Impact of COVID-19 disease on platelet reactivity and association with inflammatory parameters

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Background: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the pathogen responsible for the coronavirus disease 2019 (COVID-19) pandemic. Aside from the pulmonary manifestations, COVID-19 is associated with increased risk of venous and arterial thrombotic complications. The actual impact of SARS-CoV-2 infection on platelet reactivity and whether this is mediated by a hyperinflammatory status has not been fully elucidated to date.

Objective: To evaluate platelet reactivity in COVID-19 patients compared to healthy subjects and to assess the association between platelet reactivity and levels of inflammatory biomarkers among COVID-19 patients.

Methods: This prospective observational investigation included COVID-19 patients admitted into a tertiary care hospital and adult healthy volunteers, all of them not receiving any antiplatelet therapy. Subjects were classified in three groups: 1) Healthy subjects (HS group); 2) COVID-19 patients in a pulmonary phase (viral pneumonia and bilateral infiltrates) but without meeting criteria for systemic hyperinflammation (C19-Pulm group); and 3) COVID-19 patients in a hyperinflammation phase (C19-Infl group) meeting at least 2 of the following criteria: CRP>100mg/l, D-dimer >1000mcg/l, LDH>400U/l, ferritin>1000ng/ml, IL-6>70ng/l. Blood samples for platelet function testing and quantification of inflammatory parkers were collected at a single visit. Platelet function was measured with multiple electrode aggregometry using ADP (MEA-ADP, primary endpoint), arachidonic acid (AA) and thrombin receptor activating peptide (TRAP) as stimuli. Unadjusted analyses are presented.

Results: A total of 60 patients were included in the present investigation (20 in each group). A significantly greater platelet reactivity, measured with MEA-ADP, was observed in both groups of COVID-patients compared to healthy subjects (HS: 634,9±53,5, C19-Pulm: 919,9±53,5 and C19-Infl: 931,6±53,5 AU*min; p for C19-Pulm vs. HS <0,001, p for C19-Infl vs. HS <0,001, p for C19-Pulm vs. C19-Infl 0,878; Figure 1). Parallel findings were found when using AA as stimulus for platelet aggregation showing greater platelet aggregation in COVID-19 patients compared to healthy subjects, but numerical differences were not statistically significant when using TRAP. Among COVID-19 patients, when stratified by IL-6 levels splitted into tertiles, greater platelet reactivity was observed in patients with higher IL-6 concentrations (mid and upper tertile together) compared to those with values in the lower tertile, as assessed with MEA-ADP (lower tertile: 829,0±75,8, mid and upper tertile: 1028,7±56,2; p=0,043); a similar trend was observed with AA and TRAP as stimuli.

Conclusion: Patients with severe COVID-19 disease have greater platelet reactivity than healthy subjects. Increased IL-6 levels might be associated with the observed heightened platelet reactivity among COVID-19 patients.

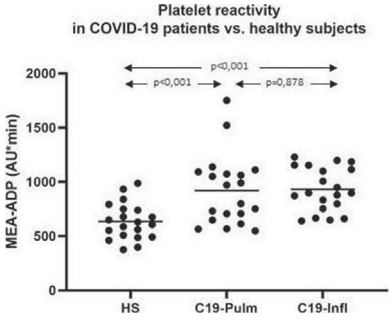

Figure 1