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Noninvasive indirect serum markers of liver fibrosis in patients with chronic viral hepatitis

To the Editor,

In the recent issue of The Turkish Journal of Gastroenterology, we read an interesting article by Gökcan et al. (1), "The predictive value of noninvasive serum markers of liver fibrosis in patients with chronic hepatitis C." However, we wanted to point out some issues related to this article.

Firstly, in the last sentence of the Materials and Methods section, the authors described hepatitis C virus (HCV) coinfection as an exclusion criterion; however, the study examined the data of patients with HCV infection. Thus, there may be an incoherence or erratum in the last sentence, which should be reviewed.

Secondly, the authors evaluated the scoring systems, which are used to predict the severity of fibrosis and consist of platelet count and/or international normalized ratio (INR), apart from patients' age, serum aspartate aminotransferase (AST), and alanine aminotransferase (ALT) levels. Nevertheless, platelet counts may be altered by infections, chronic inflammatory diseases, and some hematological disorders (2,3). Furthermore, some drugs, particularly warfarin, affect INR values. In addition, aminotransferase levels may increase in the presence of hepatosteatosis or hepatotoxic drug use and may show undulation in patients with viral hepatitis. Accordingly, as a drawback, the scoring systems used to predict the severity of fibrosis may deviate in such cases. Therefore, when using or evaluating these scoring systems, particular comorbidities or drug use that may affect the components of the scoring systems should be taken into consideration. Thus, it may be defined as a shortcoming, most likely resulting because of the retrospective nature of the analysis, that the patients in this study were not evaluated for the existence of comorbidities such as infections, chronic inflammatory diseases, hepatosteatosis, hematological disorders, or drug use, which may have affected the results; however, patients with decompensated chronic liver disease, use of alcohol, coinfection with other primary viral hepatitis, and concomitant autoimmune and metabolic disorders were excluded from the study.

Lastly, as mentioned in the article, better results could be achieved using a combination of noninvasive tests of liver fibrosis. Other than indirect or direct serum markers, including hepatic matrix metabolism markers reflecting fibrogenesis, imaging methods such as ultrasound-based transient elastography, which measures liver stiffness, can be performed to assess the degree of liver fibrosis (4). Moreover, a combination of TE and Fibrotest has been demonstrated to improve accuracy (5).

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Author's Reply

To the Editor,

We read the comments with great interest, and tried to answer them accordingly. We reviewed the predictive value of noninvasive serum markers on the hepatic fibrosis level in 120 patients with chronic hepatitis C (1). We utilized non-invasive serum markers, and Receiver Operating Characteristic (ROC) curve analyses were carried out to compare the non-invasive markers with hepatic fibrosis level.

Authors proposed a correction on the Materials and Methods section on definition of inclusion/exclusion criteria. The term "co-infection" in the articles indicates simultaneous infection of Hepatitis C with Hepatitis B. We did not feel the need to clarify the definition of co-infection as the presence of both Hepatitis B and C infections, as the name itself implies multiple infections at the same time. Therefore those patients were excluded from our study and analyses.

As a second point in their letter, authors remark a potential pitfall in the utilization of non-invasive scoring systems, as the laboratory values could have been altered due to the disease itself or co-morbid illnesses. This point could be a bias the results, if laboratory values and/or scoring parameters were used independent from each other. However, as we stated in the materials and methods, laboratory values were taken on the day of liver biopsy, and all other confounding variables were treated or removed (as using warfarin before the biopsy) for the sake of clearer analyses.

Lastly, authors pointed an important alternative method on detection of stiffness and fibrosis in liver tissue; that is elastosonography. As we stated in our discussion, better results could have been obtained using a combination of indirect serum markers, which we studied, and direct markers showing deposition or removal of extracellular matrix in the liver or liver elasticity-based imaging techniques (2,3). As these tests are expensive and have lower applicability, their feasibility in clinical practice may be difficult. However, the scoring systems that we utilized are cheap, easy to calculate, and readily available in the clinical practice.

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