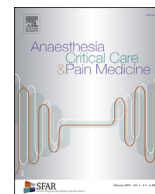




Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Correspondence

Reply to the authors of “Age-adjusted D-dimer cut-off levels to exclude venous thromboembolism in COVID-19 patients”


We thank the authors for taking interest in the 2021 updated GIHP/GFHT proposals on thromboprophylaxis for COVID-19 patients. The authors proposed to consider an age-adjusted D-dimer cut-off to exclude venous thromboembolism (VTE) in COVID-19 patients. We would like to clarify this misunderstanding regarding D-dimers during COVID-19. In non-COVID-19 patients, D-dimers have a very high sensitivity and negative predictive value to rule out VTE, thus guidelines recommend their measurement and propose an age-adjusted cut-off as an alternative to the fixed D-dimer cut-off [1,2]. Nevertheless, such guidelines concern outpatients or emergency department patients with low or intermediate clinical probability of having VTE. Guidelines also specify that D-dimer level cannot be used to rule out VTE in high-pretest probability patients. As a result, D-dimers cannot be used to exclude VTE in critically ill COVID-19 patients: they are not outpatients, their D-dimer levels are always increased and their probability of having VTE is high. In our proposals, we suggested using D-dimer level and its dynamics not to exclude VTE but to define a subgroup of critically ill COVID-19 patients exposed to a very high thrombotic risk. Indeed, a D-dimer level greater than 5 µg/mL, or an abrupt rise in D-dimer level were associated with a high positive predictive value for the diagnosis of thrombosis, with thrombosis being diagnosed in more than 50% of these patients. We chose to consider these patients as having a thrombotic complication until proven otherwise, or about to have this complication, and suggested starting therapeutic dose anticoagulation. Based on data available in the literature, about 10–15% of all critically ill patients would be concerned by this proposal [3–5].

The variation in D-dimer levels with age adds to the lack of standardisation between D-dimer assays. This highlights the value of regular biological monitoring in critically ill patients to detect a sudden increase in D-dimer levels.

In conclusion, we suggest using D-dimers as a dynamic tool to identify a small subset of critically ill COVID-19 patients with a very high risk of thrombosis, who may benefit from anticoagulation at therapeutic dose. Such a preventive anticoagulation should not go beyond 7 to 10 days without screening for thrombosis, to minimise the bleeding risk, which then becomes predominant [6].

Conflicts of interest

The authors have no competing interest to declare.

References

- [1] Sanchez O, Benhamou Y, Bertoletti L, Constant J, Couturaud F, Delluc A, et al. Recommandations de bonne pratique pour la prise en charge de la maladie veineuse thromboembolique chez l'adulte. Version courte [Recommendations of good practice for the management of thromboembolic venous disease in adults. Short version]. *Rev Mal Respir* 2019;36(February (2)):249–83. <http://dx.doi.org/10.1016/j.rmr.2019.01.003>.
- [2] Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing GJ, Harjola VP, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). *Eur Heart J* 2020;41:543–603. <http://dx.doi.org/10.1093/eurheartj/ehz405>.
- [3] Zermatten MG, Pantet O, Gomez F, Schneider A, Méan M, Mazzolai L, et al. COVID-19 Interdisciplinary Collaboration - COVIDIC initiative. Utility of D-dimers and intermediate-dose prophylaxis for venous thromboembolism in critically ill patients with COVID-19. *Thromb Res* 2020;196:222–6. <http://dx.doi.org/10.1016/j.thromres.2020.08.027>.
- [4] Whyte MB, Kelly PA, Gonzalez E, Arya R, Roberts LN. Pulmonary embolism in hospitalised patients with COVID-19. *Thromb Res* 2020;195:95–9. <http://dx.doi.org/10.1016/j.thromres.2020.07.025>.
- [5] Nauka PC, Baron SW, Assa A, Mohrmann L, Jindal S, Oran E, et al. Utility of D-dimer in predicting venous thromboembolism in non-mechanically ventilated COVID-19 survivors. *Thromb Res* 2021;199:82–4. <http://dx.doi.org/10.1016/j.thromres.2020.12.023>.
- [6] Tacquard C, Mansour A, Godon A, Gruel Y, Susen S, Godier A, et al. Anticoagulation in COVID-19: not strong for too long? *Anaesth Crit Care Pain Med* 2021;40(April (2)):100857. <http://dx.doi.org/10.1016/j.accpm.2021.100857>.

Alexandre Godon^{a,*}, Charles Ambroise Tacquard^b,
Alexandre Mansour^c, Pierre Albaladejo^a, Yves Gruel^d, Sophie Susen^e,
Anne Godier^f

^aDepartment of Anaesthesiology and Critical Care, Université Grenoble Alpes, CHU Grenoble Alpes, Grenoble, France

^bDepartment of Anaesthesia and Intensive Care, Hôpitaux Universitaires de Strasbourg, Strasbourg, France

^cDepartment of Anaesthesiology Critical Care Medicine and Perioperative Medicine, CHU de Rennes, France

^dDepartment of Haematology-Haemostasis, Hôpital Universitaire de Tours, France

^eDepartment of Haematology and transfusion, Université de Lille, Lille, France

^fDepartment of Anaesthesia and intensive care, AP-HP, Hôpital Européen Georges Pompidou, and INSERM UMRS-1140, Université de Paris, France

*Corresponding author

E-mail address: agodon1@chu-grenoble.fr (A. Godon).

Available online 13 August 2021

* Footnote: <https://doi.org/10.1016/j.thromres.2020.04.021>.