Embracing Change: From NAFLD to MASLD under the Steatotic Liver Disease Umbrella

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In 1980, a significant milestone in the field of hepatology occurred when non-alcoholic fatty liver disease (NAFLD) was brought to the forefront through the histological description of non-alcoholic steatohepatitis (NASH) by Ludwig and colleagues [1]. At the time, this groundbreaking observation shed light on a liver condition that primarily affected individuals with obesity and/or type 2 diabetes, and who consumed either minimal amounts of alcohol or abstained entirely. Little did they know that this would mark the beginning of a still ongoing journey towards a deeper understanding of steatotic liver disease.

Over the years, NAFLD has become the most prevalent liver disease in the western world and one of the leading causes of liver transplantation, there is also an increasing prevalent and disease burden in Asia. In parallel, the field of NAFLD has witnessed remarkable progress. One of the most significant advancements has been the development of non-invasive tests (NITs) that have revolutionized the diagnosis, staging, and monitoring of NAFLD/MASLD [2]. These tests have greatly reduced the need for invasive and potentially risky liver biopsies, providing both patients and clinicians with safer and more accessible tools for managing the disease. Furthermore, the field has been eagerly anticipating the first FDA and EMA approvals for novel treatments in 2024 [3], offering new hope for those affected by this condition.

Nonetheless, progress frequently presents its unique set of challenges, and this includes questioning the adequacy of the terminology in use. The concept of revising the nomenclature from NAFLD to a more encompassing term had surfaced in earlier years [4]. However, it wasn't until 2020 that specific initiatives were set in motion to rename the condition [5]. This led to the proposition of an alternative name, "metabolic-associated fatty liver disease" (MAFLD). While this undertaking aimed to enhance our comprehension of the disease, it confronted several obstacles impeding widespread adoption [6].

One primary concern was the potential for stigmatization associated with the renaming using the word “fatty”. Additionally, there was the challenge of changing the definition of the disease that would thwart advances in NITs and treatment. For instance, the term MAFLD included individuals with varying levels of alcohol consumption as well as mixing with other etiologies such as viral hepatitis [6]. Furthermore, the lack of a standardized process for renaming raised concerns about the potential confusion that could arise.

In response to these challenges, prominent organizations such as the American Association for the Study of Liver Diseases (AASLD), the European Association for the Study of the Liver (EASL), and the Latin American Association for the Study of the Liver (ALEH) spearheaded an international effort [7]. This endeavor was meticulously planned and executed, involving a steering committee with representatives from various sectors and broad geographical representation, including academia, patient advocacy groups, diverse organizations, and industry stakeholders. The approach included a Delphi process, involving multiple iterative steps to ensure a comprehensive and well-informed outcome [7].

One of the most significant achievements of this process was the introduction of "Steatotic Liver Disease" (SLD) as an overarching term encompassing all pathophysiological processes leading to liver steatosis [7]. This inclusive terminology recognized the diverse origins of this condition, which could result from metabolic factors, alcohol-related factors, or other causes.

Furthermore, and under the SLD umbrella, the renaming effort led to the transformation of NAFLD into "Metabolic-Dysfunction Associated Steatotic Liver Disease" (MASLD) and NASH into "Metabolic-Dysfunction Associated Steatohepatitis " (MASH). This evolution aimed to emphasize the alignment with the international definition of metabolic syndrome while eliminating potentially stigmatizing terms like "fatty" or "alcoholic." Recent research has shown that over 99% of NAFLD patients meet the criteria for MASLD [8], reinforcing the continuity, relevance and accuracy of this new nomenclature.

Interestingly, while these changes provide a more inclusive and accurate framework both in adults and children, there has been discussion about whether physicians will continue to use terms like "fat" or "fatty" when discussing the disease with their patients. This practice is not uncommon in medicine, where lay terms are sometimes employed to bridge the gap between technical terminology and patient understanding, much like using "heart attack" for myocardial infarction.

One of the most intriguing developments arising from this renaming process is the recognition of the impact of moderate alcohol consumption on the natural history and response to therapies in NAFLD/MASLD. To address this, a new term, "MASLD and Moderate Alcohol" (MetALD), was introduced for individuals who consume more than minimal alcohol (typically 30 g-60 g daily) but do not fit the traditional category of alcohol-related liver disease (ALD) [7]. This new classification provides an opportunity to delve into the interaction between moderate alcohol use and liver health. It also opens doors to research and treatments for a group that would otherwise be excluded from MASH clinical trials. For example, clinical trials investigating the use of GLP-1 in this cohort might be warranted, as GLP-1s have shown promise in addressing metabolic features and diminishing alcohol cravings [9, 10]. This underscores the necessity for additional research in this field.

While the terminology surrounding alcohol-related liver disease remains unchanged, the process considered various other etiologies of SLD, including drug-induced liver injury and viral hepatitis, highlighting the complexity and diversity within this field. Figure 1 summarizes the new terminology.

As with any significant change, there are bound to be questions and uncertainties along the way. The *Clinical Gastroenterology and Hepatology (CGH)* Board of Editors and stakeholders in the field of hepatology welcome these changes, and the inevitable ensuing academic debates. It is hoped that other societies will adopt this new terminology, recognizing the importance of aligning our understanding of the disease with current scientific knowledge and clinical

practices. Furthermore, they extend an invitation to researchers worldwide to explore the implications of these changes and investigate new avenues for improving the diagnosis, management, and treatment of SLD, MASLD/MASH, MetALD, and ARLD.

In conclusion, the journey of understanding and managing SLD and MASLD has come a long way since the initial description in 1980. The renaming is not just a relabeling of the same entity, but rather a more modern, comprehensive, and inclusive terminology that aims to capture the nuances of a complex and heterogeneous disorder. The commitment to research and the pursuit of better outcomes for our patients remain unwavering, and the future holds promise for further advancements in the understanding and treatment of liver diseases.

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