

# Calculating Outcome Predictors of COVID-19 Requires Inclusion of Multiple Determinants

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## Letter to the Editor

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With interest, we read the article by Lu et al. about the influence of risk factors on the course and outcome of patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease (COVID-19).<sup>1</sup> Analyzed were 239 patients from a Wuhan hospital of whom 140 were discharged (improvement group), whereas 99 died (death group).<sup>1</sup> It was concluded that patients with comorbidities, low lymphocyte counts, low platelet count, low serum albumin, and with high C-reactive protein level and renal dysfunction may have an increased risk of death compared with COVID-19 patients without these abnormalities. The study is appealing but raises the following comments and concerns.

A shortcoming of the study is that the current medication was not considered a dominant factor strongly influencing the outcome of COVID-19 patients. Though, according to the method section, the current medication was recorded<sup>1</sup>; it was obviously not included in the multivariate analysis. Though several of the drugs frequently given to patients with COVID-19, such as steroids, hydroxychloroquine, azithromycin, remdesivir, lopinavir, or tocilizumab, can be toxic, they were not considered as outcome parameters in COVID-19 patients.<sup>1</sup> Also not considered were the side effects of long-term intensive care unit treatment, such as critical illness neuropathy or critical illness myopathy. We should be told if the number of drugs, the type of drugs, and duration of application differed between the improvement and death groups.

A further shortcoming is that the number of comorbidities included in the evaluation was limited. Though disorders such as chronic obstructive pulmonary disease (COPD), lung cancer, bacterial pneumonia, pulmonary heart disease, arterial hypertension, coronary artery disease, diabetes, and cerebral infarction were considered, other pathologies did not enter the analysis. Since COVID-19 is not only a pulmonary disease, but also a multi-system disease, multi-organ and multi-tissue pathologies need to be considered when assessing the outcome of COVID-19 patients. Additionally, all comorbidities diagnosed in an individual patient prior to the SARS-CoV-2 infection need to be checked for their influence on the outcome of COVID-19 patients.

Another shortcoming is that it is unclear whether death in the 99 patients of the death group was only due to the infection of SARS-CoV-2 or whether other causes of death not related to the infection were also responsible. Furthermore, it is unclear whether the 99 patients who died underwent autopsy to confirm or exclude a particular cause of death.

Several biomarkers, such as interleukin (IL)-6, D-dimer, or interferon- $\alpha$ , have been proposed to characterize the severity of COVID-19,<sup>2,3</sup> which were not included in the calculations.

The observational period of “31 December 2020 to 20 April 2020” is implausible and should be corrected.

Overall, the presented study has several shortcomings that challenge the conclusions. The current medication, severity of COVID-19, and all comorbidities, not selected ones, should be considered in the multivariate analysis. A further strong factor determining the outcome could be the immune competence of an individual patient, which was also not included in the analysis.

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**Conflict(s) of Interest.** The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this paper.

**Ethical Standards Statement.** This study was in accordance with ethical guidelines and was approved by the institutional review board.

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