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EDITORIAL

Time to re-think how we evaluate platelet function

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Platelets are best known for their essential role in hemostasis and thrombosis. Beyond this historical role, platelets are a crucial component for many organ functions; platelets are emerging as key contributors in the immune response, including immune response against viruses. Indeed, platelets mediate the internalization of several viruses throughout the expression of different pattern recognition. The consequent platelet activation triggers the immune response against viruses throughout different mechanisms that promote endothelial activation and leukocyte migration.[1, 2]

Despite this growing knowledge, physicians usually monitor platelets function only considering their blood count. In recent years, this clinical approach has been challenged and some studies elucidated that the response of platelets to infections is not limited to a simple fall in platelets count.[3-5] Indeed changing in platelets morphology or platelet activation state, can occur even without any variations in crude blood count and are associated with unfavorable outcomes.[3, 4]

In this issue of *Minerva Anestesiologica*, Consolo *et al.*[6] evaluated the role of platelet activation state during the early stage of COVID-19. They identified a significantly increased platelet activation state at early stage of COVID-19, with significant differences among patients. These results confirmed previous studies that highlighted the platelet contribution to the progression of the COVID-19 disease; higher values of platelet aggregation (assessed by light transmission aggregometry, LTA), and increased markers of platelet activation, such as P-selectin and sCD40L, were previously associated with higher mortality.[5, 7]

These physiological results, together with the high rate of arterial thrombosis described in severe COVID-19 patients,[8] led to interventional studies investigating the potential role of antiplatelet therapy. Yet, the RECOVERY trial showed that early aspirin administration in hospitalized COVID-19 patients was not associated with lower mortality or lower risk of progression to invasive mechanical ventilation. The administration of aspirin was associated with a reduction in thrombotic events and an increase in major bleeding events.[9]

As pointed out in the study by Consolo *et al.*, patients can exhibit huge differences in platelet activation state and this heterogeneity can explain the different patients' responses to therapeutic interventions. For this reason, it is reasonable that platelet activation state can be used to design a more physiological guided interventional study. In this fashion, only patients experiencing high platelet activation state should be exposed to antiplatelet therapy, therefore minimizing the risk of major bleeding events described in the RECOVERY trial.[9]

Of note, in the study by Consolo *et al.* platelet activation state was assessed very early, *i.e.*

within 24 hours from hospital admission. This is an interesting analysis because provides a description of platelet function during initial phases of COVID-19, when platelet state is less influenced by drugs administration and other factors that occur during hospital stay. On the other hand, COVID-19 patients are usually admitted to intensive care units after some days; it means that platelet activation state may significantly differ in critical settings when compared to those describe in this study. It has been shown that platelet activation can change quickly in patients with severe infection, and the same patients may exhibit hyper or hypo platelet activation, reflecting the stage of the disease.[3] A sequential evaluation of platelet activation during hospital stay can help to identify timing of initiation of antiplatelet therapy. Conversely, in patients that exhibit platelet dysfunction, the therapeutic approach should minimize the risk of bleeding, even considering a higher platelet count thresholds for platelet transfusion.[10]

Interestingly, the method used to evaluate the platelets activation in this study is relatively new and can carry some significant advantages. Both LTA and flow cytometry are time-consuming, require an adequate equipment and are expensive. In contrast, platelet activation state assay does not require expensive reagents, equipment, or highly specialized dedicated personnel. The high reliability and simplicity of this assay could represent a step forward towards a routine platelet function assessment in real-life experiences.

Waiting for the spread of platelet activation state assessment, we must underline that a cheap and widely available tool useful for a first evaluation platelet function already exists. Platelet activation causes morphological changes (from discoid to spherical, with formation of pseudopodia) which affect the mean platelet volume (MPV) and the platelets distribution width (PDW). For this reason, we can consider PDW and MPV as surrogate markers of platelets activation.[11] Accordingly, Comer *et al.* demonstrated significantly higher MPV at admission in patients who developed severe COVID-19.[12]

In conclusion, several tools are available for the assessment of platelet function during infections. Platelet count assessment is of clear relevance but probably does not give enough information. Given the wide heterogeneity showed among patients with the same disease, assessment of platelet function during infection should guide both clinical management and the design of future interventional studies.

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