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LETTER TO THE EDITOR

Type and dose of heparin in Covid-19: Reply

We thank the authors for their comments and feedback on the International Society on Thrombosis and Haemostasis interim guidance. Hypercoagulability is indeed a significant issue in Covid-19, and the hemostatic system is shifted markedly toward the procoagulant side in these patients. However, we cannot yet be certain that unfractionated heparin (UFH) is better than low molecular weight heparin (LMWH) in this scenario. Although UFH has been used for several years, it does have practical issues, mainly with respect to the need for frequent monitoring using activated partial thromboplastin time.[1,2] In addition, as the authors pointed out correctly, markedly increased acute phase reactants including fibrinogen could contribute to heparin resistance making the use of UFH problematic (much more than LMWH).[2] Among the reasons for heparin resistance, antithrombin deficiency is not common in Covid-19 patients, at least in the published literature.[3] Despite these issues, UFH may still be preferred if there is marked renal impairment or need for reversibility for an urgent intervention.[4] One of the latter situations is if the patients progress despite anticoagulant therapy. The authors of the letter had recently published a case series on the use of tissue plasminogen activator in C,-19 patients which is certainly a consideration in patients who progress despite anticoagulant therapy.[5]

At the time of writing the interim document, our aim was to highlight the urgent need to consider thromboprophylaxis in all patients who require hospital admission for Covid-19 to mitigate poor outcomes from the marked hypercoagulability. We do recognize that, since then, it has frequently been suggested that higher doses of LMWH be given to Covid-19 patients to prevent venous thromboembolism. However, there is no demonstration that standard prophylactic doses are insufficient to prevent it. Pulmonary vessel occlusions that are observed in severe Covid-19 patients are caused by pulmonary thrombi, whose pathogenesis is unclear but likely to be associated with the severe pulmonary inflammation. Concerning the type of heparin, we cannot be certain that one type is better than the other; in other words, it is difficult to say UFH is better than LMWH. LMWH was chosen in the guidance because of the ease of use, no need for laboratory monitoring, and familiarity among the spectrum of doctors with varying experience. The question of whether *therapeutic* doses of either UFH or LMWH should be considered for all patients is currently unknown and the authors would currently reserve such a dose for those who have confirmed thrombosis including filter thrombosis. We are aware however that therapeutic dose is being administered in some centers where there is very high suspicion of pulmonary embolism and imaging is impractical. Although these approaches are reasonable, we stress that these approaches are undertaken in a trial setting.

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Final decision: David Lillicrap and 17-Apr-2020

CONFLICT OF INTEREST

Dr. Thachil has received honoraria from Bayer, BMS-Pfizer, Daichii-Sankyo, Boehringer, Mitsubishi, Novo Nordisk, Octapharma, Novartis, Amgen, Norgine, Alexion, Sobi, and CSL-Behring. All other authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Jecko Thachil and Marco Cattaneo wrote the response. Ning Tang, Satoshi Gando, Anna Falanga, Marcel Levi, Cary Clark, and Tsohiaki Iba gave comments. All authors approved the final submission.

Jecko Thachil[1]
Ning Tang[2]
Satoshi Gando[3]
Anna Falanga[4]
Marcel Levi[5]
Cary Clark[6]
Toshiaki Iba[7]
Marco Cattaneo[8]

[1]*Department of Haematology, Manchester University Hospitals, Manchester, UK*
[2]*Tongji Hospital, Huazhong University of Science and Technology, Wuhan, China*
[3]*Department of Acute and Critical Care Medicine, Sapporo Higashi Tokushukai Hospital, Sapporo, Japan*
[4]*Depatment of Medicine and Surgery, University of Milan Bicocca, Hospital Papa Giovanni, XXIII, Bergamo, Italy*
[5]*Department of Medicine and Cardio-metabolic Programme-NIHR UCLH/UCL BRC, University College London Hospitals NHS Foundation Trust, London, UK*
[6]*Director of Programs and Education, International Society on Thrombosis and Haemostasis, Carrboro, UK*
[7]*Department of Emergency and Disaster Medicine, Juntendo University Graduate School of Medicine, Tokyo, Japan*
[8]*ASST Santi Paolo e Carlo, Dipartimento di Scienze della Salute, Università degli Studi di Milano, Milan, Italy*

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Correspondence
Jecko Thachil, Department of Haematology, Manchester Royal Infirmary, Oxford Road, Manchester, M13 9WL, UK.
Email: jecko.thachil@mft.nhs.uk

ORCID

Satoshi Gando https://orcid.org/0000-0002-3525-0750

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