Fibrinolysis in COVID-19 patients with hemodynamic unstable acute pulmonary embolism: yes or no?

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To the Editor

During the current COVID-19 pandemic, different investigations are reporting a higher incidence of thrombotic events in patients with COVID-19 disease [1–4]. As suggested by a recent European Society of Cardiology (ESC) [5] and an American consensus paper [1], the treatment of COVID-19 patients with confirmed acute pulmonary embolism (PE), should be remained guided by risk stratification, as recommended by the current international guidelines. In this regard, hemodynamically unstable PE patients (defined as high-risk or massive according to the European and American nomenclature) or those hemodynamically stable having a subsequent hemodynamic deterioration during the infection, should promptly receive reperfusion treatment in absence of contraindications. In this regard, systemic thrombolysis remains the first and more appropriate therapeutic strategy, considering both the international guidelines recommendations on the management of acute PE. However, these suggestions have not considered that these patients often show peculiar clinical features and complications such as thrombocytopenia. In this regard, it has been demonstrated that thrombocytopenia occurs in a non-neglectable proportion of patients with COVID-19 infection, ranging between 5 and 42% and reaching up to 58% in subjects with severe disease [6]. Furthermore, thrombocytopenia have resulted, per se, an independent predictor of increased mortality in these subjects [7]. Despite we have no

data to establish if the thrombocytopenia could be due to a septic-induced disseminate intravascular coagulation (DIC) and/or platelet-viral interactions, this haematological profile represents a potential serious problem for the administration of fibrinolysis in hemodynamically unstable PE patients. Moreover, thrombocytopenia is per se a relative frequent event after the administration of systemic thrombolysis [8]. It appears clear that the administration of thrombolytic drugs in these patients could significantly deteriorate an already precarious haematological balance. Doubtless, a step-wise approach to diagnosis and treatment, as well as a distinguished an specific approach to critically ill patients with thrombocytopenia, with or without a bleeding phenotype must remain the basis in daily clinical practice. Indeed, the reperfusion treatment of COVID-19 patients must be tailored according to the severity of thrombocytopenia and, the interventional reperfusion, should be performed minimizing the exposure and the risk of COVID-19 transmission to healthcare workers. However, in real clinical practice, when facing with a thrombocytopenic COVID-19 patients with unstable acute PE, we cannot base our decision making only on generic rules, generally elaborated in the past when the COVID-19 was an unknown and unpredictable entity. In this regard, and especially in patients with thrombopenia, catheter directed treatment (CDT) cannot be considered only a second line therapeutic strategy, but as a potential first line therapeutic approach [9]. Probably, a simple mechanical fragmentation of the thrombus can be enough in order to reduce pulmonary vascular resistance and alleviate right ventricular overload thereby improving cardiac output and systemic arterial pressure. Moreover, a combined pharmacological approach could be also considered based on patient's profile. Now more than ever, we have been called so urgently to use all the therapeutic armamentarium against venous thromboembolism to reduce the mortality worldwide. In this regard, it is fundamental to preliminary plan specific therapeutic strategies for the treatment of thromboembolic events in COVID-19 patients, considering all the

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potential complications observed in daily clinical practice that can interfere with the traditional therapeutic protocol. As known, recommendations provided from international societies are designed to maintain a level of consistency in management as more is learned over the time. This aspect should be emphasized in this pandemic, adapting the clinical management to the continuous advancement obtained in the field of research. In this regard, particular attention will be required to investigate the pathological aspects and clinical consequences of the widespread pulmonary microthrombosis, also investigating the potential role of fibrinolysis in unstable patients without evidences of detectable pulmonary emboli. The aim should be to avoid to be unprepared in worst-case and emergency scenario.

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Compliance with ethical standards

Conflicts of interest None of the authors have conflicts of interest to declare.

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