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Reply to "Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy"

We have just read with interest the article recently published in your Journal and titled "Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy" by Tang et al¹ In this article, it is suggested that those patients with COVID-19 that accomplish the Sepsis-Induced Coagulopathy (SIC) criteria, and receive anticoagulant treatment would present a reduction of mortality rates. It is well known that both shock and disseminated intravascular coagulation (DIC) are the two major causes of organ dysfunction in sepsis.² Furthermore, DIC is a strong predictor of mortality in patients with sepsis, independently of the severity of sepsis.²

In 2017, the International Society of Thrombosis and Haemostasis (ISTH) developed a Sepsis-Induced Coagulopathy (SIC) score. It was defined for clinical practice to facilitate early recognition of DIC in

the setting of the sepsis, and to better identify those patients that are candidates for anticoagulation therapies.³ The SIC score criterion consider using the platelet count (a value lower than $100 \times 10^3/\text{mm}^3$ platelets), PT ratio and four items of the total Sequential Organ Failure Assessment (SOFA) score that defines organ dysfunction: respiratory SOFA (PaO₂/FIO₂), cardiovascular SOFA (Hypotension), hepatic SOFA (bilirubin) and renal SOFA (creatinine or urine output). Therefore, the existence of thrombopenia from the SOFA score is not taken into account for the SIC score as it is already included as a criterion.

In the article published in your Journal, Tang et al mention that "the SOFA score was developed by an international group of experts to describe the time course of six organ dysfunction using a limited number of routinely measured variables". Considering our above explanation, using together for the patient's mortality evaluation the total SOFA score with its total six variables (which includes the existence of thrombopenia) and the SIC score (which includes the platelet count as per the CID criteria) would make to count the same item twice for a patient.



We consider that the variables included in the study are not well described in the paper since the only reference in the article by Tang et al is to the original SOFA score. Furthermore, it is possible that the weight of thrombopenia in the SIC score has been magnified, since thrombopenia is a criterion included in both scores (SOFA and SIC) as individual items. As thrombopenia has been described as a frequent finding in COVID-19,⁴ it could be a consequent bias that limits the interpretation of the study.

CONFLICT OF INTEREST

Authors declare that there are no financial, labor or other relationships that may constitute a conflict of interest with respect to this work. That is to say, we have not received "benefits in money, goods, hospitality or subsidies" from any source that has a particular interest.

AUTHOR CONTRIBUTIONS

Rubén Coto-Hernández and María Teresa Fábregas Ruano contributed substantially to the discussion, research and writing of this letter to the editor. All authors discussed the results and contributed to the final manuscript.

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Response to 'Reply to Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy'

We appreciate the opportunity to respond to the comment about the Sequential Organ Failure Assessment (SOFA) score by Dr Ruben Coto. We admit that we misquoted the original SOFA score including six items¹ in our paper. But we did not double-count the thrombopenia for sepsis-induced coagulopathy (SIC) score² in practice, it's an obvious repetitive item.

The enrolled patients in our study met the definition of severe COVID-19 suggested by the National Health Commission of

China,³ which reflected respiratory insufficiency based on three parameters. As PaO₂/FiO₂ ≤ 300 mm Hg is one item of the severe COVID-19 definition, and respiratory support was given to almost all of the enrolled patients, in fact, most of our patients could get ≥2 points of respiratory SOFA score, meanwhile, some patients also got points on cardiovascular, hepatic, or renal SOFA score. Hence, the results of prothrombin time (international normalized ratio) and platelet count were commonly the determinants of SIC scoring in these patients.

We would like to modify the text about the SOFA score used in the SIC criteria before formal publication of this paper.

Manuscript handled by: David Lillcrap

Final decision: David Lillcrap, 10 April 2020