

LETTER TO THE EDITORS

Reply to 'Neutrophil and platelet-to-lymphocyte ratio: new predictors of dropout and recurrence after liver transplantation for hepatocellular cancer?'

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Dear Sirs,

With great interest, we read the reply by Tanoglu *et al.* [1], in relation to our paper focused on the interaction between inflammatory markers and hepatocellular cancer (HCC) [2]. We thank these authors for their suggestions and considerations. Tanoglu *et al.* underline in their letter that both neutrophil-to-lymphocyte (NLR) and platelet-to-lymphocyte ratios (PLR) have been recently introduced as markers of several inflammatory conditions not only in malignancies but also in other pathologies involving heart, thyroid, kidney and liver and even diabetes mellitus, metabolic syndrome and essential hypertension [3–5].

We do not fully agree with their criticisms. Tanoglu *et al.* claim that it would have been relevant to mention the presence of these affecting factors when analysing the predictive role of NLR and PLR in relation to the risk of dropout and postliver transplant (LT) tumour recurrence. Firstly, the patient population considered for LT is a very well selected one, typically free from several of the conditions (i.e. acute coronary syndrome) mentioned by the authors. Secondly, we clearly mentioned in our paper the possible biases linked to the presence of evident confounders such as hepatic function and the presence of viral infections (HBV, HCV). We, however, minimized their impact by performing subanalyses focused on specific homogeneous cohorts exclusively composed of patients with HBV and HCV infection. Even when performing such analyses, we still realize that were not fully able to minimize the selection bias as this is an intrinsic part of the study design. Indeed the sole way to perform a study excluding every possible confounder is to design a large multicentre study composed by tens of thousands cirrhotic patients. A similar remark can be made done in relation to the use of medications potentially altering the values of the inflammation markers. Unfortunately, the small sample of our study did not allow us to perform inferential

analyses focused on the construction of models aimed to identify potential factors playing a role in increasing NLR and PLR values.

We agree with the last statement by Tanoglu *et al.* that NLR and PLR alone are insufficient to select patients for dropout and post-LT tumour recurrence. More studies are needed in order to reach an international consensus, with the intent to create a new therapeutic algorithm based on the combination of different morphological and biological parameters for the selection of patients with HCC waiting for LT.

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