



Difference of coagulation features between severe pneumonia induced by SARS-CoV2 and non-SARS-CoV2

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Highlights

- In critically ill patients with SARS-CoV2 pneumonia, an early anticoagulant prophylaxis should be started in all patients.
- Further studies are needed to establish the cut off D-dimer level to switch from anticoagulant prophylaxis to anticoagulant therapy.
- The dosage of fibrinolysis inhibitors associated to doppler ultrasound could help the clinicians in the earliness of anticoagulant therapy.

We read with considerable interest the article “Difference of coagulation features between severe pneumonia induced by SARS-CoV2 and non-SARS-CoV2” wrote by Yin et al. [1]. In this retrospective study, authors compared coagulation parameters of patients with severe pneumonia induced by SARS-CoV2 and patients with pneumonia induced by other pathogens. They found that patients with pneumonia SARS-CoV2 had higher platelet count than those induced by non-SARS-CoV2. Moreover, in COVID patients when D-dimer exceeding 3.0 µg/mL the mortality was significantly lower in heparin users than nonusers. Therefore, the authors suggested, in patients infected by SARS-CoV-2, a D-dimer value exceeding 3.0 µg/mL (six-fold of upper limit of normal, 6 ULN) as cut off to start the heparin treatment.

These results and conclusions allow to make some considerations.

First point, regarding the definition of anticoagulant therapy, in the present study patients received heparin (unfractionated heparin UFH 10,000–15,000 U/day or low molecular weight heparin LMWH 40–60 U/day) according to European guidelines [2] for 7 days or longer. However, it should be noted that this dose is not an “anticoagulant therapy”, but an “anticoagulant prophylaxis”.

Second point, the authors did not indicate the severity of illness of critically ill patients (e.g. Sequential Organ Failure Assessment—SOFA): this parameter is very important when comparing two groups in term of mortality and degree of multi-organ dysfunction. Moreover, causes of mortality would be interesting especially in patients who have not received heparin prophylaxis.

Third point, in their study, Yin et al. [1] suggested that “only” the patients with markedly elevated D-dimer may benefit from anticoagulant prophylaxis with LMWH. Patients with severe pneumonia induced by SARS-CoV2 presented high D-dimer and fibrin degradation product (FDP) levels [3], which are indices of active blood clot activation. A recent retrospective study [4] showed that older age, D-dimer levels than 1 µg/L, higher level of IL-6 and higher SOFA score on admission were associated with higher in-hospital mortality.

Clinical studies [5, 6] have suggested that anticoagulant therapy, heparin, reduces the inflammatory response because thrombosis and inflammation are strictly interconnected. Heparins seems to have a biological basis as a modulator of inflammation through four ways: (1) inhibits the activation of neutrophils; (2) interacts with the vascular endothelium to prevent expression of inflammatory mediators which initiate and drive activation of the immune system; (3) inhibits proliferation of the vascular smooth muscle cells; (4) inhibits inflammatory via its anticoagulant activity: a fall in thrombin formation in turn reduce adhesion molecules as well as the platelets activation.

In term of prevention and early diagnosis, European guidelines [2] recommended against the routine use of compression Doppler ultrasound (DUS) screening of deep

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vein thrombosis in critically ill patients; however, in PREVENT study twice-weekly surveillance ultrasonography was associated with an increase in deep vein thrombosis (DVT) detection, reduction in diagnostic testing for non-lower limb DVT and pulmonary embolism (PE), earlier diagnosis of DVT and PE, and lower 90-day mortality [7].

In conclusion, in critically ill patients with SARS-CoV-2 pneumonia in which a “cytokine storm” joins to Virchow triad, it seems appropriate to highlight the need for use of early anticoagulant prophylaxis in all patients.

Further studies are needed to establish the cut off of D-dimer level to switch from anticoagulant prophylaxis to anticoagulant therapy. Perhaps a systematic research of thrombosis with ultrasound, associated with evaluation of fibrinolysis parameters could help clinicians in the earliness of anticoagulant therapy.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The article doesn't contain the participation of any human being and animal.

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