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EDITORIAL

High Neutrophil-to-Lymphocyte Ratios may Indicate Short Survival Time in Patients with Decompensated Cirrhosis

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EDITORIAL

In this issue of Clinical Laboratory, XiaoTing Qi et al. present data on the composition of white blood cells (WBC) in 144 patients with decompensated liver cirrhosis (DeCi) and chronic hepatitis B. The authors report that certain WBC ratios correlate with the 1-month survival time of these patients [1]. While the WHO has recently announced to reduce mortality related to viral hepatitis by 65% in 2030, infection with hepatitis B virus (HBV) remains a major health problem causing 820,000 deaths in 2019, approximately half of them in Eastern Asia [2]. The rational of the study is that HBV has caused a systemic inflammatory response syndrome leading to DeCi and beginning liver failure. The chronic inflammation may generate certain patterns of WBC ratios depending on the progression of the disease and the residual liver function. The retrospective study identified 21 patients who died within 30 days after hospital admission due to symptoms of DeCi. The 123 patients who survived for longer served as control group, but could not be followed for longer due to health economic limitations. The study found a marker in the neutrophil-to-lymphocyte ratio (NLR) in the WBC count which was almost as good for prediction for short-term survival as the well-established MELD score (model for end-stage liver disease score). Taken together, the MELD score and the NLR significantly improved the area under the curve (AUC) in the ROC analysis for sensitivity and specificity of the prediction from 0.87 to 0.93. The ratios between the other types of WBC were less infor-

mative and not independent in the multivariate analysis. The approach is not completely new. Li X et al. recently reported, in an almost identically designed study from the Zhejiang province in Eastern coastal China, almost identical results concerning the predictive power of a high NLR for a poor 1-month survival in HBV-related DeCi [3]. Interestingly, both reference 1 and 3 do not discuss the immediate therapeutic consequences of a poor prognosis for 1-month survival and do not pay much attention to the activity of the HBV infection. The patients reportedly received an antiviral therapy latest at admission in both studies. The levels of HBV DNA in reference 1 were relatively high with 4.6 (range 3.5 - 7.6) $\log_{10}$ IU/mL, but it was not specified whether this level referred to patients with ongoing therapy (84/144 patients) or just at the start of the therapy (44/144). Viremia levels were slightly higher in survivors than in the non-survivors reflecting the larger amount of residual functional liver tissue necessary for HBV replication in survivors. Reference 3 did not report HBV DNA levels, or details of therapy at all. Interestingly, the authors of reference 1 mention "Only 16 patients did not receive any antiviral therapy throughout the clinical course for economic or other reasons." In contrast, the European Association for the Study of the Liver (EASL) recommended in 2017: "Patients with decompensated cirrhosis should be immediately treated with a NA *(nucleoside analog)* with high barrier to resistance, irrespective of the level of HBV replication, and should be assessed for liver transplantation." [4]. Indeed, the study was done in patients of the "Xinjiang Uygur Autonomous Region" in the Northwest of China which is a region not covered by the EASL and is, furthermore, less developed than other regions of China (or Europe). A point of concern is that the authors mention "Lamivudine, Entecavir or Tenofovir" as antivirals. Entecavir and Tenofovir are state of the art drugs, but lamivudine is outdated due to rapidly developing resistance against HBV [4]. There is another peculiarity of this study: 54% of the patients belonged to the Uygur population which harbors mainly the genotype D of HBV whereas the Han population in entire China has genotypes B and C [5]. HBV genotypes may have an influence on the course of the disease [6], but this obviously does not concern the survival time with DeCi and the NLR because both studies reported very similar results.

Reference 1 and 3 studied exclusively DeCi with active HBV infection, but it appears that the role of NLR for prognosis may apply also for DeCi caused by other etiologies than HBV. Using a different study design and a broader group of patients with various etiologies (including HBV) and severity of cirrhosis, authors from Korea found the high predictive power of a high NLR along with high levels of C-reactive protein and MELD score for a poor 1-month survival in Child-Pugh class C patients (comparable to DeCi) irrespective of HBV infection [7]. A similar study from Turkey found a high NLR to be a useful prognostic marker, though not for 1-month survival, but for the 12, 24, and 36-month mortality in patients with liver cirrhosis of various etiologies and severities [8]. However, the prediction of short-term survival has highest priority because patients with the most unfavorable markers including high NLR would qualify most urgently for antiviral therapy and potentially for liver transplantation as the last remaining option. NLR together with other parameters of WBC composition has the advantage to be non-invasive unlike a liver biopsy.

The papers on the HBV positive DeCi underline the necessity of screening patients with symptoms of cirrhosis *early enough* for markers of HBV and liver function to start an efficient antiviral therapy before symptoms of DeCi become evident.

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