

Navigating the Nomenclature of Liver Steatosis: Transitioning from NAFLD to MAFLD and MASLD - Understanding Affinities and Differences

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ABSTRACT

The escalating prevalence of non-alcoholic fatty liver disease (NAFLD) represents a significant challenge to public health, with an increasing impact observed across various demographics. This review delivers a comprehensive evaluation of the evolving terminology in steatotic liver disease (SLD), documenting the transition from NAFLD to metabolic dysfunction-associated fatty liver disease (MAFLD), and progressing to the latest terms, metabolic dysfunction-associated fatty liver disease (MASLD) and MASLD with increased alcohol intake (MetALD). We conducted a comprehensive review of literature discussing the benefits and drawbacks of these nomenclatural changes. Clinical evidence supporting MASLD and MetALD, including the implications of alcohol consumption thresholds on disease classification and outcomes, was analyzed. The “MAFLD” and “MASLD” labels align with the pathophysiology of metabolic diseases, afford a positive disease connotation, and facilitate the identification of more severe diseases, such as significant fibrosis or advanced liver disease. However, the MAFLD criteria may underdiagnose lean, non-overweight, or non-obese individuals with MAFLD. The review underscores the understanding of liver diseases linked to metabolic dysfunction and alcohol use. The shift in terminology marks progress towards a clinical diagnosis that reflects underlying pathophysiology. However, additional studies are necessary to assess the long-term effects of these changes and their efficacy in enhancing patient care and health outcomes.

Keywords: NAFLD; MAFLD; MASLD; MetALD; fatty liver (Siriraj Med J 2024; 76: 234-243)

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is a prevalent condition affecting approximately one-quarter of individuals of the global population.¹⁻⁴ In a large prospective study in the US employing magnetic resonance imaging (MRI) and liver elastography, an estimated prevalence of NAFLD was 38%, with 14% categorized as non-alcoholic steatohepatitis (NASH).⁵ Similarly, a pooled analysis among European countries revealed a 26.9% NAFLD prevalence,⁶ whereas in Asia, the overall prevalence was approximately 30% which increased to

33.9% in 2017.⁷ Notably, a predicted model anticipated a further 18.3% increase in the global prevalence, with China exhibiting the highest rise owing to its aging population and diabetes.⁸ Moreover, the number of liver transplants due to hepatocellular carcinoma (HCC) from fatty liver without significant alcohol consumption between 2002 to 2012 increased by nearly 4-fold, becoming the third leading indication for liver transplantation in the US.⁹ Given the enormous burden and rapid growth of NAFLD, prevention strategies and NASH therapy are imperative.¹⁰ The spectrum of disease is heterogeneous;

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from simple steatosis, steatohepatitis, cirrhosis, and eventually HCC development, particularly in patients having advanced fibrosis and cirrhosis.¹¹ The majority of HCC in patients with NAFLD occurred in the cirrhotic background, however, a substantial proportion of up to 38% had arisen from non-cirrhosis.¹² Importantly, patients with fatty liver disease are at risk of developing not only hepatic but also extrahepatic cancers, including endometrial cancer, gastric cancer, pancreatic cancer, and colon cancer.¹³

In the past, fatty liver disease was classified into 2 groups: alcohol-associated liver disease (ALD) and NAFLD, based on the amount of alcohol consumption in individuals with evidence of hepatic steatosis.^{14–19} In 2020, an international consensus proposed a new terminology, namely metabolic dysfunction-associated fatty liver disease (MAFLD).²⁰ This change carries potential benefits in increasing awareness and in accordance with pathophysiologic aspects, as metabolic dysfunction results in a wide range of systemic derangement, including liver disease. More recently, in June 2023, the new nomenclature with the overarching term of steatotic liver disease (SLD) comes with the new subclassifications of metabolic dysfunction-associated fatty liver disease (MASLD), MASLD with increased alcohol intake (MetALD), and ALD has been introduced and endorsed by the international liver societies.^{21–23} This review focuses on the transition of nomenclature from NAFLD to MAFLD to MASLD/MetALD, and its impacts.

Naming change from NAFLD to MAFLD

In 2020, a group of international experts proposed a new nomenclature of NAFLD to MAFLD, using positive criteria (metabolic dysfunction) rather than a negative one (non-alcoholic), and did not exclude patients with significant alcohol consumption or concomitant with other chronic liver diseases.²⁰ Table 1 depicts the comparisons between NAFLD and MAFLD. The diagnostic criteria included evidence of hepatic steatosis along with one of the following: 1) overweight or obesity (≥ 23 kg/m² in Asians or ≥ 25 kg/m² in Caucasians), 2) diagnosis with type 2 diabetes, or 3) presence of at least 2 criteria of cardiometabolic and MAFLD risks. Metabolic risks from physical examination included the presence of an increase in waist circumference (WC: ≥ 90 cm or ≥ 80 cm in Asian men and women, respectively or ≥ 102 cm and ≥ 88 cm in Caucasian men and women, respectively), high blood pressure ($\geq 130/85$ mmHg) or use of antihypertensive drug.²⁰ Evidence of elevated triglycerides level (TG) (≥ 150 mg/dL), low level of HDL-cholesterol (<40 mg/dL in men or <50 mg/dL in women), prediabetes status (defined as fasting plasma glucose (FPG) levels 100–125 mg/dL or hemoglobin (Hb) A1c 5.7–6.4% or 2-hour post prandial plasma glucose levels 140–199 mg/dL), homeostasis model assessment of insulin resistance (HOMA-IR) score ≥ 2.5 , high sensitivity C-reactive protein (CRP) level >2 mg/L were considered essential metabolic risk factors for the diagnostic criteria in individuals who are non-overweight/obese and absence of diabetes mellitus.²⁰

TABLE 1. Comparisons between NAFLD and MAFLD.

Characteristics	NAFLD	MAFLD
Alcohol use	Exclude NAFLD if consume >3 drinks/day in men or >2 drinks/day in women	Can be included
Viral hepatitis	Exclude NAFLD if the presence of hepatitis B or hepatitis C	Can be included
Other chronic liver diseases	Exclude NAFLD	Can be included, such as drug-induced liver injury, autoimmune hepatitis
Cirrhosis	Mostly diagnosed with cryptogenic cirrhosis	Can be diagnosed with MAFLD-related cirrhosis if having evidence of steatosis in the past or present with risk factors of MAFLD
Alternative cause of fatty liver	Previously defined as a secondary cause	no more 'primary' or 'secondary' causes of fatty liver, only MAFLD and alternative causes of fatty liver

Reasons for the name change

While the term NAFLD has been widely used for a long-term, it appears to have certain significant drawbacks. NAFLD is a term with a negative connotation (non-) and can stigmatize those with alcohol use issues. Additionally, NAFLD fails to encapsulate the primary pathogenesis of the disease, which is metabolic derangement. Contrarily, the new term, MAFLD, provides greater mechanistic insight into metabolic dysregulation including inflammatory markers such as highly sensitive CRP, and uses the positive criteria to establish the diagnosis. Furthermore, other causes of chronic liver disease (CLD) need to be excluded in the diagnosis of NAFLD, while MAFLD, covers patients with dual liver pathology e.g., MAFLD with hepatitis C virus, MAFLD with autoimmune hepatitis, or when associated with ALD. Additionally, NAFLD studies often rely on histology for eligibility, potentially impeding trial endpoints. Using the term MAFLD and understanding its multiple phenotypes may be beneficial for clinical trial design and developing therapies targeted to different subtypes of MAFLD. Lastly, renaming NAFLD to MAFLD could improve public recognition and increase the chance of receiving funds, as it acknowledges that fatty liver can be associated with metabolic dysregulation rather than just liver disease alone.

Diagnosis of MAFLD with other etiologies

MAFLD can coexist with other CLDs, accelerating the progression of liver fibrosis and cancer development. The most common etiology that is associated with MAFLD is ALD.²⁴ In the presence of dual causes, the patients were more likely to be younger, with male sex preponderance, elevated liver enzymes, and higher Aspartate Aminotransferase (AST) to Platelet Ratio Index.²⁵ The positive criteria for the diagnosis of MAFLD reflect the real situation in clinical practice where many etiologies of CLD might coexist in a single patient. The NAFLD criteria allowed the alcohol intake with certain cutoff levels (<3 drinks/day in men and <2 drinks/day in women).^{14–16} Currently, there is no longer a so-called ‘safe amount’ of alcohol intake.²⁶ A large database study that included 28 million individuals globally indicated that the level of alcohol consumption that can minimize the harm of alcohol is zero.²⁷ Similarly, a 4.9-year follow-up study of 58,927 Korean patients with NAFLD reported that light and moderate drinkers were also associated with worsening fibrosis scores.²⁸ Another study also supported alcohol abstinence to minimize the risk of fibrosis progression, particularly in patients with metabolic syndrome.²⁹

However, MAFLD in combination with chronic hepatitis B (CHB) infection, still exhibited controversial

results for the long-term outcomes when compared with those associated with CHB alone. The presence of hepatic steatohepatitis has been shown to be a strong predictor of having significant fibrosis (odds ratio [OR] 10.0, 95% confidence interval [CI], 2.08–48.5) and advanced fibrosis (OR 3.45, 95% CI, 1.11–10.7).³⁰ Hepatic steatosis was also significantly associated with a 4-fold increased risk of all-cause mortality and cancer.³¹ Another long-term cohort study, including more than a thousand patients from 2 tertiary centers in Canada and Netherlands, demonstrated that 27.5% of patients with CHB were concomitant with MAFLD, and was proven histologically,³² while those with MAFLD had an increased risk of decompensation (adjusted hazard ratio [HR] 2, 95% CI 1.26–3.19) and HCC (adjusted HR 1.93, 95%CI 1.17–3.21). Recently, a study from Rugivarodom et al, reported that patients with CHB with concomitant hepatic steatosis on liver biopsy were at a higher risk of developing liver-related mortality (HR 3.7).³³ Contradictorily, few studies also demonstrated that the liver-related complications were not statistically significantly different between patients with CHB with and without hepatic steatosis.³⁴

Hepatitis C infection, particularly in genotype 3, is directly associated with causing hepatic steatosis.³⁵ Other genotypes were associated with steatosis via the mechanism of insulin resistance.³⁶ Overall, the prevalence of dual chronic hepatitis C (CHC) infection and fatty liver was approximately 27%–44.8%.^{37,38} Concomitant hepatic steatosis and CHC accelerated fibrosis progression and extrahepatic events including cardiovascular, renal events and cancer development.^{39,40}

In summary, a combination of other causes of CLD with MAFLD was generally associated with poor outcomes, as well as both hepatic and extrahepatic complications. Nonetheless, it has been concluded that virological suppression and sustained virological response in individuals with CHB and CHC can improve hepatic fat.^{31,41}

Comparisons of NAFLD and MAFLD

Table 2 illustrates studies comparing NAFLD and MAFLD. The vast majority of patients with fatty liver can be included by either using the NAFLD or MAFLD criteria. Although some studies showed the same producibility and characteristics of patients in the diagnosis of fatty liver between NAFLD and MAFLD criteria^{42–44}, several others reported the advantages of MAFLD criteria over NAFLD, including enhanced detection of patients with significant or advanced hepatic fibrosis, cardiovascular risk,^{25,32,45–50} as well as a higher all-cause mortality.⁵¹ Interestingly, non-obese MAFLD may be overlooked due

TABLE 2. Summarized comparative studies between MAFLD and NAFLD.

Author, year	Sample size	Study design	Key results	Implication
Lin <i>et al.</i> ⁵³ , 2020	13,083	Retrospective study using data from the third National Health and Nutrition Examination Surveys of the United States, 1988-1994 (NHANES III)	MAFLD prevalence 31.24% NAFLD prevalence 33.23% Patients with MAFLD had higher age, higher body mass index, higher diabetes, hypertension, insulin resistance, hepatic enzymes, and liver fibrosis score (NFS score, FIB-4 score, and BARD score)	MAFLD criteria can better identify patients with advanced fibrosis when compared with the NAFLD criteria.
Wong <i>et al.</i> ⁴² , 2020	1,013	Retrospective study from Hongkong census database, using MRI, liver stiffness measurement (FibroScan®)	MAFLD 25.9% NAFLD 25.7% NAFLD only 5.1% Only one with both MAFLD and NAFLD had FibroScan® ≥10 kPa.	MAFLD criteria did not show a significant change in NAFLD prevalence.
Yamamura <i>et al.</i> ⁴⁵ , 2020	765	Retrospective study in health check-up, Japan, using FIB-4, liver stiffness measurement	MAFLD 79.6% NAFLD 70.7% MAFLD (OR 4.401; 95% CI 2.144–10.629; $p<0.0001$), alcohol intake (OR 1.761; 95% CI 1.081–2.853; $p=0.0234$), and NAFLD (OR 1.721; 95%CI 1.009–2.951; $p=0.0463$) associated with F2 fibrosis.	MAFLD criteria could identify more patients with significant fibrosis.
Baratta <i>et al.</i> ⁵² , 2021	795	Cohort study (The Plinio Study), Italy	96.5% of NAFLD identified with MAFLD MAFLD criteria missed 28 in 68 patients of lean NAFLD (41%).	Most NAFLD patients overlapped with MAFLD. However, a substantial lean NAFLD may be missed.
Ciardullo <i>et al.</i> ⁴⁴ , 2021		A cross-sectional study of NHANES, 2017-2018, using controlled attenuation parameter (CAP) and transient elastography	NAFLD 37.1% MAFLD 39.1% Similar risk of advanced fibrosis (7.5% vs. 7.4% among NAFLD and MAFLD, respectively)	The new MAFLD criteria had the same diagnostic yield when compared with that of the NAFLD criteria.

TABLE 2. Summarized comparative studies between MAFLD and NAFLD. (Continue)

Author, year	Sample size	Study design	Key results	Implication
Fujii <i>et al.</i> ⁴⁷ , 2021	2,254	A cross-sectional study in Japan, using FibroScan-aspartate aminotransferase (FAST) score to identify progressive liver disease.	MAFLD 35% NAFLD 27.4% MAFLD criteria had a higher FAST score (≥ 0.35) than did NAFLD criteria (8.6% vs. 7.7%).	MAFLD criteria may identify progressive liver disease by FAST score.
Guerreiro <i>et al.</i> ⁴⁸ , 2021	1,233	Retrospective study, biopsy-proven, 2013-2018, Brazil	MAFLD had numerically higher cardiovascular event incidences than did NAFLD (20.1% vs. 12.8%, $p=0.137$). MAFLD with viral hepatitis had a higher 10-year cardiovascular risk than negative viral hepatitis MAFLD (21.1% vs. 4.3%, $p=0.02$)	MAFLD with other HBV+/- HCV infection had a higher 5-fold risk of cardiovascular event when compared with MAFLD associated with no viral hepatitis infection.
Huang <i>et al.</i> ⁴⁶ , 2021	175	Retrospective study, National Taiwan University Hospital, Taiwan	Both MAFLD and NAFLD 41.1% MAFLD 43.8% NAFLD only 4.9% MAFLD only 10.3% MAFLD only had high bilirubin levels, low platelet count, high NAS score, and advanced cirrhosis percentage (48.1% vs 0%, $p<0.05$).	MAFLD only without NAFLD had severe disease and severe histology than patients with NAFLD only.
Huang <i>et al.</i> ⁵⁴ , 2021	1,217	Retrospective study, Fujian Hospital, China, biopsy-proven	MAFLD 35% NAFLD 48.07% MAFLD did not capture steatosis 13.8%.	MAFLD criteria may overlook steatosis.
Niriella <i>et al.</i> ⁴⁹ , 2021	2,985	Retrospective study, community-based cohort in Sri Lanka	MAFLD 33.1% NAFLD 31.5% In patients with MAFLD but not NAFLD (2.9%) had higher odds of developing incident general obesity, central obesity, diabetes, and cardiovascular events.	Patients with MAFLD have high risks for metabolic and cardiovascular events.

TABLE 2. Summarized comparative studies between MAFLD and NAFLD. (Continue)

Author, year	Sample size	Study design	Key results	Implication
Tsutsumi <i>et al.</i> ⁵⁰ , 2021	2,306	Cohort study, Japan	MAFLD 80.7% NAFLD 63.4% MAFLD (HR 1.08, 95% CI 1.02–1.15, $p=0.014$) and alcohol consumption (20–39 g/day; HR 1.73, 95% CI 1.26–2.36, $p=0.001$) were independently associated with worsening of the Suita score.	MAFLD criteria better identified patients with a higher risk of cardiovascular disease.
Van kleeef <i>et al.</i> ⁵⁵ , 2021	5,445	A cross-sectional analysis within the Rotterdam Study (large prospective population-based cohort), ultrasound-based	MAFLD 34.3% NAFLD 29.5% MAFLD only 5.9% NAFLD only 1% MAFLD only was strongly associated with fibrosis (adjusted OR 5.3).	MAFLD criteria improved the detection of fibrosis.
Zhang <i>et al.</i> ⁴³ , 2021	19,617	Retrospective study from NHANES, 1999-2016	MAFLD increased from 28.4% to 35.8% and was higher than NAFLD (33%). MAFLD and NAFLD had similar 10-year cardiovascular risk (13.2% vs. 12.9%) and chronic kidney disease (18.7% vs. 18.8%).	MAFLD had the same cardiovascular and renal dysfunction compared with NAFLD.
Kim <i>et al.</i> ⁵¹ , 2021	7,761	Participants in the NHANES III with linked mortality data	Prevalence of any fatty liver was 32.6% -23.5% concordant between NAFLD and MAFLD -6.1% NAFLD only -2.4% MAFLD only Hazard ratio (HR) for all-cause mortality: -MAFLD+/NAFLD+ 1.26 (95%CI: 1.16-1.38) -MAFLD-/NAFLD+ 0.90 (95%CI: 0.56-1.43) -MAFLD+/NAFLD- 1.97 (95%CI: 1.47-2.64)	MAFLD was significantly associated with increased mortality while NAFLD without metabolic risk factors was not.

Abbreviations: ALD, alcoholic associated liver disease; CAP, controlled attenuation parameter; FAST, FibroScan-aspartate aminotransferase score; FIB-4, Fibrosis-4; HBV, hepatitis B virus; HCV, hepatitis C virus; MAFLD, metabolic dysfunction-associated fatty liver disease; NAFLD, non-alcoholic fatty liver disease; NAS score, non-alcoholic fatty liver disease activity score; NFS, NAFLD fibrosis score; NHANES III, the third National Health and Nutrition Examination Surveys of the United States

to the absence of any obvious metabolic dysregulation under the new criteria.⁵² This drawback might stem from the lack of inflammatory or insulin resistance markers in retrospective studies, which are now incorporated in the new MAFLD criteria if the patients are non-obese or non-diabetic.

Most recent nomenclature: MASLD and MetALD

More recently, in June 2023, the newest nomenclature of the MASLD under the overarching term of SLD, was introduced in the International Liver Congress held in Vienna. This nomenclature was derived from the Delphi consensus process and endorsed by the major hepatology societies.^{21–23} In this updated nomenclature, not only is the term “MASLD” introduced, but for the first time, another unique category of MetALD was established.

In the transition from NAFLD to MAFLD, the authors proposed replacing the term “nonalcoholic” with “metabolic dysfunction” to better reflect the etiology of the disease rather than merely excluding significant alcohol consumption in patients with hepatic steatosis. However, the term “fatty” in MAFLD is considerably stigmatizing for the patients, whereas “steatotic” in MASLD is more neutral and medically inclined.^{21–23} The term “steatotic” may cause confusion for patients regarding the disease due to its medical nature. Nevertheless, the impact of potentially stigmatizing terms in non-English speaking countries, such as Thailand, where both “fatty” and “steatotic” translate to the same word in Thai, remains unknown, potentially leading to uniform communication regarding the nomenclature of the disease between doctors and patients.

Furthermore, beyond the distinction between “fatty” and “steatotic”, there are differences in the diagnostic criteria for MAFLD and MASLD.^{20–23} The variations in the definitions of MAFLD and MASLD are depicted in [Table 3](#). The most significant differences are the alcohol threshold and the number of cardiometabolic risks required for the diagnosis under each terminology. While MAFLD emphasizes the number of cardiometabolic risks and categorizes patients into obese, lean/normal weight, and type 2 diabetes MAFLD, the diagnosis of MASLD mandates the exclusion of significant alcohol consumption. For MASLD, if patients exhibit both cardiometabolic risk(s) and alcohol consumption >20/30 gm in women/men but less than 50/60 gm/day in women/men, they would be categorized as MetALD, and if the alcohol consumption exceeds 50/60 gm/day in women/men, regardless of cardiometabolic risk presence, they would be categorized as ALD.

Clinical evidence of the MASLD and MetALD nomenclature

Given that the alcohol intake threshold for diagnosing MASLD is the same as the previous criterion for diagnosing NAFLD, a clinical question arises regarding the potential utilization of existing NAFLD data under the new MASLD definition. Recent studies conducted in the US, Korea, and Hong Kong have demonstrated that the characteristics of individual patients with NAFLD and MASLD are nearly identical, with an overlap of up to 98% to 99% of patients.^{56–58} Therefore, in general, the term MASLD can be used interchangeably with the previous term NAFLD. A study from India reported that the MASLD criteria is superior to MAFLD in diagnosing the disease in patients with normal weight/lean. Nevertheless, the major caveat is that this study was retrospective, and the HOMA-IR and the hs-CRP were unavailable for the majority of patients in that cohort.⁵⁹ The data regarding the comparisons between the MAFLD and MASLD criteria in both patients’ characteristics and longitudinal outcomes are very limited, at this point.

MetALD, introduced for the first time, has its own definition due to concerns regarding the potential impact of varying alcohol intake on clinical outcomes in patients with cardiometabolic risk and the presence of hepatic steatosis. For instance, in patients with type 2 diabetes and fatty liver, it is unclear whether no/minimal alcohol intake or consuming moderate amounts would have different effects. The usefulness of determining this MetALD subcategory is yet to be explored. Some studies have indicated a higher risk of long-term overall and cardiovascular mortality in individuals with MASLD and MetALD compared to those without SLD.^{57,60} However, specific comparisons between MASLD and MetALD groups to assess the effect of alcohol consumption in patients with cardiometabolic features, using the same dataset of NHANES III dataset, have yielded a non-significantly higher risk of long-term overall mortality compared to the MASLD group at an adjusted hazard ratio of 1.11 (95%CI: 0.90–1.38, $p=0.337$), after adjusting the age, sex, smoking status, race-ethnicity, and liver fibrosis category level using a noninvasive biomarker. [unpublished data, the results of our analysis were presented at the EASL SLD summit in September 2023.]

Lastly, there are some challenges associated with the transition from the nomenclature NAFLD to MAFLD and MASLD. First, these terms may confuse patients because there are two terms, MAFLD and MASLD. Second, it is unclear whether the clinical trial endpoints for new drugs are the same for or differ between these two terms. Lastly, there is inconsistency in the adoption of the new term

TABLE 3. The differences in the definitions of MAFLD and MASLD.

Domain	MAFLD	MASLD
Identification of hepatic steatosis	Either imaging techniques, blood biomarkers/scores, or liver histology	Imaging or histology
Alcohol consumption	At any level can be included	<20/30 gm/day in women/men
Cardiometabolic risk	<p>If the presence of obesity or type 2 diabetes → MAFLD</p> <p>If no DM and normal weight → need ≥2 of the following to diagnose:</p> <p>1) WC ≥102/88 cm in men/women (≥90/80 in Asians).</p> <p>2) Prediabetes (HbA1c of 5.7–6.4%, or FPG of 5.6–6.9 mmol/L, or 2-hour post-load glucose levels of 7.8–11.0 mmol/L).</p> <p>3) Blood pressure ≥130/85 mmHg or under anti-hypertension therapy.</p> <p>4) HDL-c <1.0/1.3 mmol/L for men/women.</p> <p>5) TG ≥1.70 mmol/L or specific drug treatment.</p> <p>6) HOMA-IR score ≥2.5.</p> <p>7) hs-CRP level >2 mg/L.</p>	<p>≥1 of 5 cardiometabolic risk factors:</p> <p>1) BMI ≥ 25 kg/m² [23 Asia] or 94 cm (M) 80 cm (F) or ethnicity adjusted</p> <p>2) FPG ≥ 5.6 mmol/L [100 mg/dL] or 2-hour post-load glucose levels ≥ 7.8 mmol/L or HbA1c ≥ 5.7% [39 mmol/L] or type 2 diabetes or treatment for type 2 diabetes</p> <p>3) Blood pressure ≥ 130/85 mmHg or specific antihypertensive drug treatment</p> <p>4) TG ≥ 1.70 mmol/L [150 mg/dL] or lipid lowering treatment</p> <p>5) HDL-cholesterol ≤ 1.0 mmol/L [40 mg/dL] (M) and ≤ 1.3 mmol/L [50 mg/dL] (F) or lipid lowering treatment</p>
Subtypes	<p>1. obese MAFLD</p> <p>2. lean/normal weight MAFLD</p> <p>3. type 2 diabetes MAFLD</p>	None, but those with alcohol consumption between 20/30 and 50/60 gm/d in women/men were categorized into MetALD.

by international liver societies; for example, MASLD is endorsed by the European Association for the Study of the Liver (EASL) and the American Association for the Study of Liver Diseases (AASLD), whereas MAFLD is endorsed by the Asian Pacific Association for the Study of the Liver (APASL).

CONCLUSION

In conclusion, efforts to improve disease nomenclature based on the underlying pathophysiology, as well as raising awareness among doctors, patients, and the public awareness on fatty liver disease, have been made substantial in recent years. Emphasizing the role of metabolic dysfunction as a cause of disease and acknowledging its significant long-term cardiometabolic morbidity and mortality risk is crucial. Nonetheless, further investigation is necessary to determine whether the MASLD and MetALD definitions offer superior diagnostic and prognostic value compared to the MAFLD definition.

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Conflict of interest

Kaewdech A. and Sripongpun P. declare no conflicts of interest.

REFERENCES

- Huang DQ, El-Serag HB, Loomba R. Global epidemiology of NAFLD-related HCC: trends, predictions, risk factors and prevention. *Nat Rev Gastroenterol Hepatol*. 2021;18(4):223-38.
- Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease—meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology*. 2016;64(1):73-84.
- Dufour JF, Scherer R, Balp MM, McKenna SJ, Janssens N, Lopez P, et al. The global epidemiology of nonalcoholic steatohepatitis (NASH) and associated risk factors—A targeted literature review. *Endocr Metab Sci*. 2021;3:100089.
- Younossi Z, Anstee QM, Marietti M, Hardy T, Henry L, Eslam M, et al. Global burden of NAFLD and NASH: trends,

- predictions, risk factors and prevention. *Nat Rev Gastroenterol Hepatol*. 2018;15(1):11-20.
5. Harrison SA, Gawrieh S, Roberts K, Lisanti CJ, Schwobe RB, Cebe KM, et al. Prospective evaluation of the prevalence of non-alcoholic fatty liver disease and steatohepatitis in a large middle-aged US cohort. *J Hepatol*. 2021;75(2):284-91.
 6. Cholongitas E, Pavlopoulou I, Papatheodoridi M, Markakis GE, Bouras E, Haidich AB, et al. Epidemiology of nonalcoholic fatty liver disease in Europe: a systematic review and meta-analysis. *Ann Gastroenterol*. 2021;34(3):404-14.
 7. Li J, Zou B, Yeo YH, Feng Y, Xie X, Lee DH, et al. Prevalence, incidence, and outcome of non-alcoholic fatty liver disease in Asia, 1999-2019: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol*. 2019;4(5):389-98.
 8. Estes C, Anstee QM, Arias-Loste MT, Bantel H, Bellentani S, Caballeria J, et al. Modeling NAFLD disease burden in China, France, Germany, Italy, Japan, Spain, United Kingdom, and United States for the period 2016-2030. *J Hepatol*. 2018;69(4):896-904.
 9. Wong RJ, Cheung R, Ahmed A. Nonalcoholic steatohepatitis is the most rapidly growing indication for liver transplantation in patients with hepatocellular carcinoma in the U.S. *Hepatology*. 2014;59(6):2188-95.
 10. Lazarus JV, Colombo M, Cortez-Pinto H, Huang TTK, Miller V, Ninburg M, et al. NAFLD — sounding the alarm on a silent epidemic. *Nat Rev Gastroenterol Hepatol*. 2020;17(7):377-9.
 11. Clinical outcomes in adults with nonalcoholic fatty liver disease | NEJM [internet]. *New England Journal of Medicine* [cited Jan 24 2022]. Available from: <https://www.nejm.org/doi/10.1056/NEJMdo006255/full/>.
 12. Stine JG, Wentworth BJ, Zimmet A, Rinella ME, Loomba R, Caldwell SH, et al. Systematic review with meta-analysis: risk of hepatocellular carcinoma in non-alcoholic steatohepatitis without cirrhosis compared to other liver diseases. *Aliment Pharmacol Ther*. 2018;48(7):696-703.
 13. Allen AM, Hicks SB, Mara KC, Larson JJ, Therneau TM. The risk of incident extrahepatic cancers is higher in non-alcoholic fatty liver disease than obesity – A longitudinal cohort study. *J Hepatol*. 2019;71(6):1229-36.
 14. Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, et al. The diagnosis and management of nonalcoholic fatty liver disease: practice guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2018;67(1):328-57.
 15. European Association for the Study of the Liver (EASL), European Association for the Study of Diabetes (EASD), European Association for the Study of Obesity (EASO). EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. *J Hepatol*. 2016;64(6):1388-402.
 16. Wong VWS, Chan WK, Chitturi S, Chawla Y, Dan YY, Duseja A, et al. Asia-Pacific Working Party on Non-alcoholic Fatty Liver Disease guidelines 2017-Part 1: Definition, risk factors and assessment. *J Gastroenterol Hepatol*. 2018;33(1):70-85.
 17. Chitturi S, Wong VWS, Chan WK, Wong GLH, Wong SKH, Sollano J, et al. The Asia-Pacific Working Party on Non-alcoholic Fatty Liver Disease guidelines 2017-Part 2: Management and special groups. *J Gastroenterol Hepatol*. 2018;33(1):86-98.
 18. National guideline centre (UK). Nonalcoholic fatty liver disease: assessment and management [internet]. London: National Institute for Health and Care Excellence. UK; 2016 [cited Jan 24 2022]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK374135/>. (National Institute for Health and Care Excellence. Guidance).
 19. Italian Association for the Study of the Liver (AISF) (AISF). AISF position paper on nonalcoholic fatty liver disease (NAFLD): updates and future directions. *Dig Liver Dis*. 2017;49(5):471-83.
 20. Eslam M, Newsome PN, Sarin SK, Anstee QM, Targher G, Romero-Gomez M, et al. A new definition for metabolic dysfunction-associated fatty liver disease: an international expert consensus statement. *J Hepatol*. 2020;73(1):202-9.
 21. Rinella ME, Lazarus JV, Ratziu V, Francque SM, Sanyal AJ, Kanwal F, et al. A multi-society Delphi consensus statement on new fatty liver disease nomenclature. *Hepatology*. 2023;78(6):1966-86.
 22. Rinella ME, Lazarus JV, Ratziu V, Francque SM, Sanyal AJ, Kanwal F, et al. A multi-society Delphi consensus statement on new fatty liver disease nomenclature. *Ann Hepatol*. 2024;29(1):101133.
 23. Rinella ME, Lazarus JV, Ratziu V, Francque SM, Sanyal AJ, Kanwal F, et al. A multi-society Delphi consensus statement on new fatty liver disease nomenclature. *J Hepatol*. 2023;79(6):542-56.
 24. Eslam M, Sanyal AJ, George J. Toward more accurate nomenclature for fatty liver diseases. *Gastroenterology*. 2019 Sep;157(3):590-3.
 25. Lin S, Huang J, Wang M, Kumar R, Liu Y, Liu S, et al. Comparison of MAFLD and NAFLD diagnostic criteria in real world. *Liver Int*. 2020;40(9):2082-9.
 26. Eslam M, Sarin SK, Wong VWS, Fan JG, Kawaguchi T, Ahn SH, et al. The Asian Pacific Association for the Study of the Liver clinical practice guidelines for the diagnosis and management of metabolic associated fatty liver disease. *Hepatol Int*. 2020;14(6):889-919.
 27. GBD 2016. Alcohol collaborators. Alcohol use and burden for 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2018;392(10152):1015-35.
 28. Chang Y, Cho YK, Kim Y, Sung E, Ahn J, Jung HS, et al. Nonheavy drinking and worsening of noninvasive fibrosis markers in nonalcoholic fatty liver disease: A cohort study. *Hepatology*. 2019;69(1):64-75.
 29. Åberg F, Helenius-Hietala J, Puukka P, Färkkilä M, Jula A. Interaction between alcohol consumption and metabolic syndrome in predicting severe liver disease in the general population. *Hepatology*. 2018;67(6):2141-9.
 30. Charatcharoenwittaya P, Pongpaibul A, Kaosombattawattana U, Bhanthumkomol P, Bandidniyamanon W, Pausawasdi N, et al. The prevalence of steatohepatitis in chronic hepatitis B patients and its impact on disease severity and treatment response. *Liver Int*. 2017;37(4):542-51.
 31. Peleg N, Issachar A, Sneh Arbib O, Cohen-Naftaly M, Braun M, Leshno M, et al. Liver steatosis is a strong predictor of mortality and cancer in chronic hepatitis B regardless of viral load [internet]. *JHEP Rep*. 2019;1(1):9-16.
 32. van Kleef LA, Choi HSJ, Brouwer WP, Hansen BE, Patel K, de Man RA, et al. Metabolic dysfunction-associated fatty liver disease increases risk of adverse outcomes in patients with chronic hepatitis B. *JHEP Rep*. 2021;3(5):100350.
 33. Rugivarodom M, Pongpaibul A, Chainuvati S, Nimanong S,

- Chotiayaputta W, Tanwandee T, et al. Prognostic relevance of metabolic dysfunction-associated steatohepatitis for patients with chronic hepatitis B. *J Clin Transl Hepatol*. 2023;11(1):76-87.
34. Lee YB, Ha Y, Chon YE, Kim MN, Lee JH, Park H, et al. Association between hepatic steatosis and the development of hepatocellular carcinoma in patients with chronic hepatitis B. *Clin Mol Hepatol*. 2019;25(1):52-64.
 35. Chan A, Patel K, Naggie S. Genotype 3 infection- the last stand of hepatitis C virus. *Drugs*. 2017;77(2):131-44.
 36. Kralj D, Virović Jukić LV, Stojasavljević S, Duvnjak M, Smolić M, Čurčić IB. Hepatitis C virus, insulin resistance, and steatosis. *J Clin Transl Hepatol*. 2016;4(1):66-75.
 37. Sirinawasatien A, Techasirioangkun T. The prevalence and determinants of hepatic steatosis assessed by controlled attenuation parameter in Thai chronic hepatitis C patients. *Gastroenterol Res Pract*. 2020;2020:8814135.
 38. Fernandez-Fuertes M, Macías J, Corma-Gómez A, Rincón P, Merchante N, Gómez-Mateos J, et al. Similar prevalence of hepatic steatosis among patients with chronic hepatitis C with and without HIV coinfection. *Sci Rep*. 2020;10(1):6736.
 39. Adinolfi LE, Restivo L, Zampino R, Guerrera B, Lonardo A, Ruggiero L, et al. Chronic HCV infection is a risk of atherosclerosis. Role of HCV and HCV-related steatosis. *Atherosclerosis*. 2012;221(2):496-502.
 40. Khat tab MA, Eslam M, Mousa YI, Ela-adawy N, Fathy S, Shatat M, et al. Association between metabolic abnormalities and hepatitis C-related hepatocellular carcinoma. *Ann Hepatol*. 2012;11(4):487-94.
 41. Nouredin M, Wong MM, Todo T, Lu SC, Sanyal AJ, Mena EA. Fatty liver in hepatitis C patients post-sustained virological response with direct-acting antivirals. *World J Gastroenterol*. 2018;24(11):1269-77.
 42. Wong VWS, Wong GLH, Woo J, Abrigo JM, Chan CKM, Shu SST, et al. Impact of the new definition of metabolic associated fatty liver disease on the epidemiology of the disease. *Clin Gastroenterol Hepatol*. 2021;19(10):2161-2171.e5.
 43. Zhang HJ, Wang YY, Chen C, Lu YL, Wang NJ. Cardiovascular and renal burdens of metabolic associated fatty liver disease from serial US national surveys, 1999-2016. *Chin Med J (Engl)*. 2021;134(13):1593-601.
 44. Ciardullo S, Perseghin G. Prevalence of NAFLD, MAFLD and associated advanced fibrosis in the contemporary United States population. *Liver Int*. 2021;41(6):1290-3.
 45. Yamamura S, Eslam M, Kawaguchi T, Tsutsumi T, Nakano D, Yoshinaga S, et al. MAFLD identifies patients with significant hepatic fibrosis better than NAFLD. *Liver Int*. 2020;40(12):3018-30.
 46. Huang SC, Su HJ, Kao JH, Tseng TC, Yang HC, Su TH, et al. Clinical and histologic features of patients with biopsy-proven metabolic dysfunction-associated fatty liver disease. *Gut Liver*. 2021;15(3):451-8.
 47. Fujii H, Fukumoto S, Enomoto M, Uchida-Kobayashi S, Kimura T, Tamori A, et al. The FibroScan-aspartate aminotransferase score can stratify the disease severity in a Japanese cohort with fatty liver diseases. *Sci Rep*. 2021;11(1):13844.
 48. Guerreiro GTS, Longo L, Fonseca MA, de Souza VEG, Álvares-da-Silva MR. Does the risk of cardiovascular events differ between biopsy-proven NAFLD and MAFLD? *Hepatol Int*. 2021;15(2):380-91.
 49. Niriella MA, Ediriweera DS, Kasturiratne A, De Silva ST, Dassanayaka AS, De Silva AP, et al. Outcomes of NAFLD and MAFLD: results from a community-based, prospective cohort study. *PLoS One*. 2021;16(2):e0245762.
 50. Tsutsumi T, Eslam M, Kawaguchi T, Yamamura S, Kawaguchi A, Nakano D, et al. MAFLD better predicts the progression of atherosclerotic cardiovascular risk than NAFLD: generalized estimating equation approach. *Hepatol Res*. 2021;51(11):1115-28.
 51. Kim D, Konyon P, Sandhu KK, Dennis BB, Cheung AC, Ahmed A. Metabolic dysfunction-associated fatty liver disease is associated with increased all-cause mortality in the United States. *J Hepatol*. 2021;75(6):1284-91.
 52. Baratta F, Ferro D, Pastori D, Colantoni A, Cocomello N, Coronati M, et al. Open Issues in the Transition from NAFLD to MAFLD: The Experience of the Plinio Study. *Int J Environ Res Public Health*. 2021;18(17):8993.
 53. Lin S, Huang J, Wang M, Kumar R, Liu Y, Liu S, et al. Comparison of MAFLD and NAFLD diagnostic criteria in real world. *Liver Int*. 2020;40(9):2082-9.
 54. Huang J, Xue W, Wang M, Wu Y, Singh M, Zhu Y, et al. MAFLD Criteria May Overlook a Subtype of Patient with Steatohepatitis and Significant Fibrosis. *Diabetes Metab Syndr Obes*. 2021;14:3417-25.
 55. van Kleef LA, Ayada I, Alferink LJM, Pan Q, de Knecht RJ. Metabolic dysfunction-associated fatty liver disease improves detection of high liver stiffness: The Rotterdam Study. *Hepatology*. 2022;75(2):419-29.
 56. Lee BP, Dodge JL, Terrault NA. National prevalence estimates for steatotic liver disease and subclassifications using consensus nomenclature. *Hepatology*. 2024;79(3):666-73.
 57. Lee HH, Lee HA, Kim EJ, Kim HY, Kim HC, Ahn SH, et al. Metabolic dysfunction-associated steatotic liver disease and risk of cardiovascular disease. *Gut*. 2024;73(3):533-40.
 58. Song SJ, Lai JCT, Wong GLH, Wong VWS, Yip TCF. Can we use old NAFLD data under the new MASLD definition? *J Hepatol*. 2024;80(2):e54-6.
 59. De A, Bhagat N, Mehta M, Taneja S, Duseja A. Metabolic dysfunction-associated steatotic liver disease (MASLD) definition is better than MAFLD criteria for lean patients with NAFLD. *J Hepatol*. 2024;80(2):e61-2.
 60. Kim D, Wijarnpreecha K, Cholanteril G, Ahmed A. Metabolic dysfunction-associated steatotic liver disease and all-cause/cause-specific mortality among adults in the United States. *J Hepatol*. 2024;80(2):e79-81.