



Review Article

Non-alcoholic fatty liver disease to metabolic dysfunction-associated steatotic liver disease: Changing terminology in the understanding of liver disease

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ABSTRACT

Over the past few decades, non-alcoholic fatty liver disease (NAFLD) has become a major concern in global public health due to its rising prevalence, particularly with the increasing rates of obesity, type 2 diabetes, and metabolic syndrome. Traditionally, NAFLD was the primary term used to describe liver conditions characterized by fat accumulation in the liver, without significant alcohol consumption to explain it. However, recent developments in the field of hepatology have led to a shift in terminology, and Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is defined as presence of hepatic steatosis with one or more cardiometabolic risk factors, and no other identifiable cause of steatosis. Cardiometabolic risk factors are an increase in body mass index or waist circumference; impaired glucose metabolism; high blood pressure; high triglyceride levels; and low levels of high-density cholesterol.

Keywords: Insulin resistance, MASLD, Metabolic syndrome, NAFLD

INTRODUCTION

Over the past few decades, non-alcoholic fatty liver disease (NAFLD) has become a major global public health concern due to its rising prevalence, particularly with the increasing rates of obesity, type 2 diabetes, and metabolic syndrome.¹ Traditionally, NAFLD was the primary term used to describe liver conditions characterized by fat accumulation in the liver, without significant alcohol consumption to explain it. However, recent developments in the field of hepatology have led to a shift in terminology, and NAFLD is being replaced with a new term: metabolic dysfunction-associated steatotic liver disease (MASLD). This transition is not just a lexical change but a reflection of deeper insights into the underlying mechanisms of the disease.

THE HISTORY AND LIMITATIONS OF NAFLD

NAFLD, by definition, refers to a condition in which fat accumulates in the liver in individuals who consume little or no alcohol. The term was introduced to differentiate this condition from alcoholic liver disease. NAFLD encompasses a spectrum of liver conditions, ranging from simple steatosis (fatty liver) to more severe forms, such as non-alcoholic steatohepatitis (NASH), which can lead to cirrhosis and liver failure.

While NAFLD has been useful in diagnosing and understanding this group of liver diseases, it also has notable limitations. One of the most prominent issues with the term NAFLD is its inability to reflect the root cause of the disease, which is more closely related to metabolic dysfunction

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rather than just the absence of alcohol consumption. NAFLD fails to adequately capture the complex interplay of obesity, insulin resistance, diabetes, hypertension, and dyslipidemia, all of which are central to the development of liver damage.

Furthermore, the term “non-alcoholic” has been criticized for being too narrow, as it could imply that the condition only develops in people who do not consume alcohol at all. However, the liver disease process in NAFLD patients is driven more by metabolic factors, and alcohol consumption in small amounts may also exacerbate or modify the condition.²

TRANSITIONING TO MASLD: A MORE COMPREHENSIVE TERMINOLOGY

In response to these limitations, the term NAFLD is gradually being replaced with MASLD. This new terminology was proposed by an international group of liver disease experts and hepatologists in 2020. It has since gained traction in scientific literature and clinical practice. On June 24, 2023, the American Association for the Study of Liver Diseases, the European Association for the Study of Liver, and the Latin American Association for the Study of Liver jointly led a global Delphi consensus process that suggested changing the terminology from NAFLD to MASLD.³ This change reflects a broader and more accurate understanding of the disease process, which centers around metabolic dysfunction. MASLD is defined as the presence of hepatic steatosis with one or more cardiometabolic risk factors (CMRF) and no other identifiable cause. Cardiometabolic risk factors refer to an increase in BMI or waist circumference, impaired glucose metabolism, high blood pressure, high triglyceride levels, and low high-density cholesterol levels.

MASLD is not just a rebranding; it represents a shift in focus toward the underlying metabolic dysfunctions that drive the accumulation of fat in the liver. This term acknowledges that fatty liver disease is part of a wider syndrome of metabolic derangements that often includes conditions such as obesity, insulin resistance, and type 2 diabetes.⁴ MASLD also emphasizes that the condition is closely linked to the dysfunction of multiple organ systems, particularly the liver, but also the cardiovascular system and other metabolic processes.⁵

KEY COMPONENTS OF MASLD

The concept of MASLD integrates several key elements:

1. **Metabolic dysfunction:** The primary driver of MASLD is metabolic dysfunction, which encompasses factors like insulin resistance, obesity, and disturbances in lipid metabolism. These factors contribute to the accumulation of fat in the liver.

2. **Steatosis:** The term "steatosis" refers to fat accumulation in liver cells, which is a hallmark feature of the disease. In MASLD, the extent of steatosis can vary, ranging from mild to severe.
3. **Associated diseases:** MASLD often coexists with other metabolic disorders, including type 2 diabetes, hypertension, dyslipidemia, and cardiovascular disease. This reflects the interconnected nature of metabolic disorders and their shared risk factors.
4. **Progression to severe forms:** Similar to NAFLD, MASLD can progress to more severe forms, such as NASH, which can lead to cirrhosis, liver failure, and an increased risk of liver cancer.

WHY CHANGE THE TERMINOLOGY?

The shift from NAFLD to MASLD is not just about semantics. It's about better understanding the disease and improving clinical care for patients. Here are several reasons why this change is important:

1. **Focus on the root cause:** By emphasizing metabolic dysfunction, MASLD highlights the need for interventions that target the underlying risk factors, such as obesity and insulin resistance, rather than simply focusing on the liver. This approach encourages a holistic treatment strategy.
2. **Improved patient care:** MASLD provides a more accurate diagnosis, helping healthcare providers better assess the risk of progression to severe liver disease. By recognizing the metabolic roots of liver fat accumulation, clinicians are better equipped to provide personalized care, targeting the full spectrum of metabolic disorders.
3. **Aligning with current research:** As research into liver disease advances, scientists are uncovering new insights into how metabolic dysfunctions contribute to the development of fatty liver disease. MASLD is better aligned with the current understanding of these complex pathophysiological mechanisms, which could help lead to new therapeutic approaches.
4. **Reducing stigma:** The term "non-alcoholic" in NAFLD has sometimes caused confusion and may carry a stigma, as patients might believe their condition is related to alcohol use. The new terminology helps shift the focus away from alcohol consumption and onto the metabolic issues that truly drive the disease.

CHALLENGES AND FUTURE DIRECTIONS

While MASLD represents a more accurate and comprehensive understanding of liver disease, the transition will not be without challenges. One significant challenge is ensuring widespread adoption of the new term across medical communities and clinical settings. Many clinicians and

researchers are still more familiar with NAFLD and may resist changing the terminology, particularly if it has been deeply entrenched in clinical practice and diagnostic criteria.

Moreover, this shift may require updates to clinical guidelines, educational materials, and diagnostic tools, all of which take time and effort. It will also be essential to establish standardized definitions and diagnostic criteria for MASLD to ensure consistency and reduce potential confusion.

CONCLUSION

The transition from NAFLD to MASLD represents an important step forward in understanding liver disease. By embracing a more accurate terminology that reflects the underlying metabolic dysfunction, MASLD promises to lead to better diagnoses, improved treatments, and a deeper understanding of the complex relationship between the liver and metabolic health. As the medical community continues to refine its approach to liver disease, the adoption of MASLD will likely play a crucial role in addressing the growing global burden of metabolic-associated liver diseases.

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