



## COVID-19 Is Not Over and Needs Prediction Scores: An Endless Road!

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Following the broad spread of SARS-CoV-2 in Wuhan City from December 2019, the World Health Organization (WHO) declared the novel coronavirus disease (COVID-19) a public health emergency of international concern; by 11 March 2020, the COVID-19 outbreak was declared a global pandemic (1, 2). Until now, no specific therapies have yet been developed to prevent or reduce the risk of developing complications and organ dysfunction of COVID-19 (3). Therefore, early and accurate identification of patients at higher risk of developing severe disease is so crucial (4) both as part of guidance for clinical treatment and resource allocation as well as to highlight the likely groups benefiting from novel disease-modifying therapies.

With the fast-changing pandemic landscape and emerging new information regarding therapeutic options, immune response, and virus mutations, it seems impossible that one prediction score can answer all questions. Many studies have been performed and shown the predictive value of different scores in multicenter studies, but their external clinical utility and face validity have not been established in independent cohorts (5, 6).

Recently, more than 20 specific scores for COVID-19 patients have been developed and introduced (7). Some of them are simple, but some are more complex systems using a combination of clinical and laboratory markers and comorbidities to predict the development of critical illness among hospitalized patients infected with COVID-19 (8, 9). Acute physiology and chronic health evaluation (APACHE) is one of the most common prediction scores used in critically ill patients and is widely used as a predictor in critically ill patients. Karthick et al. showed that APACHE II could be used as a predicting score for hospital mortality in COVID-19 patients, especially when the score is more than 17. They emphasized that APACHE II was an early warning predictor of mortality and could guide physicians in conducting therapeutic protocol (10). The results of another

study in COVID-19 showed that the APACHE II score was an effective clinical score for mortality prediction compared to the sequential organ failure assessment (SOFA) score and confusion, urea, respiratory rate, blood pressure, > 65 years of age (CURB-65) score (11).

As we know, the most common reason for mortality in COVID-19 patients is acute respiratory distress syndrome (ARDS). On the other hand, a definite dissociation between a clinically happy/silent hypoxemia and profound hypoxemic pulmonary failure is frequently seen. Thus, relying on this situation can misguide physicians regarding future intervention and deciding treatment protocols. The lung mechanic indices are well-preserved in the first days of the disease, and there is no increased airway resistance or dead space ventilation; thus, the respiratory center does not sense an uncomfortable sensation of breathing. Considering ARDS as the most common reason for mortality in COVID-19 patients and concurrent happy/silent hypoxemia on the first day of the disease, it seems that prediction scores that rely on pulmonary variables (such as partial pressure of oxygen [ $P_{aO_2}$ ],  $P_{aO_2}$ /fraction of inspired oxygen [ $F_{iO_2}$ ]) can be misleading in diagnosing the severe/critically ill COVID-19 patients (12-15).

The problem arises when these scores are used to predict long-term mortality, especially after intensive care unit (ICU) discharge. The mortality of COVID-2019 patients was higher than that previously seen in critically ill patients for some reasons as follows: First, a large number of COVID-19 cases that occurred in a short period led to difficulty in hospitalization treatment. Second, the lack of information regarding clinical characteristics and pathophysiological features of the disease. Third, the APACHE II score was assessed by the characteristics of the patients on the first day of ICU admission, which, based on the mentioned comments regarding pulmonary involvement and happy hypoxemia, can be misinterpreted as normal

or near-normal values. Forth, regarding the possibility of adhering to some national guidelines of “stay at home,” patients were referred to hospitals with more severe disease, which made their management difficult. Based on big data and problems regarding COVID-19 management, Ko et al. developed an artificial intelligence model using blood biomarkers at the time of hospital admission for mortality prediction in COVID-19 patients with an accurate validity (16).

Finally, considering the fact that mortality prediction is neither perfect nor absolute, it seems that considering clinical symptoms of patients and increasing the level of standard of care and healthcare workers' information are the most important points for the best treatment strategy and decreasing the mortality of COVID-19 patients. However, using a simple bedside score to predict the possibility of severe disease/mortality of COVID-19 patients can help physicians regarding their treatment options. We recommend future studies with adequate inclusion/censoring and description of the study population, defining the time horizon of the prediction, and structured and standard reporting of results (17); however, they need external validation and other studies to prove their usefulness.

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## Footnotes

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