Comment on "Prognostic Value of Neutrophil-to-Lymphocyte Ratio in Cirrhotic Patients with Acute-on-Chronic Liver Failure"

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Dear Editor,

We read with interest the study by Stefan et al[1] entitled "Prognostic Value of Neutrophil-to-Lymphocyte Ratio in Cirrhotic Patients with Acute-on-Chronic Liver Failure" which was recently published in *Turk J Gastroenterol*. The authors found that the neutrophil-to-lymphocyte ratio (NLR) was significantly higher in non-survivors of acute-on-chronic liver failure (ACLF) and can be used as a biomarker for predicting ACLF outcome. Although we fully agree with the conclusions of this study, the following issues need to be addressed.

First, in the CANONIC study, of all ACLF patients, 51.3%, 35.1%, and 13.4% were of grade 1, grade 2, and grade 3, respectively.[2] And other subsequent studies also confirmed a similar proportion of ACLF grading.[3,4] However, in the present study, 82.8% of ACLF patients had grade 3 ACLF. Such an extraordinarily high percentage of grade 3 ACLF may be related to the ICU circumstance. In addition, a very limited number of 58 ACLF patients were included in the statistical analysis. The selection bias and the limited sample size would inevitably introduce bias and weaken the statistical power. For example, as shown in Table 1, the median value of bilirubin of ACLF patients was 3.7 mg/dL, higher than that of non-ACLF (1.61 mg/dL), but did not reach statistical significance (P = .68). The interquartile range of bilirubin in this study is larger than the median, which suggests significant data heterogeneity. The comparison was biased by selection bias and limited sample size and thereby the finding was inconsistent with previous studies. Second, since there is a relationship between high NLR and poor prognosis in ACLF patients, the authors should further prove that the effect of NLR was independent of other confounding variables such as the CTP score. In our opinion, it is essential to perform a multivariate logistic regression analysis or Cox hazard proportional analysis to confirm whether NLR was an independent risk factor of poor outcome in ACLF patients, as previous studies did.[5]

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