Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Heart & Lung 50 (2021) 298

Contents lists available at ScienceDirect

Heart & Lung

journal homepage: www.heartandlung.com

D-dimer and poor clinical outcome in patients with COVID-19: lessons from meta-analysis of case-control studies

Saeed Shoar

Department of Clinical Research, ScientificWriting Corporation, 3403 Garth Rd., Ste#1305, Baytown, TX, United States

ARTICLE INFO

Article History:
Received 2 January 2021
Accepted 6 January 2021
Available online 12 January 2021

Dear Editor,

Over a year has passed since the coronavirus diseases 19 (COVID-19) has been with us. During this time, an exponentially increasing number of papers describing risk scores, outcome assessment questionnaires, and mortality predictors, have been published with heterogeneous validity and uncertain clinical utility. Nevertheless, systematic reviews and meta-analysis are always an important tool in highlighting high-quality clinical studies and determining our current place in an extensively broad literature.

The recent publication of a systematic review and meta-analysis by Bansal et al. in the first issue of Heart & Lung Journal in 2021 addresses the long discussion about clinical utility of D-dimer serum levels in predicting a poor outcome in patients with COVID-19.[1] The pooled standardized mean difference of D-dimers from six case-control studies has been significantly higher in patients with COVID-19, who encountered a composite clinical outcome of acute respiratory distress syndrome, intensive care unit (ICU) admission, and death (SMD = 1.67 μg/mL). A subgroup analysis of studies, which reported the association of D-dimer only with mortality, also showed a higher SMD for D-dimer in patients with COVID-19, who encountered the endpoint of mortality (SMD = 2.5 μg/mL). While the study concludes that the higher level of D-dimer is associated with worse clinical outcome and can guide the clinicians in their decision making, it remains to consider important flaws inherited by its included studies and some different perspectives to analyze the data from.

The included studies in this systematic review are retrospective cohorts in which the underlying comorbidities of patients with COVID-19 might not have evenly distributed between case and control groups or adequately adjusted for. Such a heterogeneity might simply be transferred to the pooled effect size rendered by this meta-analysis, which is clearly obvious from its high heterogeneity (I^2 = 98%). For instance, kidney function before developing COVID-19 and during the course of hospital stay is an important predictor of clinical outcome and accounts for variations in serum levels of D-dimer.[2] Such a parameter needs to be taken into account, when trying to speculate determinants of outcome.

As depicted in their summary table, the composite endpoint of this meta-analysis is a combination of the primary endpoint by the included studies. This might be a major source of large heterogeneity within the pooled analysis as are the wide confidence intervals of median D-dimer serum levels in each study. One potential way to reduce such a heterogeneity is to perform sub-group analysis for each outcome measure or pooling studies with a similar composite endpoint in the same group. Also, one might question the reliability of pooling different values of D-dimer from several studies with different outcome measures such as in-hospital mortality, ICU admission, and ARDS to estimate a composite endpoint.[3]

Although D-dimer is an important marker in predicting coagulopathy and adverse outcome in patients with COVID-19, cardiovascular instability and other metabolic derangements play an undeniably pivotal role in determining the clinical fate.[4] For this reason, D-dimer does not seem to be an independent predictor of poor clinical outcome or mortality in patients with COVID-19, or at least cannot be concluded solely by pooling the data from retrospective studies with different endpoints, heterogenous patient population, and variable treatment strategy at the index institutions. Not to mention that the clinical management of patients with COVID-19 has substantially evolved since early 2020 and that also has a substantial impact on patient outcome.

No funds have been received in any forms.

Declaration of Competing Interest

None.

References

1 Bansal A, Singh AD, Jain V, et al. The association of D-dimers with mortality, intensive care unit admission or acute respiratory distress syndrome in patients hospitalized with coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. *Heart Lung*. 2021;50:9–12.
2 Schefold JC, Gerber JL, Angehrn MC, et al. Renal function-adjusted D-dimer levels in critically ill patients with suspected thromboembolism. *Crit Care Med*. 2020;48: e270–e276.
3 Wu C, Chen X, Cai Y, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with Coronavirus disease 2019 Pneumonia in Wuhan, China. *JAMA Intern Med*. 2020;180:934–943.
4 Shoar S, Hosseini F, Naderan M, Mehta JL. Meta-analysis of Cardiovascular events and related biomarkers comparing survivors versus non-survivors in patients with COVID-19. *Am J Cardiol*. 2020;135:50–61.

E-mail address: saeedshoar@scientificwriting.org

https://doi.org/10.1016/j.hrtlng.2021.01.004