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Correspondence

The authors respond: Anticipating Covid prognosis from white blood cell count

To the Editor

We thank Dr. Akinori Higaki for their interest in our article *"Increased age, neutrophil-to-lymphocyte ratio (NLR) and white blood cells count are associated with higher COVID-19 mortality"*. In the following paragraphs, we try to address comments noted by Dr. Akinori Higaki.

Concerning the employment of both NLR and WBC as explanatory variables in the multivariate model, we agree that existence of strong multicollinearity among explanatory variables would lead to biased results in multivariate models. So, in our analysis, we did check the correlation among explanatory variables and drew the correlation matrix table prior to running the multivariate model, but no correlation was found between NLR and WBC nor NLR and age; so, it was concluded that no multicollinearity existed [1,2]. Similar to our finding, several studies have included WBC and NLR together in multivariate models [3,4]. Consistent with our study in which, increased WBC count was tnot seen in all patients, Selim [5] indicated that patients with COVID-19 pneumonia may have normal, low, or high leukocyte count [5].

Besides, concerning the cut-off value used in the survival analysis, it should be noted that in several disorders, NLR can be considered a prognostic marker [6-10]. As there exist controversies in the optimal NLR cut-off value for increased risk of death, in studies reporting cut-off values for severity/mortality in COVID-19 patients, a wide range of NLR values has been considered [11]. Nevertheless, no NLR cut-off value to detect normal and increased NLR values, especially for COVID-19 patients, has been introduced. In a recent meta-analysis, four studies with NLR values of 3.3–5.9 to predict severity [12-15], two studies of NLR 7.9–11.8 to predict mortality [16,17] were considered. Such variations in NLR value reflect that it is difficult to have similar optimal cut-off values for different populations [18]. At the time of writing our manuscript, and during the revisions, we chose 3.3 as a cut-off value based on the study cited in our article [12]; a similar cut-off value was considered by another study [19].

Importantly, it should be emphasized that the primary aim of our study was investigating the association of various factors such as age (as a continuous variable), sex, predisposing factors, and WBC (as a continuous variable), NLR (as a continuous variable), etc. and the survival of COVID-19 patients. Determining the optimal cut-off point and grouping the patients based on at-admission NLR for predicting risk of mortality, was not the aim of our study and Fig. 2 (in which the cut-off value 3.3 is noted) was drew as per the comment of the respected reviewers. Choosing this cut-off level for NLR was done based on the available literature (at the time of making revisions) and any level that was chosen could have raised questions such as "why the other levels were not considered?"

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