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EDITORIAL

Metabolic Dysfunction-Associated Steatotic Liver Disease vs. Metabolic Dysfunction-Associated Fatty Liver Disease: Which Option is the Better Choice?

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Abstract

Non-alcoholic fatty liver disease (NAFLD) is a leading cause of chronic liver disease and is linked to metabolic syndrome components such as insulin resistance and obesity. In 2020, the term "metabolic dysfunction-associated fatty liver disease (MAFLD)" was introduced, incorporating metabolic risk factors and including patients with other liver conditions. However, concerns about the term "fatty" led to the proposal of the term "metabolic dysfunction-associated steatotic liver disease (MASLD)", which refined diagnostic criteria but excluded patients with significant alcohol consumption or liver comorbidities. Although MASLD improves NAFLD in some respects, its exclusion of comorbid conditions may hinder comprehensive care for metabolic dysregulation. A proposed solution is "combinatorial MASLD", which would better address patients with liver comorbidities. Further studies are necessary to determine the most appropriate nomenclature for clinical practice.

Key words: MASLD; nomenclature; semantic improvement

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Introduction

Non-alcoholic fatty liver disease (NAFLD) is defined by the accumulation of fat in hepatocytes that is not caused by excessive alcohol use or other concomitant causes of liver disease (Chen et al, 2024). Currently, NAFLD is one of the most frequent causes of chronic liver disease in the world and ranges from simple hepatic steatosis to cirrhosis. It can be considered a clinical manifestation of the metabolic syndrome associated with insulin resistance, obesity, dyslipidemia, and hypertension. For this reason, the scientific community proposed the new nomenclature "metabolic dysfunction-associated fatty liver disease (MAFLD)" in 2020 (Eslam et al, 2020). Unlike the previous definition, MAFLD does not exclude patients with significant alcohol consumption or other liver conditions and, at the same time, establishes new inclusion criteria for the presence of at least two signs of metabolic syndrome, including type 2 diabetes mellitus and overweight/obesity. Despite the progress represented by MAFLD, some experts have raised doubts about the appropriateness of the term "fatty", which has been considered stigmatizing. Consequently, the new nomenclature of metabolic dysfunction-associated steatotic liver disease (MASLD) was proposed for further conceptual evolution. This new term

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introduces more specific diagnostic criteria, requiring the presence of liver steatosis associated with at least one of the five cardiometabolic risk factors without excessive alcohol consumption or another concomitant liver disease (Rinella et al, 2023). Fig. 1 summarizes NAFLD, MAFLD, MASLD, and non-alcoholic steatohepatitis (NASH) diagnostic criteria.

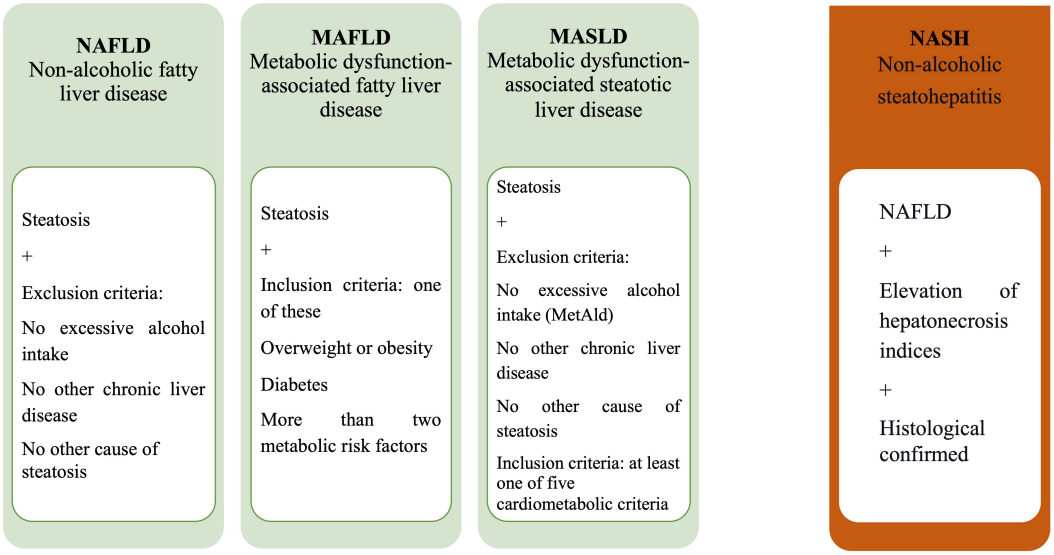

Fig. 1. Summary of NAFLD, MAFLD, MASLD, and NASH diagnostic criteria.

Criticality of the Nomenclature

The term NAFLD has some limitations, particularly in emphasizing the role of metabolic dysfunction in the pathogenetic process. To solve this issue, the MAFLD nomenclature was introduced, which takes into consideration the metabolic and hepatic conditions associated with liver steatosis. This new term seems better at representing the patients' hepatic and extrahepatic clinical features. Recent studies underlined that patients with NAFLD have a better liver profile than those with MAFLD. Indeed, MAFLD patients showed a more advanced fibrotic stage and more significant liver damage (Yamamura et al, 2020).

Furthermore, MAFLD has been associated with an increased risk of kidney and cardiovascular diseases and consequent increased mortality (Kim et al, 2021). Therefore, there is a need for multidisciplinary approaches to managing metabolic and hepatic comorbidities. Although MAFLD nomenclature better framed the hepatic and extrahepatic clinical features of patients with liver steatosis, the term "fat" was replaced with "steatotic" in the MASLD acronym due to the perceived stigma that the former creates. However, MASLD, in contrast with MAFLD, excludes patients with other liver diseases and includes more 'lean' patients, thus excluding the metabolic comorbidities present in MAFLD. In this regard, in a comparative analysis between MASLD, MAFLD, and NAFLD, MAFLD showed worse liver damage and comorbidities outcomes than NAFLD, whereas MASLD presented similar features to NAFLD (Chen et al, 2024). Due to these differences, MASLD tends

to reproduce the NAFLD scenario closely, whereas MAFLD better captures some hepatic and extrahepatic outcomes.

Possible Solutions

Recent studies suggest that MASLD overlaps with NAFLD, which is related to MASLD's diagnostic criteria applying to a more significant number of lean patients, thus with a better metabolic profile, than MAFLD subjects (Chen et al, 2024; Ramírez-Mejía et al, 2024; Colaci et al, 2024). Moreover, both in NAFLD and MASLD, the exclusion of patients with liver comorbidities would lead to a gap in the management of metabolic dysregulation, especially in those individuals who would require more intensive and targeted medical intervention and care. Indeed, this exclusion determines a lower understanding of the severity of liver damage with a reduction of the possibility of managing or preventing any disease related to extrahepatic manifestations. Therefore, a crucial dilemma arises: does MASLD represent only a semantic improvement over MAFLD?

From a metabolic point of view, patients with MASLD have a better profile than those with MAFLD. However, further studies are needed to clarify the best and most precise nomenclature to adopt in clinical practice. The other crucial aspect is the exclusion of patients with liver comorbidities. One solution proposed by Wang et al (2024) is the introduction of the term "combinatorial MASLD". This new nomenclature could ensure patients with liver comorbidities are managed appropriately in multidisciplinary settings.

In conclusion, the literature suggests that MASLD is a more inclusive term than MAFLD. However, the exclusion of patients with liver comorbidities limits both the understanding of the severity of the disease and the possibility of providing appropriate management. Therefore, further studies are required to determine the best nomenclature, including the proposal to use the term "combinatorial MASLD" to integrate patients with different comorbidities into a multidisciplinary approach.

Key Points

- The term MASLD represents a semantic evolution in the classification of patients with hepatic steatosis.
- Unlike MAFLD, MASLD includes patients with a better metabolic profile and excludes patients with hepatic comorbidities.
- The exclusion of patients with hepatic comorbidities may lead to overlooking the holistic management of those patients, who often present with more significant liver damage.
- Adopting the combinatorial term MASLD would allow for a more integrated therapeutic approach for patients with hepatic comorbidities, improving overall clinical outcomes.

Availability of Data and Materials

All data included in this study are available upon request by contact with the corresponding author.

Author Contributions

MLG and LA conceived and collaborated on the project. Both authors contributed to drafting the manuscript and suggesting key revisions to the body of the text. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

LA is serving as one of the Editorial Board members of this journal. We declare that LA had no involvement in the review of this article and has no access to information regarding its review. MLG declares no conflict of interest.

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