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.

Thrombosis Research 191 (2020) 29

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Editorial

Where do we stand with antithrombotic prophylaxis in patients with COVID-19?

From Dec 2019 onwards, an outbreak of cases of pneumonia associated with novel Coronavirus (SARS-CoV2) has been reported in China. The disease, defined 'COVID-19', since Jan 2020 has spread in Italy, particularly in Milan and other cities in Northern Italy. On March 11, the WHO declared COVID-19 a pandemic. The mortality rate in Italy exceeds 12% and is up to 26% in intensive care units (ICUs) [1]. After an early phase characterized by mild symptoms, patients with COVID-19 infection may develop an interstitial pneumonia associated with an acute inflammatory state [2]. Autopsy findings showed the occlusion on the small vessels of the lungs (and also other organs) [3], possibly because of an intense cytokines secretion associated to an endothelial impairment bringing to the activation of the coagulation cascade.

An interim guidance on COVID-19 coagulopathy released on Mar 25 by experts of the International Society of Thrombosis and Haemostasis (ISTH) suggests a conventional prophylactic dose of enoxaparin 4000 U (or equivalent dose of another low molecular weight heparin) once daily [4]. However, the same prophylactic dose is insufficient to prevent venous thromboembolism in non-COVID-19 ICU patients, who develop pulmonary embolism 10% of cases [5]. This figure was perceived even higher since the beginning of epidemic in many ICUs, and Klok and colleagues confirmed a 31% cumulative incidence of thrombosis in a cohort of 184 ICU patients with COVID-19, despite antithrombotic prophylaxis at least at the conventional doses. The vast majority of the events (81%) were pulmonary emboli [6]. It is easy to imagine how pulmonary embolism can dramatically worsen the respiratory function of COVID-19 patients and increase their mortality. Another aspect that should be considered is the difficulty to perform CT-scan in many hospitals due to the emergency that several countries are facing. Not all ICU patients who deserve a chest CT scan for suspected pulmonary embolism are promptly diagnosed and indirect objective examinations, i.e., echocardiography or lung ultrasonography do not help. It may be that an unexpected worsening of the respiratory function together with a sudden increase of D-dimer levels are suggestive of pulmonary embolism, but this remains to be demonstrated. To date, D-dimer levels help in predicting the severity of the disease and patient's prognosis, as patients with high levels at admission die more than those with normal levels [7].

With this panorama and all the uncertainties of care of ICU patients with COVID-19, we believe that when pulmonary embolism is suspected objective diagnosis should be performed quickly and appropriate heparin doses administered. If diagnosis is delayed, consider subtherapeutic or therapeutic heparin regimens in patients with low risk of bleeding. On Apr 11, the Italian Medicines Agency (AIFA) published a document on heparin use in COVID-19 patients, suggesting doses close to therapeutic ones in severe cases, despite the lack of scientific evidence. Further studies are urgently needed to establish the optimal heparin treatment in ICU patients with COVID-19.

Funding

The authors received no specific funding for this work.

Declaration of competing interest

The authors do not declare any conflict of interest.

References

[1] G. Grasselli, A. Zangrillo, A. Zanella, Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy, JAMA (2020), https://doi.org/10.1001/jama.2020.5394.
[2] C.C. Lai, T.P. Shih, W.C. Ko, et al., Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): the epidemic and the challenges, Int. J. Antimicrob. Agents 55 (3) (2020) 105924.
[3] T. Zhang, L.X. Sun, R.E. Feng, et al., Comparison of clinical and pathological features between severe acute respiratory syndrome and coronavirus disease 2019, Zhonghua Jie He He Hu Xi Za Zhi 43 (0) (2020) E040.
[4] J. Thachil, N. Tang, S. Gando, et al., ISTH interim guidance on recognition and management of coagulopathy in COVID-19, J. Thromb. Haemost. (2010), https://doi.org/10.1111/jth.14810 (in press).
[5] M. Bahloul, K. Regaieg, M. Dlela, et al., Pulmonary embolism in intensive care units: more frequent or more known, Clin. Respir. J. 13 (8) (2019) 513–520.
[6] F.A. Klok, M.J.H.A. Kruip, N.J.M. van der Meer, et al., Incidence of thrombotic complications in critically ill ICU patients with COVID-19, Thromb. Res. (2020), https://doi.org/10.1016/j.thromres.2020.04.013.
[7] N. Tang, D. Li, X. Wang, Z. Sun, et al., Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia, J. Thromb. Haemost. 18 (4) (2020) 844–847.

Alessandro Ciavarella[a,b], Flora Peyvandi[b,c], Ida Martinelli[b,*]
[a] *Interdisciplinary Department of Medicine, University of Bari, Bari, Italy*
[b] *Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico, A. Bianchi Bonomi Hemophilia and Thrombosis Center, Milan, Italy*
[c] *Department of Pathophysiology and Transplantation for Health, University of Milan, Milan, Italy*
E-mail address: ida.martinelli@policlinico.mi.it (I. Martinelli).

* Corresponding author at: Fondazione IRCCS Ca' Granda-Ospedale Maggiore Policlinico, A. Bianchi Bonomi Hemophilia and Thrombosis Center, via Pace 9, Milan 20122, Italy.

https://doi.org/10.1016/j.thromres.2020.04.023
Received 16 April 2020; Accepted 17 April 2020
Available online 20 April 2020
0049-3848/