism, active malignancy, major surgery within the last 3 months, BMI >30 kg/m^2, persistent reduced mobility, sickle cell disease, etc.) who do not have a high risk of bleeding.
- At present, there are no data supporting the use of direct oral anticoagulants for pharmacological thromboprophylaxis in COVID-19 patients.
- We suggest daily coagulation monitoring including prothrombin time (Quick), D-dimers, fibrinogen, and platelet count. Monitoring of antithrombin is not required routinely but can be considered on an individual basis (e.g., in DIC, sepsis-induced coagulopathy, heparin resistance). LDH, creatinine, ALT, and ferritin should also be monitored regularly (at least 2-3x/week).
- Anti-Xa activity should be monitored when indicated (e.g., severe renal insufficiency, UFH at therapeutic dose, suspected reduced heparin efficacy).
- Possible heparin-induced thrombocytopenia (HIT) should be considered in patients with fluctuating platelet counts or signs of heparin resistance.
- Wherever possible, patients should be offered participation in clinical trials (e.g., COVID-HEP, NCT 04345848)

Working Party of Hemostasis: Lorenzo Alberio, Anne Angelillo-Scherrer, Alessandro Casini, Pierre Fontana, Bernhard Gerber, Lukas Graf, Inga Hegemann, Wolfang 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; doi: 10.1001/jamainternmed.2020.0994.
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.
5. Paranipe I, Fuster V, Lala A, et al. Association of treatment dose anticoagulation with in-hospital survival among hospitalized patients withnCOVID-19. J Am Coll Cardiol 2020; doi: 10.1016/j.jacc.2020.05.001.