

# Rebuttal to letter "Is thromboprophylaxis with high-dose enoxaparin really necessary for COVID-19 patients? A new "prudent" randomised clinical trial"

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Dear Sir,

We appreciate the interest of Cattaneo and Morici in the Siset position paper on COVID-19 and haemostasis<sup>1,2</sup>.

In their comments<sup>1</sup>, they underline several interesting points relevant to the management of venous thrombosis prophylaxis in COVID-19 patients.

We agree that stronger evidence from properly designed, randomised controlled trials is urgently needed. It would be desirable that clinical trials compare efficacy and safety of different doses and schedules of administration of either unfractionated heparin (UFH) or low molecular weight heparin in improving the clinical course of the disease in a well-characterised clinical subset of COVID-19 patients. Achieving this goal requires careful stratification of their thrombotic risk, taking into consideration the care setting (i.e., intensive or less intensive care units) in which the patients were treated. Apparently, the trial designed by Cattaneo and Morici will only enrol patients admitted to non-intensive care units.

Pending further evidence, our recommendation regarding the need to provide antithrombotic prophylaxis to all hospitalised COVID-19 patients, is a reasonable one, and is in agreement with that provided by the World Health Organization<sup>3</sup>. Indeed, it is well known that hospitalised patients with acute medical illness, including infections such as pneumonia, are at increased risk of VTE.

We are aware that there are no risk assessment models that have been specifically validated in this particular setting. Nevertheless, most hospitalised COVID-19 patients have multiple risk factors for venous thromboembolism (VTE), such as age >70 years, reduced mobility, and obesity, besides the impending inflammatory status, meaning they should be considered for VTE prophylaxis according to the Padua score. Moreover, there are increasing laboratory data showing a state of hypercoagulability in severe COVID-19 patients, thus supporting the use of antithrombotic prophylaxis or treatment<sup>4</sup>.

In our paper, we wanted to suggest that the rate of micro-pulmonary embolism could be actually higher than that reported, since it is difficult to obtain a confirmed diagnosis, either objective or autoptical. Indeed, we are aware that the question about the rate of objectively confirmed VTE in more severe COVID-19 patients is still unanswered, given the paucity of data about the incidence of VTE according to the severity of the disease.

Arrived: 27 April 2020

Accepted: 28 April 2020

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In this regard, an incidence of symptomatic pulmonary embolism of approximately 20% has been reported in COVID-19 patients admitted to intensive care units, despite properly administered VTE prophylaxis<sup>5</sup>.

We strongly endorse any effort by the scientific community to rapidly collect evidence from basic and clinical research to improve our ability to tackle this global health issue.

*The Authors declare no conflicts of interest.*

## REFERENCES

1. Cattaneo M, Morici N. Is thromboprophylaxis with high-dose enoparin really necessary for COVID-19 patients? A new “prudent” randomized clinical trial. *Blood Transfus* 2020; **18**: 237-8.
2. Marietta M, Ageno W, Artoni A, et al. COVID-19 and haemostasis: a position paper from Italian Society on Thrombosis and Haemostasis (SISET). *Blood Transfus* 2020; **18**: 167-9.
3. World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected. Interim guidance 28 January 2020. Accessible at: <https://www.who.int/docs/defaultsource/coronaviruse/clinical-management-of-novel-cov.pdf>. Accessed on 27/04/2020.
4. Panigada M, Bottino N, Tagliabue P, et al. Hypercoagulability of COVID-19 patients in Intensive Care Unit. A Report of thromboelastography findings and other parameters of hemostasis. *J Thromb and Haemost* 2020; doi: 10.1111/jth.14850. [Epub ahead of print]
5. Poissy J, Goutay J, Caplan M, et al. Lille ICU Haemostasis COVID-19 group. Pulmonary embolism in COVID-19 patients: awareness of an increased prevalence. *Circulation* 2020; doi: 10.1161/CIRCULATIONAHA.120.047430. [Epub ahead of print].



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