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.

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Letter to the Editors-in-Chief

COVID-19 associated pulmonary thrombosis

Dear editor,

I have read with great interest the recent article by Klok et al., showing that the cumulative incidence of thrombotic complications in patients with COVID-19 admitted to the intensive care unit (ICU), is extremely high (> 30%) [1]. The authors note that the most frequent complication was pulmonary embolism (PE), despite the use of thrombosis prophylaxis with low molecular weight heparin (LMWH).

'Embolism' comes from the Greek émbolos, meaning 'stopper' or 'plug'. In case of PE, the general concept of its pathophysiology lies in the formation of thrombi in the deep veins of the legs, pelvis or arms, that after dislodging circulate throughout the bloodstream and then blocks ('embolize') the pulmonary arteries [2].

However, in case of COVID-19, is has been hypothesized that the pathophysiology of PE is different, and local thrombi are formed in the lung vessels due to a local inflammatory process rather than the classical emboli coming from elsewhere out of the body [3].

It is known that the coagulation pathway can be activated through the contact system and kallikrein/kinin system (KKS) [4]. Because the KKS is dysregulated by binding of SARS-CoV-2 to the ACE-2 receptor of the type II pneumocytes, this may be a plausible mechanism for the noted interaction between COVID-19 and thrombosis of lung vessels [5]. While this is believed to be a relative late manifestation of severe COVID-19, it is of interest whether the observed median duration of 7 days to the thrombotic event is truly the median days after first onset of COVID-19 symptoms [1].

Furthermore, as the pathophysiology of thrombotic disease differs, it can be questioned whether the standard therapy of PE (either prophylactic or therapeutic) with LMWH, direct oral anticoagulants or vitamin K antagonist, will have similar efficacy and safety in COVID-19 patients. In the study of Klok et al., prophylactic use of different doses of LMWH did not prevent thrombotic complications but, as all patients did use LMWH, it may have been a much higher incidence without LMWH prophylaxis or an even lower incidence in case therapeutic anticoagulation had been used [1]. Therefore, as 9% of the patients did use therapeutic anticoagulation at admission, it would be of special interest to know whether the cumulative incidence of thrombotic complications within this subgroup was indeed lower.

A recent retrospective study showed that the use of thrombosis prophylaxis was associated with a lower 28-day mortality in COVID-19 patients, but only in those with either a high sepsis-induced coagulopathy score (≥4) or high D-dimer result (≥3.0 mg/l) [6]. The study by Klok et al. also illustrated that coagulopathy in COVID-19 is strongly associated with thrombosis [1]. These data suggest that thrombotic complications particularly occur at a relative late stage of severe and prolonged inflammation in COVID-19 disease (e.g. the ICU setting) [3,5]. Based on their findings, the authors recommend to use high-dose prophylactic LMWH for all COVID-19 patients, including those admitted at the general ward [1]. Though, I agree with it, it should be stressed that this recommendation is not yet evidence-based. Ideally, randomized controlled clinical trials should evaluate the benefit and risks of different doses of LMWH or other anticoagulants in COVID-19 patients. Moreover, as an inflammatory cascade seems to be the driving force behind thrombotic events, the authors should also discuss the potential role of anti-inflammatory strategies to prevent thrombosis.

Finally, the term PE should be avoided in COVID-19 patients as this might be misleading. Therefore, I'll suggest to use a new name such as 'COVID-19 associated pulmonary thrombosis' or as others propose 'Microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome (MicroCLOTS)' [3].

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None.

Declaration of competing interest

None to declare.

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