LETTERS TO THE EDITOR

Neutrophil-lymphocyte ratio is useful for the prognosis of patients with hepatocellular carcinoma

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Abstract

There is increasing evidence that neutrophil-lymphocyte ratio (NLR) may play a role in predicting recurrence in patients with hepatitis B virus-related hepatocellular carcinoma (HCC) after liver transplantation. In the original study by Yan *et al*, it was aimed to determine whether an elevated NLR is associated with tumor recurrence. Total tumor size (> 9 cm) and macro-vascular invasion were found to be more significant than NLR according to the multivariate logistic regression analysis. Therefore, substantive significance should be emphasized rather than NLR because total tumor size and macro-vascular invasion are easier and more expressive than NLR in assessing HCC recurrence. NLR and platelet-lymphocyte ratio (PLR) are markers which are easy to obtain and can be used as inflammation indicators. Moreover, assessment of both NLR and PLR may add some value as a good predictor of risk for post-liver transplantation HCC recurrence. However, while the study was constructed on whole blood analysis, further details about the features and performance characteristics of the whole-blood analyzer, and preanalytical/analytical variables should also be mentioned.

Core tip: Neutrophil-lymphocyte ratio (NLR), total tumor size (> 9 cm) and macro-vascular invasion may play a role in the prediction of recurrence in patients with hepatitis B virus-related hepatocellular carcinoma after liver transplantation. Assessment of both NLR and platelet-lymphocyte ratio, as inflammation markers, may increase the prediction rate for these patients. Factors affecting the laboratory results should also be evaluated, in such a study.

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TO THE EDITOR

We read with great interest the recently published article by Xiao *et al*[1] regarding the value of neutrophil-lymphocyte ratio (NLR) for predicting recurrence in patients with hepatocellular carcinoma after liver transplantation. In the original study, it was aimed to determine whether an elevated NLR is associated with tumor recurrence in patients with hepatitis B virus (HBV)-related hepatocellular carcinoma (HCC) after liver transplantation (LT), and to determine the optimal predictive NLR cut-off value. They concluded that preoperative elevated NLR

significantly predicted an increased risk for tumor recurrence in HCC patients after LT. The study is important because it provides scientific information on this clinically relevant condition. However, we think that some points should be discussed.

Firstly, some of the parameters shown to be significant in univariate analysis were evaluated by multivariate logistic regression analysis, and ultimately total tumor size (> 9 cm) and macro-vascular invasion were found to be more significant than NLR. Therefore, substantive significance should be emphasized rather than NLR because total tumor size and macro-vascular invasion are easier and more expressive than NLR in assessing HCC recurrence. Additionally, performing a forward stepwise multivariate logistic regression analysis can give the chance to establish a regression equation including the most significant parameters in enhancing diagnostic accuracy of just one single test parameter, NLR.

Secondly, systemic inflammation has been linked to poor outcome and increased tumor progression. Such systemic inflammatory responses have been investigated using markers such as the elevation of NLR and platelet-to-lymphocyte ratio (PLR)[2-4]. These studies focusing on the impact of these parameters on recurrence after LT may contribute to the selection criteria of HCC liver recipients, in addition to the combination of NLR and PLR by regression analysis may increase the accuracy of the selection process[3]. In the light of this information, assessing PLR besides NLR may add some value as a good predictor of risk for post-LT HCC recurrence while analyzing the whole blood count in the current study.

Thirdly, although the study was constructed on the basis of whole blood analysis, further details about the features and performance characteristics of the whole-blood analyzer, and preanalytical/analytical variables were not specified. It is well-known that the WBC reference ranges may vary depending on many factors such as the population studied, individual laboratory, and instruments or measurement methods used (*e.g.*, waiting period prior to analysis)[5]. The types of collection tubes, waiting period prior to analysis, instrumental parameters and reference ranges for each parameter must be specified as they are easily affected by analytical and pre-analytical variables in studies based on laboratory results[6]. The authors stated that the preoperative NLR is affected by many factors, such as unidentified sepsis, weight loss, massive hemorrhage and instrumental error, which make the NLR inaccurate. Therefore, samples should also be analyzed more than once to avoid random error in such studies.

In conclusion, although easily measured, NLR is more complicated due to being a combined factor of inflammation and immune reaction. It would be better to assess NLR with other inflammation markers to predict inflammatory tumor micro-environment. Possible causes affecting neutrophil and lymphocyte counts and the confounding factors, which have a considerable effect on the clinical availability of NLR, should be discussed in more detail in this study population.

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