Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Clinical Microbiology and Infection 27 (2021) 1188–1189

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Letter to the Editor

Personalized prophylactic anticoagulation in hospitalized patients with Covid-19 – The role of anti-Xa monitoring

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ARTICLE INFO

Article history:
Received 14 December 2020
Received in revised form
8 April 2021
Accepted 21 April 2021
Available online 29 April 2021

Editor: J. Rodriguez-Baño

To the Editor,

COVID-19 is a public health emergency. Over the last few months, there has been increasing evidence of a strong association between severe COVID-19 and a prothrombotic state, which has been attributed to inflammatory immunopathology and endothelial inflammation [1]. We read with great interest two recent studies reporting on the prevalence of venous thromboembolism in patients with COVID-19 [2,3]. Interestingly, the prevalence of deep venous thrombosis (DVT) and pulmonary embolism (PE) is over 10% in almost all studies, implying that one of the primary therapeutic goals should be the implementation of adequate thromboprophylaxis in these patients. Accordingly, in a clinical vignette that was recently published in the *New England Journal of Medicine*, a clinical scenario of a patient hospitalized with severe COVID-19 was presented, and two different anticoagulation strategies discussed [4]. Most experts suggest an intensified anticoagulation regimen, mostly including an intermediate dose of low molecular weight heparin (e.g. enoxaparin, 0.5 mg/kg twice daily), even though there is no clear clinical evidence supporting the efficacy of this strategy in patients with COVID-19, as was also recently shown in critically ill patients with COVID-19 [5]. Indeed, this intermediate dosing regimen of enoxaparin, which appears to be safe in patients with COVID-19, has been extrapolated from studies in trauma patients [6].

Instead, anti-Xa monitoring of low molecular weight heparin is recommended for patients with renal dysfunction, severe obesity or patients at high risk for thrombosis/bleeding. In our department, we followed a protocol of an individualized prophylactic anticoagulation based on anti-Xa measurement. Specifically, we used sequential anti-Xa measurement to tailor the dose of enoxaparin, aiming for anti-Xa levels of 0.4–0.5 IU/mL (the higher tertile of prophylactic range). Anti-Xa was measured every 2–3 days after every dose change of enoxaparin. Surprisingly, among 16 patients admitted due to COVID-19 (Table 1) who were initially treated with enoxaparin 40 mg/daily, 13 (81.3%) patients needed dose adjustment due to lower than 0.4 IU/mL anti-Xa levels (interestingly, 2 of 13 (15.4%) patients had anti-Xa levels <0.2 IU/mL). Based on this approach, a median enoxaparin dose of 60 mg (interquartile range 50–80 mg) once daily was needed to successfully tailor prophylaxis in 11 out of 13 patients (84.6%), with only one (7.7%) having levels above the target, and only one (7.7%) having levels between 0.3 and 0.4 IU/mL. Importantly, no patient in our small case series died or developed clinically evident thrombosis or bleeding. Thus, sequential anti-Xa measurement could be a safe method to successfully tailor an individualized prophylactic anticoagulation treatment in hospitalized COVID-19 patients. To that end, a future randomized study comparing patients treated with prophylactic enoxaparin to patients treated with a tailored approach based on anti-Xa monitoring could be performed.

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https://doi.org/10.1016/j.cmi.2021.04.024

Table 1
Characteristics of patients hospitalized with COVID-19

	COVID-19 patients ($n = 16$)
Age (years), median (IQR)	57 (46.8–65)
Male gender, *n* (%)	11 (68.8)
Severe COVID-19[a], *n* (%)	13 (81.3)
Duration of symptoms (days) before admission, median (IQR)	7 (5–7.8)
Lower pO_2/FiO_2 ratio, mmHg (IQR)	199.3 (132.6–274.6)
Maximum oxygen requirements (%FiO_2), median (IQR)	38 (26.3–50)
Patients admitted to the ICU[b], *n* (%)	3 (18.8)
CRP (mg/L), median (IQR)	6.7 (5.1–13.4)
D-dimers (ng/mL), median (IQR)	0.43 (0.27–-0.7)
Anti-Xa on enoxaparin 40 mg once a day (IU/mL), median (IQR)	0.28 (0.22–0.35)
Anti-Xa on tailored enoxaparin dose (IU/mL), median (IQR)	0.46 (0.44–0.48)
Duration of hospitalization (days), median (IQR)	8 (6–13)

CRP, C-reactive protein; ICU, intensive care unit; IQR, interquartile range; IU, international units.
[a] Severe COVID-19 defined as dyspnoea, respiratory frequency 30/min, blood oxygen saturation ≤93%, partial pressure of arterial oxygen to fraction of inspired oxygen ratio <300, and/or lung infiltrates >50% within 24 to 48 hr.
[b] No patient developed bleeding, thrombosis, need for intubation, and no patients died.

Transparency declaration

This research has not received funding from any source. D.P.K. reports lecture honoraria from Pfizer, MSD, ViiV and Angelini. T.D.F. reports lecture honoraria from Boehringer Ingelheim, Mylan, Astra Zeneca, Lilly, Recordati, Bausch Health, Servier and Innovis. P.I., E.K. and G.C. have no conflict of interest.

Author contributions

D.P.K. contributed to the conceptualization, investigation, methodology, project administration, supervision and writing of the original draft. P.I. and T.D.F. contributed to data curation, formal analysis, investigation, methodology, software, validation, and writing of the original draft. E.K. and G.C. contributed to validation and writing, review and editing of the manuscript.

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