Letter: there is something about the Neutrophil-to-Lymphocyte ratio (NLR). . .—authors’ reply

SIRS,
We recently published a study titled “A nomogram for predicting prognostic value of inflammatory response biomarkers in decompensated cirrhotic patients without acute-on-chronic liver failure”, demonstrating that neutrophil-to-lymphocyte ratio (NLR) and lymphocyte-to-monocyte ratio (LMR) were independent predictive factors for mortality of decompensated cirrhotic patients without acute-on-chronic liver failure. In response, Dr Forrest put forward his insightful comments that the prognostic value of NLR in cirrhosis might be associated with sarcopenia. As NLR or lymphopenia has been recognised to be strongly associated with malnutrition or sarcopenia in other illnesses, we agree with his sentiment that the higher NLR is more than a reflection of systemic inflammation and subclinical endotoxemia but also an indication of the poor nutritional status.

Sarcopenia is a pathological disorder characterised by progressive and generalised loss of skeletal muscle mass and strength. Studies have demonstrated that sarcopenia is a frequent complication in cirrhosis and predictor for increased mortality of cirrhotic patients. However, its pathogenesis is poorly understood. Gastrointestinal dysfunction leading to inadequate nutrients intake is an important aetiology of sarcopenia. Interestingly, there is also increasing evidence that altered gut motility, small bowel bacterial overgrowth and changes to the gut microbiota in cirrhosis can each affect both absorption and utilisation of nutrients. Moreover, an experimental study demonstrated that the endotoxemia could induce the body weight loss and the protein catabolic state in skeletal muscle. It seems that there is a link exists between sarcopenia and increased bacterial translocation or endotoxemia in patients with cirrhosis. Furthermore, chronic low-grade inflammatory profile (CLIP) has also been recognised as an important causative factor for sarcopenia. The presence of cytokines such as TNF-alpha can also cause loss of appetite. Cirrhosis is a pro-inflammatory state, in which levels of inflammatory mediators such as TNF-alpha and interleukin 1 are elevated. From the above, we can find that the systemic inflammatory response and endotoxemia both contribute to the development of sarcopenia. Closed interactions exist between systemic inflammatory response, endotoxemia and sarcopenia in decompensated cirrhosis.

Hence, we are more inclined to believe that the poor prognosis of cirrhosis may be the consequence of combined effect of high systemic inflammatory status, endotoxemia and sarcopenia.

As a limitation of our study, we did not explore the potential mechanism of increased NLR in assessing prognosis in cirrhosis. Indication of sarcopenia is a reasonable explanation for the unfavourable outcomes. However, the relationship between sarcopenia and increased NLR for the mortality in cirrhosis remains elucidated. Further studies are needed to investigate the potential mechanism of the prognostic value of NLR in liver diseases.

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Letter: direct-acting agent therapy and HCV-related Child C cirrhosis

SIRS,

Guarino et al.’s systematic review of interferon-free regimens for patients with HCV-related Child C cirrhosis deserves comment.1

Although the rate of sustained virological responses with Direct-Acting Agent Therapy (DAAT) is impressive, sustained virological response is only a surrogate. Interferon-based regimens were proven to have efficacy on the rate of progression to cirrhosis and the incidence of hepatocellular carcinoma. Long-term randomisation on clinically relevant outcomes (benefits and harms) or post-marketing surveillance programs are needed in Child C patients.

Indeed, as usual safety concerns are rising after the marketing authorisation.2 The list is growing3-5 and the most serious concerns is occurrence of hepatocellular carcinoma.5 Although data are scant and controversial (https://www.aasld.org/events-professional-development/liver-meeting/press/there-increased-risk-cancer-after-taking-direct-acting-antiviral-medication), a fourfold increase in serum vascular endothelial growth factor during DAAT is a serious case for concern.6

Last, Guarino et al. disclosed that MELD score was only available for 103 of the 228 treated Child C patients.1 This underlines that quality and accessibility of data from patients who participated to published trials are always major critical issues.7

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