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Correspondence

Potential multicollinearity among NLR and other variables in the prediction model for the COVID-19 mortality

To the Editor,

I read with great interest the article by Vafadar Moradi et al. reporting the predictive role of neutrophil-to-lymphocyte ratio (NLR) on the one-month mortality of COVID-19 patients [1]. Based on the multivariate Cox regression analysis, authors concluded that older age, increased NLR and white blood cells (WBC) count were associated with the one-month mortality. I agree with their interpretation that increased NLR reflects an imbalance of the inflammatory response in COVID-19 patients, leading to the fatal outcome. However, I found some methodological issue to be considered in this study. When constructing the multivariate model, the authors employed both NLR and WBC as explanatory variables. Since the majority of leukocytes are neutrophils and the increase in WBC count in infectious disease is mainly due to the increase in neutrophils, there should be a significant correlation between NLR and WBC. However, the authors did not discuss this potential multicollinearity problem. In the recent study by Caillon et al., there was a strong correlation between NLR and WBC count in the COVID-19 patients, and neither of them was used in their prediction model for the in-hospital mortality [2]. Another concern in this study is the cut-off value they used in the survival analysis. The authors employed NLR value ≥3.3 as the threshold of predicting severe disease according to the previous study [3]. The first strange point is seen in the demographic data; the median values of NLR in the two groups, divided by oxygen saturation levels, are both higher than 3.3 (5.0 and 4.1 respectively). It is also unreasonable that the cut-off value for "disease severity" was used for the "mortality" analysis in the Kaplan-Meier curve. According to the recent meta-analysis by Li et al., half of the included studies used cut-off value greater than 6.5 for the mortality [4]. In view of this result, the cut-off value used by the authors seems to be a little too low. As a matter of fact, contributing factors to COVID-19 fatality depend on the characteristics of the cohort in which the study was conducted [5]. Therefore, the optimal cut-off value for the one-month mortality should be determined based on their own dataset. Taking into account the association between cardiovascular disease and COVID-19 severity [6], as well as the association between immune disease and cardiovascular disease [7], the NLR cut-off value can be largely influenced by the proportion of patients with cardiovascular comorbidities. Although I am not questioning the predictive role of NLR in COVID-19, above all issues should be cleared before the results of their research will be applied to the clinical practice.

Declaration of Competing Interest

None declared.

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