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

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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], [4], [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].

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