



Waiting for Multi-Stakeholders' Consensus Position Statement on New Nonalcoholic Fatty Liver Disease Nomenclature

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See "Metabolic Dysfunction-Associated Fatty Liver Disease Predicts Long-term Mortality and Cardiovascular Disease" by Joon Ho Moon, et al. on page 433, Vol. 16, No. 3, 2022

In this issue of *Gut and Liver*, Moon *et al.*¹ reported on the effects of metabolic dysfunction-associated fatty liver disease (MAFLD) on future mortality and cardiovascular disease using a prospective community-based cohort. Presence of MAFLD independently predicted overall mortality after adjustment for confounders, but the presence of nonalcoholic fatty liver disease (NAFLD) did not.¹ Hot discussions for and against the nomenclature of MAFLD are ongoing. The nomenclature task force, including representatives of the major international liver societies, set forth to evaluate whether this newly emerging concept on the phenotypes of fatty liver could or should be incorporated into the discussions on naming.

MAFLD is known to be better at stratifying those at a higher risk for advanced liver fibrosis and overall mortality than the previous NAFLD definition.²⁻⁴ Due to the exclusive nature of the NAFLD definition, we could not call comorbid hepatic steatosis as NAFLD when it co-exists with viral hepatitis, for example. However, MAFLD includes those patients with other chronic liver diseases permitting dual etiologies in a same patient. In this regard, the diagnoses of "MAFLD and alcoholic liver disease" or "MAFLD and chronic hepatitis B" can be made. Recently, it is known that the burden of metabolic risk factors are associated with the increasing risks of hepatocellular carcinoma and all-cause mortality in patients with chronic hepatitis B.⁵ Therefore, MAFLD definition supports the holistic approach for a patient with varying number of co-existing liver diseases frequently met in real-life practice.⁶

However, there are following major concerns with the newly emerging definition of MAFLD. First, higher risk

of overall mortality in MAFLD is mainly due to increasing mortality of other cancers as seen in this study.¹ Furthermore, it is unclear whether the liver-related mortality increases in those with MAFLD.³ Second, the increasing overall mortality in MAFLD is mainly seen in MAFLD subgroups II (lean with metabolic dysfunction) and III (diabetes), but not clear in subgroup I (simple obese). Nevertheless, the majority of MAFLD in real-life practice is compatible to subgroup I. In previous study, nearly 90% of MAFLD subjects were categorized into subgroup I.⁷ Third, high-density lipoprotein cholesterol, high-sensitivity C-reactive protein, hemoglobin A1c, and insulin levels need to be measured for the accurate diagnosis of MAFLD according to the definition, but most physicians do not test these markers as their routine labs in patients with fatty liver. Fourth, many previous reports suggested that prevalence of MAFLD is higher than that of NAFLD in the same population.^{7,8} If we apply the newly proposed definition of MAFLD in the outpatient clinic, the prevalence of fatty liver of medical interest would be significantly increased. Unfortunately, the data on the cost effectiveness on the application of MAFLD definition is lacking. Further studies would be needed whether the application of new MAFLD definition would reduce the social costs by active screening of those at a higher risk from the general population and thereby facilitating active referral and treatment. Fifth, there are so many factors which can affect the pathogenesis of fatty liver, not only the metabolic abnormalities but also the metabolism of bile acid, dysbiosis, sarcopenia, and diet. Therefore, the MAFLD definition would paradoxically misdirect therapeutic approaches only to the metabolic ab-



normalities.

To summarize, the newly proposed MAFLD concept has a positive aspect reminding several components of its pathogenesis (e.g., metabolic dysfunction, presence of diabetes, etc.) which underlies the fatty liver disease.⁹ MAFLD additionally raised important questions about the ambiguous nomenclature system of the conventional NAFLD definition. However, we believe that the new nomenclature requires agreement among the pan-national stakeholders and needs more clinical data for its wide acceptance in clinical practice. It would be prudent to wait for the outcome of the multi-stakeholders' consensus position statement for the new NAFLD nomenclature.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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