Letter

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Re: Thromboelastography demonstrates progressive hypercoagulability in COVID-19 patients admitted to ICU with respiratory failure

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We read with interest the article by Joshi et al., comparing the thromboelastographic results of patients with and without COVID-19, showing that COVID-19 infection causes a functional increase in fibrinogen activity without an increase in Clauss fibrinogen levels, and an increase in R time as a measure of clot initiation,[1] suggesting that changes in platelet or fibrinogen activity may be responsible for the increased thromboembolic risk.

Our team has analysed our ROTEM thromboelastometry data, where we similarly found an increase in fibrin activity, but with a corresponding association with fibrinogen levels, and no change in the equivalent clot initiation time indices. We also found no change in platelet activity, suggesting that the fibrin activity has predominant effects.

In a retrospective analysis, we compared all ROTEM data for patients on our adult intensive care unit between June 2020 and February 2021. We included 163 patients: 12 with a positive SARS-CoV-2 result in the preceding 28 days and 151 without. All included patients had contemporaneous plasma Clauss fibrinogen assay results.

None of the EXTEM, INTEM and HEPTEM assays showed any differences in any measures between patients with and without COVID-19 infection, including the clotting time, analogous to the TEG R time, different to that found by Joshi et al.

However, FIBTEM analysis showed a significant difference in the fibrin component of clot strength in patients with COVID-19 infection compared with those without. The amplitude at 5 minutes (A5) and maximum clot firmness (MCF) were larger in the COVID-19 cohort. The median A5 was 21 vs 13 mm, and the median MCF was 25 vs 16 mm ($p < 0.05$, $r = 0.178$; and $p < 0.05$, $r = 0.159$, respectively, by the Mann–Whitney U test).

Comparing with the data reported by Joshi et al., this correlates with their inference of greater fibrinogen function. Additionally, we also demonstrated a higher fibrinogen concentration in patients with COVID-19 infection (median 6.2 vs 3.05 g/L, $p < 0.01$, $r = 0.183$). In a linear regression model, the MCF was positively correlated with fibrinogen concentration in all patients ($p < 0.001$, adjusted $R^2 = 0.809$), also maintained in COVID-19 patients ($p < 0.001$, adjusted $R^2 = 0.8944$), consistent with a previous study in patients without COVID-19,[2] but different to a previous study, which showed that COVID-19 infection was associated with a reduced clotting time and an increased MCF overall, but no difference in the FIBTEM MCF in COVID-19 patients.[3]

Despite several limitations, we believe our work adds weight to Joshi and colleagues' proposal of functional changes in the fibrin component of coagulation in coagulopathy associated with COVID-19, but in addition does show a significant correlation with higher plasma fibrinogen concentrations, without changes in clot initiation time, contrary to the data from Joshi and colleagues. Joshi et al. suggest that targeting either fibrinogen or platelet activity may be of benefit; with no observed change in clot thickness indices other than the fibrinogen component, we suggest that the former may be more significant than the latter.

Yours faithfully,
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