Using the neutrophil-to-lymphocyte ratio to estimate the severity of coronavirus disease 2019

To the editor We have read with great interest a recent article by Zeng et al,[1] who described a notable relevance of the neutrophil-to--lymphocyte ratio (NLR) to identify patients with severe coronavirus disease 2019 (COVID-19). As low levels of leukocytes and, conversely, high levels of neutrophils are observed in patients with a severe status of COVID-19, the NLR can exaggerate the converse direction of neutrophils and lymphocytes. This finding is clinically useful, because the NLR is easily calculated during routine blood tests even at community clinics and hospitals (where many patients with COVID-19 are seen).
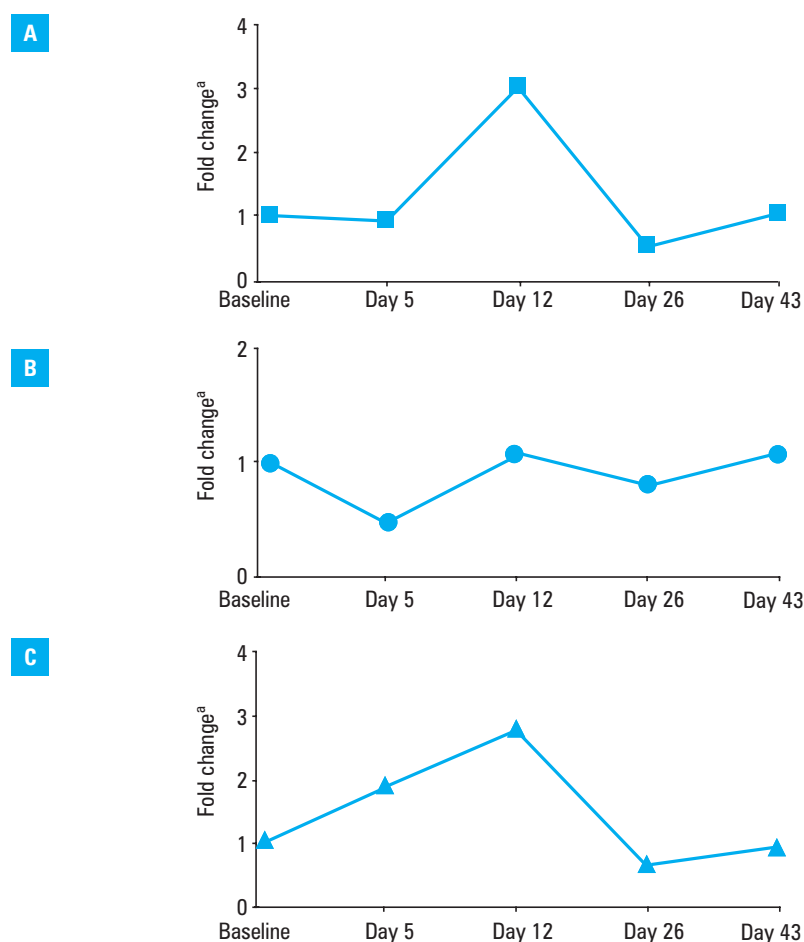
FIGURE 1 Changes in the neutrophil count (**A**), lymphocyte count (**B**), and neutrophil-to-lymphocyte ratio (**C**) in a patient with severe coronavirus disease 2019 (a recovered case). The lowest count of lymphocytes was seen early. The highest neutrophil count was seen following the lowest leukocyte count, and the lowest neutrophil count was noted later.

a Y axis shows changes in concentrations with regard to baseline values.

We would like to provide some suggestions related to the use of the NLR. Although the NLR measured at a single point was reported in most studies, as analyzed in the article by Zeng et al,[1] the nadir (the lowest point) for leukocytes and the peak (the highest point) for neutrophils can differ during the clinical course of COVID-19. For instance, early lymphopenia and late neutropenia have been reported during the course of influenza.[2] In our experience of treating an adult patient with severe COVID-19, such phenomena were indeed observed (FIGURE 1). Monitoring the NLR (eg, by the change rate) may produce a sensible finding of the disease conditions. Additionally, the cutoff values of the NLR remain to be determined in order to predict the severity of COVID-19. It is seemingly necessary to establish the cutoff values considering the transiently different behaviors of both leukocytes and neutrophils. Further studies to effectively use the NRL are therefore warranted.

ARTICLE INFORMATION

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Authors' reply We would like to thank Prof. Kotani et al for their interesting comments to our article on the clinical value of the neutrophil-to--lymphocyte ratio (NLR) to estimate the severity of coronavirus disease 2019 (COVID-19).[1] Kotani et al closely tracked the dynamic changes of neutrophils, lymphocytes, and the NLR in a patient with severe COVID-19 for 43 days from admission. They concluded that the NLR, a marker easily accessible from the routine blood test, could be used to predict the severity of COVID-19, which was consistent with our previous finding.[1]

Furthermore, Kotani et al observed that the time of the leukocyte nadir is not the same as that of the neutrophil peak in a patient with severe COVID-19. Lu et al[2] and Sun et al,[3] who observed patients with severe COVID-19, supported the finding. We are not surprised by the observations. However, if you check the data carefully, you will find different dynamic changes even in neutrophils, lymphocytes, and the NLR between these patients with severe COVID-19 (FIGURE 1). Besides, the dynamic changes were inconsistent even in patients with different degrees of disease severity.[3] Based on that, more caution needs to be taken when drawing conclusions on the time difference between the leukocyte nadir and the neutrophil peak. More importantly, nowadays, there is no evidence suggesting that the difference could dampen the predictive value of the NLR, which reflects the progress of the disease course.[3] Therefore, we should not care too much about the difference, but pay more attention to the dynamic change of the NLR.

Additionally, Kotani et al demonstrated that the cutoff of the NLR should be determined for clinical use. We appreciate their proposal and, nowadays, there are some studies on this issue. For example, through maximizing the Youden index in the receiver operating characteristic curve, Tatum et al[4] identified 4.94, 9.95, and 11.4 as the NLR cutoffs for endotracheal intubation and mortality prediction on days 1, 2, and 5. They found out that the NLR is a prognostic factor for endotracheal intubation and an independent predictor of mortality risk in patients with COVID-19. Moreover, Ma et al[5] used the median as the cutoff (9.8) to divide the patients into 2 groups. They found that the high--NLR group showed a higher incidence of acute respiratory distress syndrome and a higher rate of noninvasive and invasive mechanical ventilation. To conclude, the NLR cutoff should be determined according to the clinical purpose and disease progression. It is not reasonable to determine a specific value for the NLR cutoff in all clinical circumstances.

Thank you for your comments again. Taken together, the NLR is a prognostic predictor of COVID-19 severity, but it is a long way to go to determine its cutoff in different clinical circumstances.
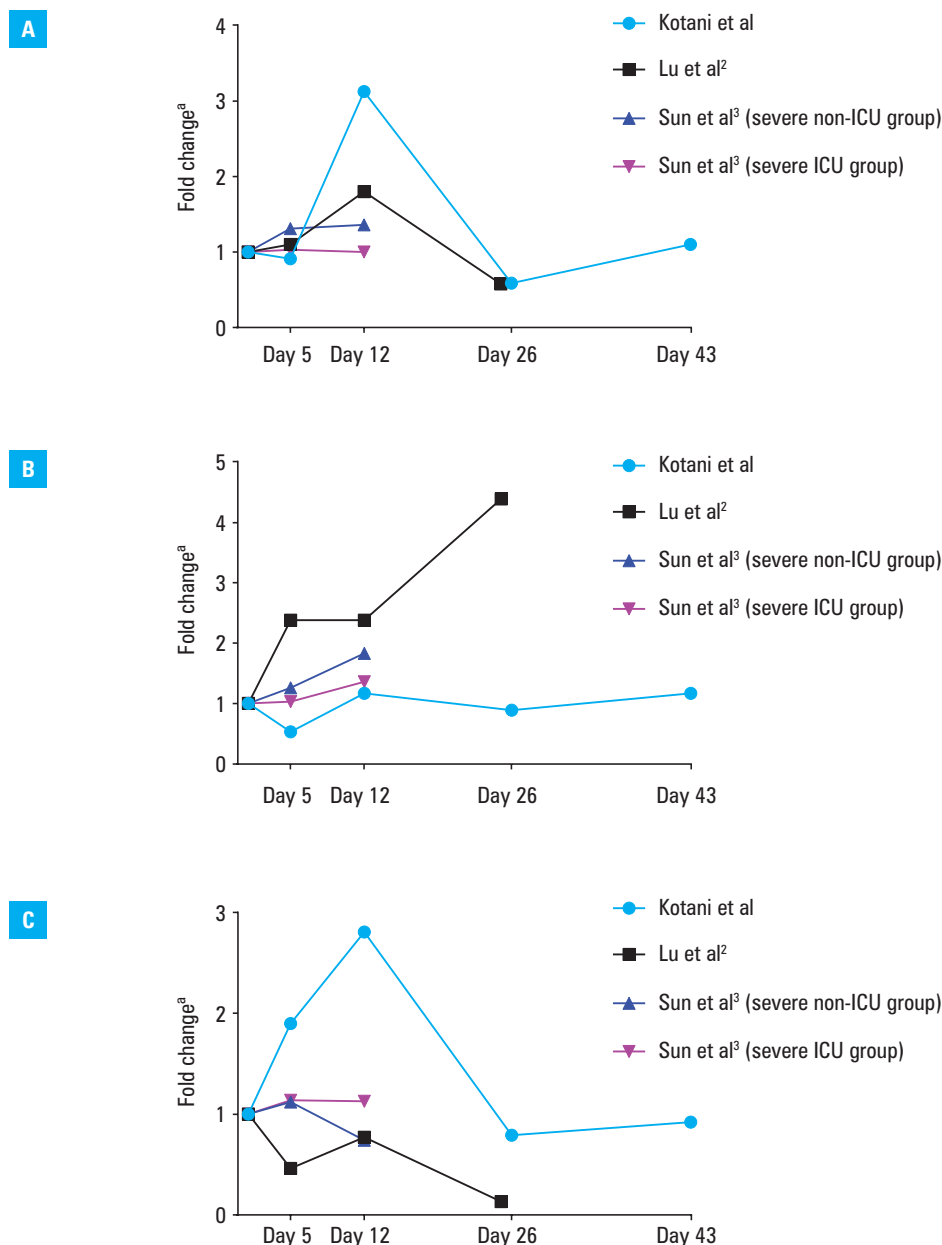
FIGURE 1 Dynamic changes in the neutrophil count (**A**), lymphocyte count (**B**), and neutrophil-to-lymphocyte ratio (**C**) observed in different studies of patients with severe coronavirus disease 2019

Abbreviations: ICU, intensive care unit

a Y axis shows changes in concentrations with regard to baseline values.

ARTICLE INFORMATION

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