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332.ANTICOAGULATION AND ANTITHROMBOTIC THERAPY | NOVEMBER 5, 2020

# COVID-19-Associated Coagulopathy: Safety and Efficacy of Prophylactic Anticoagulation Therapy in Hospitalized Adults with COVID-19

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***Blood*** **(2020) 136 (Supplement 1) : 11.**

**http://doi.org/10.1182/blood-2020-141951**

**Background:**

COVID-19-associated coagulopathy increases mortality in patients with COVID-19 infection. The International Society of Thrombosis and Hemostasis (ISTH) has published a guidance document recommending thromboprophylaxis with low-molecular weight heparin (LMWH) for all hospitalized patients with COVID-19. Despite standard dose LMWH thromboprophylaxis, arterial and venous thrombotic events occur in up to 30-40% of COVID-19 patients admitted to the intensive care unit (ICU). It is not known if patients with coagulopathy from COVID-19 benefit from higher levels of prophylactic anticoagulation therapy. No data exist regarding the comparative safety or efficacy of intermediate dose versus standard prophylactic dose LMWH.

**Study Design and Methods:**

This is a multi-center, randomized, open-label study (NCT04360824) comparing standard prophylactic dose enoxaparin (40 mg SC daily if BMI < 30 kg/$m^2$; 30 mg SC twice daily or 40 mg SC twice daily if BMI ≥ 30 kg/$m^2$) versus intermediate-weight adjusted dose enoxaparin (1 mg/kg SC daily if BMI < 30 kg/$m^2$ or 0.5 mg/kg SC twice daily if BMI ≥ 30 kg/$m^2$) in hospitalized patients with laboratory-confirmed SARS-CoV-2 infection who are either admitted to an intensive care unit or have a modified ISTH Overt DIC score ≥ 3.

**Objectives:**

The primary endpoint is to compare all-cause 30-day mortality of patients treated with standard prophylactic dose versus intermediate-dose enoxaparin. The secondary endpoints are to determine whether the use of standard prophylactic dose versus intermediate dose enoxaparin impacts major bleeding, arterial thrombosis, venous thrombosis, time to intubation or transfusion of blood products. The exploratory endpoints are to determine the effects of SARS-CoV-2 infection on laboratory coagulation parameters to better understand the mechanism of COVID-19 coagulopathy compared to healthy control subjects; parameters include citrullinated histone H3 (H3Cit), a component of neutrophil extracellular traps. The null hypothesis is that intermediate dose enoxaparin (intervention arm) will have a mortality rate that is not less than standard prophylactic dose enoxaparin (standard of care arm). Assuming a true margin of 20%, a sample size of 82 patients in each arm of the study is required to have 80% power when testing for a difference.

**Baseline Data:**

Three centers are currently enrolling patients. As of August 1, 2020, we have enrolled 52 patients (28 males and 24 females) with a median age of 61 years (range 24-80). 51% were Caucasian, 36% Hispanic, and 16% other ethnicities. Median BMI was 31 kg/$m^2$ (range 20-52). Baseline D-Dimer was elevated in 95% of participants with a median of 2.23 mg/mL (range 0.39-40.32). The majority of participants had normal baseline PT, PTT, and platelet levels. All patients had fibrinogen levels over 100 mg/dL with a median of 607 mg/dL. Plasma H3Cit was elevated significantly in patients with COVID-19 (n = 21) vs healthy control subjects (n = 10) (6.48 vs 1.09 ng/mL, P = 0.001).

**Conclusion:**

Baseline data for the first 52 patients enrolled confirm the presence of multiple risk factors for thrombosis such as elevated BMI, D dimer, and plasma markers of neutrophil extracellular traps. In contrast to initial

reports from China, the prevalence of thrombocytopenia and hypofibrinogenemia was very low in our cohort. Hispanics represented 36% of our study population, compared with 19% of overall COVID-19 infections in the region, suggesting a higher severity of illness in this subpopulation. The enrollment of this trial is ongoing with the addition of sites that have larger African American populations. As safety and efficacy data mature, this study will help clarify the optimum dose of prophylactic enoxaparin to prevent COVID-19 associated coagulopathy.

**Disclosures**

No relevant conflicts of interest to declare.

# Author notes

* Asterisk with author names denotes non-ASH members.

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