be attributed to the above reasons. Furthermore, because of the limited data Dr Gris et al provided, we also do not know whether there were differences in the baseline characteristics. In this case, it would be better to establish a suitable cutoff value and evaluate the predictive value of D-dimer in COVID-19 based on their own population.

The potential use of D-dimer in COVID-19 based on recent evidence has been simply summarized in our previous response. There are still many uncertainties and potential uses of D-dimer in COVID-19, such as whether it can be used to guide anticoagulation adjustment, initiate mechanical ventilation, and de-escalating critical care support,[9] all of which are worthwhile to expect the further studies to describe in more detail.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest regarding this article.

KEYWORDS

COVID-19, C-reactive protein, D-dimer, mortality, SARS-CoV-2

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What do monitoring platelet counts in COVID-19 teach us?

Yang and colleagues published the relevance of thrombocytopenia in COVID-19 patients and its association with mortality in this condition in the *Journal of Thrombosis and Haemostasis*.[1] The authors are to be applauded for the largest so-far analysis in the epidemiology of thrombocytopenia in patients with COVID-19. In addition to the association with mortality, there may be several other findings in this interesting paper that deserve mention. First of all, the study confirms that COVID-19 is not associated with significant thrombocytopenia (only 20.7% had counts < 125×10^9/L, the lower range in this study).[2,3] The "higher" platelet counts for an illness as severe as COVID-19 is unusual and likely points toward liver activation and thrombopoietin release. After all, platelets can also be considered an acute phase reactant (such as ferritin, fibrinogen, C-reactive protein, which are all markedly raised in this disease) because of its antimicrobial repertoire, which is increasingly recognized by the thrombosis and hemostasis community.[4-6] The lung-specific entry

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of SARS-CoV-2 suggests these platelets are one of the first lines of defense and gives proof to the concept of the presence of functional megakaryocytes in the lungs. In other words, the lung megakaryocytes (a previously disputed concept) in response to the liver thrombopoietin produce a large number of platelets locally to help in the host defense.[7] In support of this, the authors do hypothesize SARS-CoV-2 could entrap megakaryocytes and block the release of platelets as another reason for thrombocytopenia, which is interesting. But what would explain the poor prognosis from the lower platelet counts noted by Yang and colleagues?

Platelet counts < 50 × 10^9/L are extremely rare in COVID-19. According to the current study, the range of nadir platelet counts was 43 to 129 × 10^9/L. Although the authors suggest bone marrow involvement by the virus as another cause for the thrombocytopenia, that the rest of the blood counts are not always significantly affected in COVID-19 (hemoglobin and white cell counts apart from lymphopenia) points away from this mechanism. A more plausible reason is platelet being consumed to form pulmonary thrombi. Thrombus formation as an anti-infective process gained momentum in the past 2 decades.[8] To serve this purpose, a bronchoalveolar hemostatic system exists to stop pathogen invasion into the bloodstream,[9] but can be deleterious to the host if it is widespread. Pulmonary microthrombi occur when multiple efforts (including that of the platelets) to stop the infection have not succeeded and blocking the viral invasion has become necessary. In keeping with this hypothesis, Yang et al also show that in those who had nadir platelet counts, the mortality decreased with the increasing of platelet count, suggesting the thrombotic process has abated and platelets are no more consumed into the clot. The significance of this finding is that monitoring platelet counts in COVID-19 (and other infections and inflammatory states) is paramount because a decrease in the count after an initial surge may suggest the start of a process which may be harmful to the host (eg, microthrombi). For the same reason, improvement of the platelet counts may signify imminent clinical improvement. This approach would certainly benefit clinicians in low-resource settings where access to laboratory tests may be limited but a full blood count may be relatively easily performed.

Based on the "platelet consumption" reason for thrombocytopenia and thus poor prognosis, in future studies, it would be useful to examine the following.

1. Whether antiplatelet agents are useful especially if anticoagulant drugs fail to stop the thrombotic process in COVID-19.
2. If inhalational antiplatelet drugs like heparin and prostacyclin analogues may be beneficial in worsening patients, similarly
3. If patients already on antiplatelet agents for various cardiovascular disorders (and compliant with it) may be protected from severe COVID-19
4. The timing of antiplatelet therapy – at a stage when they participate in microthrombi formation much more than the early phases when they may play a beneficial role (as described earlier)

Platelets continue to surprise us by being much more than the cellular component of the hemostatic system. And studies like that of Yang and colleagues help us to understand more about these multifaceted platelets, which do far more than just forming clots.

CONFLICT OF INTEREST

None.

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