The concept of MAFLD gathers patients with distinct disease progression trajectories

To the Editor:
We read with great interest the article of Staufer et al. on the rate of alcohol consumption in patients with presumed non-alcoholic liver disease (NAFLD). The authors made a substantial effort to reclassify patients according to the recent definition of metabolic dysfunction-associated liver disease (MAFLD). The findings of this study further illustrate the wide heterogeneity that this nomenclature englobes.

The concept of MAFLD was introduced in 2020 by Eslam et al. as an alternative to describing liver disease associated with an underlying metabolic dysfunction for several reasons that will not be expanded on here. As a result, this definition includes all patients with hepatic steatosis and metabolic abnormalities regardless of alcohol intake. Hence, a significant proportion of patients with alcohol-related liver disease (ALD) now falls into this category.3

In their study, Staufer et al. included 184 patients, 114 with presumed NAFLD and 70 with ALD, and made important observations. First, more than 90% of their population that could be reclassified according to MAFLD criteria belong to this category. This result is not surprising as the median BMI was 30, and 68% of patients had type 2 diabetes or glucose intolerance. Second, patients with ALD differed from a clinical point of view on age, sex ratio, BMI, and prevalence of glucose metabolism abnormalities from those with presumed NAFLD. This indicates that the MAFLD nomenclature gathers patients with distinct clinical profiles. Third, considerable differences in rates of cirrhosis were observed between presumed NAFLD and ALD (11% vs. 87%, respectively). Although NAFLD and ALD have similar pathogenic features and patients share common clinical risk factors for disease progression, the natural history of the disease differs. In addition, this discrepancy in cirrhosis rate also shows that patients with NAFLD and ALD have different progression trajectories.

The discrepancy in the natural history of ALD and NAFLD has already been documented. Previous studies indicated that the risk of cirrhosis differs between patients with ALD and NAFLD. In a study including 106 patients with ALD and 109 with NAFLD, the incidence of cirrhosis was 21% in the first group of patients and 1% in the latter.4 In addition, the risk of liver-related mortality is known to be low in patients with NAFLD and conversely high in patients with ALD. In a large study enrolling more than 3,000 individuals with biopsy-proven ALD, 5-year mortality was 41%.5 In contrast, this rate was less than 5% in patients without fibrosis and around 10% in those with fibrosis in another study population with biopsy-proven NAFLD.6

Overall, there is no doubt that ALD and NAFLD share similar pathogenic pathways, that excessive alcohol consumption and features of the metabolic syndrome are frequently associated in a significant proportion of patients seen in daily clinical practice and have a synergistic effect on disease progression. However, several lines of evidence indicate that liver-related morbidity and mortality are mainly driven by alcohol use. The article by Staufer et al. provides additional evidence that patients with ALD and NAFLD should not be grouped into a unique set of patients under the current MAFLD definition.

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