D-dimer is Associated with Severity of Coronavirus Disease 2019: A Pooled Analysis

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A new infective outbreak, sustained by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and defined coronavirus disease 2019 (COVID-19), is now spreading all around the world.1 The clinical course of this respiratory disease is complicated in up to 15% of infected patients by onset of interstitial pneumonia, evolving toward acute respiratory distress syndrome needing mechanical ventilation or admission to the intensive care unit (ICU), and is also often accompanied by multiorgan failure.2 Since there is now incontrovertible evidence that laboratory hemostasis provides an essential contribution to decision-making and care of the vast majority of human pathologies,3 we aimed to explore here whether increased D-dimer values—which are a frequent occurrence in patients with COVID-194—may be associated with disease severity.

An electronic search was performed in Medline (PubMed interface), Scopus, and Web of Science, using the keywords "laboratory" and "COVID-19" or "coronavirus 2019" or "2019-nCoV" or "SARS-CoV-2," between 2019 and present time (i.e., March 4, 2020), with no language restriction. The title, abstract, and full text of all documents that could be identified based on these search criteria were analyzed, and those reporting infor-...
patients who died (median: 5.2 mg/L; IQR: 1.5–21.1 mg/L) than in those who survived (median: 0.6 mg/L; IQR: 0.3–1.0 mg/L; p < 0.001). In the study of Guan et al, who extracted data on 1,099 patients with laboratory-confirmed COVID-19 infection from 552 hospitals located in 30 Chinese territories, the risk of having D-dimer values above the locally defined cut-off (i.e., ≥0.5 mg/L) was more frequent in patients with severe disease (65/109, i.e., 59.6%) than in those without (195/451, i.e., 43.2%; p = 0.002). The WMD of the four studies which reported continuous values (totaling 553 patients, 22% with severe disease)\(^6\)–\(^9\) is summarized in Fig. 1, showing that D-dimer values are considerably higher in COVID-19 patients with severe disease than in those without (WMD: 2.97 mg/L; 95% CI: 2.47–3.46 mg/L). The heterogeneity across the studies was found to be relatively high (i.e., \(I^2\), 94%; \(p < 0.001\)).

Recent literature data show that D-dimer values are frequently enhanced in patients with COVID-19, being variably observed in 36 to 43% of positive cases.\(^4\) Nonetheless, what clearly emerges from the results of our pooled analysis is that D-dimer values are even higher in patients with severe COVID-19 than in those with milder forms and therefore, D-dimer measurement may be associated with evolution toward worse clinical picture, though serial measurement would not be easily feasible at present in COVID-19 patients. Notably, Tang et al also recently highlighted that the vast majority of COVID-19 patients who died during hospital stay fulfilled the criteria for diagnosing disseminated intravascular coagulation (71.6 vs. 0.6% in survivors).\(^7\) Although D-dimer elevations recognize multifactorial etiology, our findings would lead us to conclude that D-dimer elevations and disseminated coagulopathy may be commonplace in patients with severe forms of COVID-19 as in other severe infections disease such as systemic human immunodeficiency virus,\(^8\) Ebola\(^9\) and Zica, and Chikungunya virus\(^10\) so that urgent studies shall be planned to define whether adjunctive antithrombotic therapies (e.g., anticoagulants, antithrombin or thrombomodulin) may be helpful in patients with severe COVID-19.

Conflict of Interest
None declared.

References

Fig. 1  Weighted mean difference and 95% confidence interval of D-dimer values between patients with or without severe form of coronavirus disease 2019.