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Implications of the new nomenclature of steatotic liver disease and definition of metabolic dysfunction-associated steatotic liver disease

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Summary

Background: The American and European liver associations have endorsed new nomenclature of steatotic liver disease (SLD) and definition of metabolic dysfunction-associated steatotic liver disease (MASLD).

Aims: To review the historical development leading to the changes and to discuss the implications of the changes on research and clinical practice

Methods: We performed a literature search using keywords related to MASLD and non-alcoholic fatty liver disease (NAFLD).

Results: The SLD umbrella allows classification of patients under the key categories of MASLD, alcohol-associated liver disease and a new entity termed MetALD, which represents MASLD with increased alcohol intake. The diagnosis of MASLD requires the demonstration of hepatic steatosis and at least one metabolic risk factor, whereas MASLD can co-exist with other liver diseases such as chronic viral hepatitis. Despite the change in definition, over 95% of patients previously known as having NAFLD fulfil diagnostic criteria for MASLD. It is conceivable that future clinical trials and biomarker studies will continue to exclude concomitant liver diseases. As most patients

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AUTHOR CONTRIBUTIONS

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AUTHORSHIP

Guarantor of the article: Rohit Loomba and Vincent Wong.

with MASLD are seen at primary care and non-hepatology settings, communication with other stakeholders is essential to ensure disease awareness and smooth adoption of the changes.

Conclusions: The new nomenclature is both a challenge, given the need for dissemination and education across the spectrum of stakeholders, and an opportunity to bring everyone together and spark new research to better understand epidemiology, natural history, diagnosis, biomarkers and management strategies across the spectrum of SLD.

1 | INTRODUCTION

Metabolic dysfunction-associated steatotic liver disease (MASLD), previously known as non-alcoholic fatty liver disease (NAFLD), is currently the most common chronic liver disease affecting over 30% of the general adult population globally.[1] It is particularly common among patients with type 2 diabetes and obesity,[2–4] and has emerged as one of the leading causes of end-stage liver disease and carcinoma (HCC).[5,6]

In 2023, after a four-round Delphi process, an international panel of 225 participants (comprising hepatologists, gastroenterologists, endocrinologists, primary care physicians and patient representatives) led by the American Association for the Study of Liver Diseases (AASLD), European Association for the Study of the Liver (EASL) and Asociación Latinoamericana para el Estudio del Hígado (ALEH) decided to change the nomenclature of NAFLD to MASLD, with corresponding changes in the classification and definition of the disease.[7–9] It is, thus, timely to review the reasons for the change and explore the potential implications. In future, all manuscripts published in the *Alimentary Pharmacology and Therapeutics* (*AP&T*) will utilise the new nomenclature, and this commentary will serve as a guide for the authorship and readership of *AP&T*.

2 | WHY THE CHANGE?

In 1836, Addison first described fatty liver related to alcohol use (Figure 1).[10] It was later apparent that similar histological features could happen in non-drinkers with metabolic risk factors. For example, Adler and Schaffner described ‘fatty liver hepatitis and cirrhosis in obese patients’.[11] In 1980, Ludwig and colleagues coined the term ‘non-alcoholic steatohepatitis (NASH)’.[12] This, along with the more general term NAFLD, took hold and became the standard terms to describe hepatic steatosis in the absence of excessive alcohol consumption in the next 40 years.

However, there are certain issues surrounding the terminology and definition of NAFLD and NASH. Above all, they are diagnoses of exclusion. While it is common practice to adopt diagnoses of exclusion for uncommon conditions with poorly characterised pathophysiology, this approach is inappropriate for the most common liver disease worldwide. Besides, over time, the medical field has firmly established the link between NAFLD and various metabolic conditions, and the pathophysiology of NAFLD and NASH, albeit complicated and heterogeneous, is reasonably characterised.[13] Moreover, there are concerns that the word ‘alcoholic’ in NAFLD is stigmatising, especially as liver disease is already perceived as linked to alcohol use and other undesirable behaviours in some countries.[14] Another operational issue is that the diagnosis of NAFLD requires the exclusion of not only

excessive alcohol consumption but also other liver diseases such as chronic viral hepatitis and autoimmune liver disease. This approach trivialises the contribution of metabolic risk factors and hepatic steatosis to the natural history of liver diseases, but in fact multiple studies have shown that type 2 diabetes, obesity and perhaps hepatic steatosis increase the risk of cirrhosis, hepatic decompensation and HCC in patients with chronic viral hepatitis and alcohol-related liver disease.[15,16]

For these reasons, a group of hepatologists from Europe, South America and the Asia-Pacific region published a paper in 2020 to propose a nomenclature change from NAFLD to metabolic (dysfunction)-associated fatty liver disease (MAFLD).[17] This was accompanied by a proposal to change in the disease definition. To diagnose MAFLD, a patient should have hepatic steatosis together with one of the following metabolic conditions: (1) type 2 diabetes, (2) overweight or obesity and (3) 2 or more other metabolic risk factors. Conversely, MAFLD can co-exist with excessive alcohol consumption, concomitant liver diseases or secondary causes of hepatic steatosis.

The publication of the MAFLD proposal was soon followed by cautionary remarks from hepatologists from the United States and Europe.[18,19] The concern was that the proposal had not been thoroughly discussed, particularly among other stakeholders such as patients, policymakers, the industry and healthcare providers outside the hepatology field. Additionally, the impact of the changes on biomarker and drug development was not adequately considered. A change in the nomenclature may also hamper efforts in raising awareness.

As a result, the AASLD and EASL, in collaboration with ALEH, decided to convene a panel of wider representation to discuss the matter. The process involved 4 rounds of online Delphi process and a large-group hybrid meeting in Chicago in July 2022 for in-depth discussion between the second and third round surveys. All recommendation statements were voted by the panellists, with a ≥67% (supermajority) agreement to define consensus. The final report was published in the three society journals.[7–9]

3 | THE NEW NOMENCLATURE AND DEFINITION

During the discussion, patient representatives raised that both ‘alcoholic’ and ‘fatty’ in the original terminology of NAFLD were stigmatising. Apart from the semantic association with alcoholism as discussed above, the word ‘fatty’ could cause fat shaming.[20] Finally, the panel decided to adopt ‘steatotic liver disease’ (SLD) as the overarching term to describe patients with hepatic steatosis (Figure 2).[7–9] Under this umbrella, MASLD would replace NAFLD as the preferred term to describe patients with hepatic steatosis and metabolic risk factors. Metabolic dysfunction-associated steatohepatitis (MASH) would replace NASH to describe patients with MASLD and active necroinflammation characterised by the presence of lobular inflammation and hepatocyte ballooning. A particularly new entity is MASLD and increased alcohol intake, termed as both metabolic dysfunction and alcohol-associated liver disease, abbreviated as MetALD, which includes patients with MASLD together with moderate-alcohol consumption (30–60 g per day or 210–420 g per week in men, 20–50 g per day or 140–350 g per week in women). Other entities under SLD include alcohol-related

liver disease, specific aetiology SLD (drug-induced hepatic steatosis, monogenic diseases, miscellaneous) and cryptogenic SLD (i.e. hepatic steatosis in lean individuals with no additional metabolic risk factors).

Similar to the MAFLD definition, the diagnosis of MASLD also requires the presence of metabolic risk factors. The main difference is that the diagnosis of MASLD only requires one or more additional metabolic risk factors out of (1) overweight, obesity or central obesity, (2) hyperglycaemia, (3) high blood pressure, (4) increased plasma triglycerides and (5) reduced plasma high-density lipoprotein-cholesterol. The components are in line with the multi-society harmonised definition of metabolic syndrome with the exception of including both body mass index and waist circumference in point 1 (the metabolic syndrome criteria only consider waist circumference but not body mass index).[21] This may facilitate adoption of the MASLD definition in a wider community as primary care physicians, endocrinologists and cardiologists are familiar with the diagnosis of metabolic syndrome.

Table 1 summarises the similarities and differences in the definitions of NAFLD, MAFLD and MASLD.

4 | IMPLICATIONS ON RESEARCH

4.1 | Past and ongoing research

One concern about the change in the disease definition is the impact on research. If the definition results in the identification of grossly different patient populations, previous research on the epidemiology, biomarker use and treatment of NAFLD cannot be extrapolated to MASLD. Nonetheless, emerging data consistently support that over 97% of patients with hepatic steatosis would fulfil at least one of the metabolic criteria of MASLD.[22,23] The concordance is even higher among patients with biopsy-proven NAFLD (>99%).[22] In reality, most clinical trials in NASH have metabolic factors (e.g. minimal body mass index, prediabetes or diabetes) in the inclusion criteria anyway. Thus, effectively all clinical trial data represent patients with MASH, and no further adaptation is required.

4.2 | Future research

In contrast, most previous studies of NAFLD and NASH did exclude patients with excessive alcohol consumption and concomitant liver diseases (except studies specifically looking at the impact of concomitant conditions). This special population is indeed different from those with NAFLD alone. For example, the optimal cut-offs for liver stiffness measurement by ultrasound-based elastography to diagnose advanced liver fibrosis or cirrhosis differ by aetiology.[24] Untreated concomitant liver diseases will definitely influence the natural history of liver disease, thus affecting event rate (e.g. proportion of patients developing fibrosis progression and hepatic decompensation) and response rate. This may also make an investigational drug look less promising when the concomitant aetiology is not well controlled, even though less stringent inclusion criteria may speed up enrolment. As the path to successful introduction of a drug for MASH is already very challenging, in the foreseeable future, it is conceivable that biomarker studies and clinical trials will continue to exclude patients with excessive alcohol consumption and concomitant liver diseases. There

will be no fundamental changes in study design. However, the performance of biomarkers and the response to pharmacological treatments in patients with dual aetiologies or MetALD will be fertile ground for future research. Accumulation of new data may also encourage future studies to better define the effect of alcohol consumption on the natural history of SLD.

4.3 | Bench research

In the past decade, the field has witnessed numerous examples of treatments that worked well in animal models, only failing to demonstrate a therapeutic effect in subsequent clinical trials. The relative merits and limitations of various in vitro and in vivo models of MASH are beyond the scope of this article.[25] Nonetheless, the adoption of the MASLD nomenclature and definition will stimulate laboratory studies to emphasise the importance of using models that mimic not only the histological features of MASH but also the phenotype of metabolic dysfunction. For example, the methionine-choline-deficient diet can induce steatohepatitis and liver fibrosis rapidly, but the animals would lose weight and not develop insulin resistance. Future studies will likely require the use of at least one model that recapitulates the metabolic features of MASH.

On a separate note, there have been few preclinical studies on MetALD. Animal studies with both metabolic dysfunction and various degrees of alcohol consumption will shed light on the interaction between these two important risk factors.

5 | IMPLICATIONS FOR CLINICAL PRACTICE

The new terminology for SLD provides new opportunities to educate clinicians and providers across a spectrum of medical specialties including general practice, internal medicine, endocrinology, gastroenterology, hepatology and cardiology among others. To make it easier for the clinicians to utilise the new nomenclature in their clinical practice, the following terms may be used in place of the previous terminology. NAFLD is now termed as MASLD. MASLD can be broadly sub-divided into two broad sub-types including metabolic-dysfunction associated steatotic liver (MASL) (this was previously termed as non-alcoholic fatty liver [NAFL]), the non-progressive sub-type of MASLD and metabolic dysfunction-associated steatohepatitis (MASH) (this was previously termed as non-alcoholic steatohepatitis [NASH]), the progressive sub-type of MASLD (Figure 3). NASH-related fibrosis is termed as MASH-related fibrosis. As clinicians evaluate patients with suspected SLD in their clinic, it has become imperative that they pay close attention to their alcohol use and pattern and quantity of alcohol consumption. This will allow for improved recognition of alcohol use disorder among patients with SLD.

Furthermore, patients who are lean and have concomitant hepatic steatosis but no metabolic risk factors are now called cryptogenic SLD. In previous studies, such individuals tend to have milder liver disease and better prognosis than those with overweight/obesity with hepatic steatosis.[26,27] Whether the term ‘cryptogenic SLD’, which suggests uncertainty, on one hand it may create anxiety among patients, but on the other hand it may even lead to disruptive innovations and advances in diagnostic workup but this remains to be seen. It is

likely that this may lead to a paradigm shift in clinical utility of genetic testing in this patient population in the liver clinics with parallel advances in the genetics of liver disease.[28]

The biggest impact in terms of clinical practice will likely be the recognition of the contribution of MASLD in patients with dual or multiple aetiologies such as chronic viral hepatitis, autoimmune liver disease and alpha-1-antitrypsin deficiency. This empowers clinicians to describe the disease clearly and manage different causes of liver disease at the same time.

The Food and drug administration (FDA) have indicated that they would be willing to entertain both the new as well as the previous terminology interchangeably and the change in the nomenclature will not have any impact on clinical drug and biomarker development. As the new terminology gains greater adoption and recognition, the next steps would be to implement changes in the International Classification of Disease (ICD-11).

6 | ISSUES RELATED TO MetALD

Both metabolic-dysfunction and alcohol-associated liver disease (MetALD) comprises of individuals who have metabolic risk factors but consume more than 20 g (and less than 50 g/day) per day of alcohol for women and more than 30 g (and less than 60 g/day) per day of alcohol for men, respectively. This new entity is likely to ignite new research in understanding the joint effects of metabolic syndrome and excessive alcohol use and its impact on liver disease progression and long-term clinical outcomes.[16] It will also allow for improved understanding of whether novel therapies for reversal of MASH-related fibrosis will also work in patients with MetALD who have stage 2 fibrosis or higher. The biomarkers that can easily and readily differentiate MASLD versus MetALD versus alcohol-associated steatotic liver disease would also be needed to better characterise these disease entities.

One related issue is the way we quantify alcohol consumption. In the real world, patients report the number of drinks rather than the amount of alcohol in grams. The National Institute on Alcohol Abuse and Alcoholism states that 1 standard drink contains roughly 14 g of pure alcohol, and this is roughly equivalent to 12 ounces of regular beer (around 5% alcohol), 5 ounces of wine (around 12% alcohol) and 1.5 ounces of distilled spirits (around 40% alcohol). However, it should be noted that such a definition is not universal. For example, European and British guidelines define 1 standard drink as containing 10 and 8 grams of alcohol, respectively.[29] Furthermore, it is common for patients to underreport the amount of alcohol consumption. The role of alcohol biomarkers in clinical practice and case definition should be better defined.[30]

7 | CONCLUSIONS

In summary, the new nomenclature is both a challenge given the need for dissemination and education across the spectrum of stakeholders as well as an opportunity to bring everyone together and spark new research to better understand epidemiology, natural history, diagnosis, biomarkers as well as management strategies across the spectrum of SLD. We welcome submissions to AP&T to fill this gap-in-knowledge. In addition, while the word ‘steatotic’ may be less stigmatising, it is also less commonly used among patients and the

public. It is thus imperative that clinicians explain the meaning of the terminology clearly to patients and help promote awareness.

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REFERENCES

1. Wong VW, Ekstedt M, Wong GL, Hagstrom H. Changing epidemiology, global trends and implications for outcomes of NAFLD. J Hepatol. 2023;79:842–52. [PubMed: 37169151]
2. En Li Cho E, Ang CZ, Quek J, Fu CE, Lim LKE, Heng ZEQ, et al. Global prevalence of non-alcoholic fatty liver disease in type 2 diabetes mellitus: an updated systematic review and meta-analysis. Gut. 2023;72:2138–48. [PubMed: 37491159]
3. Quek J, Chan KE, Wong ZY, Tan C, Tan B, Lim WH, et al. Global prevalence of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in the overweight and obese population: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol. 2023;8:20–30. [PubMed: 36400097]
4. Ajmera V, Cepin S, Tesfai K, Hofflich H, Cadman K, Lopez S, et al. A prospective study on the prevalence of NAFLD, advanced fibrosis, cirrhosis and hepatocellular carcinoma in people with type 2 diabetes. J Hepatol. 2023;78:471–8. [PubMed: 36410554]
5. Lim WH, Ng CH, Tan D, Tseng M, Xiao J, Yong JN, et al. Natural history of NASH cirrhosis in liver transplant waitlist registrants. J Hepatol. 2023;79:1015–24. [PubMed: 37307997]
6. Huang DQ, Singal AG, Kono Y, Tan DJH, el-Serag HB, Loomba R. Changing global epidemiology of liver cancer from 2010 to 2019: NASH is the fastest growing cause of liver cancer. Cell Metab. 2022;34:969–977.e2. [PubMed: 35793659]
7. Rinella ME, Lazarus JV, Ratziu V, Francque SM, Sanyal AJ, Kanwal F, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. Hepatology. 2023;78:1966–86. [PubMed: 37363821]
8. Rinella ME, Lazarus JV, Ratziu V, Francque SM, Sanyal AJ, Kanwal F, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. J Hepatol. 2023;79:1542–56. [PubMed: 37364790]
9. Rinella ME, Lazarus JV, Ratziu V, Francque SM, Sanyal AJ, Kanwal F, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. Ann Hepatol. 2023;29:101133. [PubMed: 37364816]
10. Addison T. Observations on fatty degeneration of the liver. Guys Hosp Rep. 1836;1:485.
11. Adler M, Schaffner F. Fatty liver hepatitis and cirrhosis in obese patients. Am J Med. 1979;67:811–6. [PubMed: 507094]

12. Ludwig J, Viggiano TR, McGill DB, Oh BJ. Nonalcoholic steatohepatitis: Mayo Clinic experiences with a hitherto unnamed disease. Mayo Clin Proc. 1980;55:434–8. [PubMed: 7382552]
13. Wong VW, Chitturi S, Wong GL, et al. Pathogenesis and novel treatment options for non-alcoholic steatohepatitis. Lancet Gastroenterol Hepatol. 2016;1:56–67. [PubMed: 28404113]
14. Younossi ZM, AlQahtani SA, Alswat K, Yilmaz Y, Keklikkiran C, Funuyet-Salas J, et al. Global survey of stigma among physicians and patients with nonalcoholic fatty liver disease. J Hepatol. 2023. 10.1016/j.jhep.2023.11.004.
15. Wong GL, Wong VW, Choi PC, et al. Metabolic syndrome increases the risk of liver cirrhosis in chronic hepatitis B. Gut. 2009;58:111–7. [PubMed: 18832522]
16. Younossi ZM, Stepanova M, Ong J, Yilmaz Y, Duseja A, Eguchi Y, et al. Effects of alcohol consumption and metabolic syndrome on mortality in patients with nonalcoholic and alcohol-related fatty liver disease. Clin Gastroenterol Hepatol. 2019;17:1625–1633.e1. [PubMed: 30476585]
17. 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;73:202–9. [PubMed: 32278004]
18. Ratziu V, Rinella M, Beuers U, Loomba R, Anstee QM, Harrison S, et al. The times they are a-changin' (for NAFLD as well). J Hepatol. 2020;73:1307–9. [PubMed: 32890593]
19. Younossi ZM, Rinella ME, Sanyal AJ, Harrison SA, Brunt EM, Goodman Z, et al. From NAFLD to MAFLD: implications of a premature change in terminology. Hepatology. 2021;73:1194–8. [PubMed: 32544255]
20. Rubino F, Puhl RM, Cummings DE, Eckel RH, Ryan DH, Mechanick JI, et al. Joint international consensus statement for ending stigma of obesity. Nat Med. 2020;26:485–97. [PubMed: 32127716]
21. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation. 2009;120:1640–5. [PubMed: 19805654]
22. Song SJ, Lai JC, Wong GL, Wong VW, Yip TC. Can we use old NAFLD data under the new MASLD definition? J Hepatol. 2023. 10.1016/j.jhep.2023.07.021
23. Ratziu V, Boursier J, AFEF Group for the Study of Liver Fibrosis. Confirmatory biomarker diagnostic studies are not needed when transitioning from NAFLD to MASLD. J Hepatol. 2023. 10.1016/j.jhep.2023.07.017.
24. European Association for the Study of the Liver. EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis - 2021 update. J Hepatol. 2021;75:659–89. [PubMed: 34166721]
25. Denk H, Abuja PM, Zatloukal K. Animal models of NAFLD from the pathologist's point of view. Biochim Biophys Acta Mol Basis Dis. 2019;1865:929–42. [PubMed: 29746920]
26. Leung JC, Loong TC, Wei JL, et al. Histological severity and clinical outcomes of nonalcoholic fatty liver disease in nonobese patients. Hepatology. 2017;65:54–64. [PubMed: 27339817]
27. Younes R, Govaere O, Petta S, Miele L, Tiniakos D, Burt A, et al. Caucasian lean subjects with non-alcoholic fatty liver disease share long-term prognosis of non-lean: time for reappraisal of BMI-driven approach? Gut. 2022;71:382–90. [PubMed: 33541866]
28. Lin H, Wong GL, Whatling C, et al. Association of genetic variations with NAFLD in lean individuals. Liver Int. 2022;42:149–60. [PubMed: 34610207]
29. European Association for the Study of the Liver. EASL clinical practice guidelines: management of alcohol-related liver disease. J Hepatol. 2018;69:154–81. [PubMed: 29628280]
30. Staufer K, Huber-Schönauer U, Strebinger G, et al. Ethyl glucuronide in hair detects a high rate of harmful alcohol consumption in presumed non-alcoholic fatty liver disease. J Hepatol. 2022;77:918–30. [PubMed: 35605744]

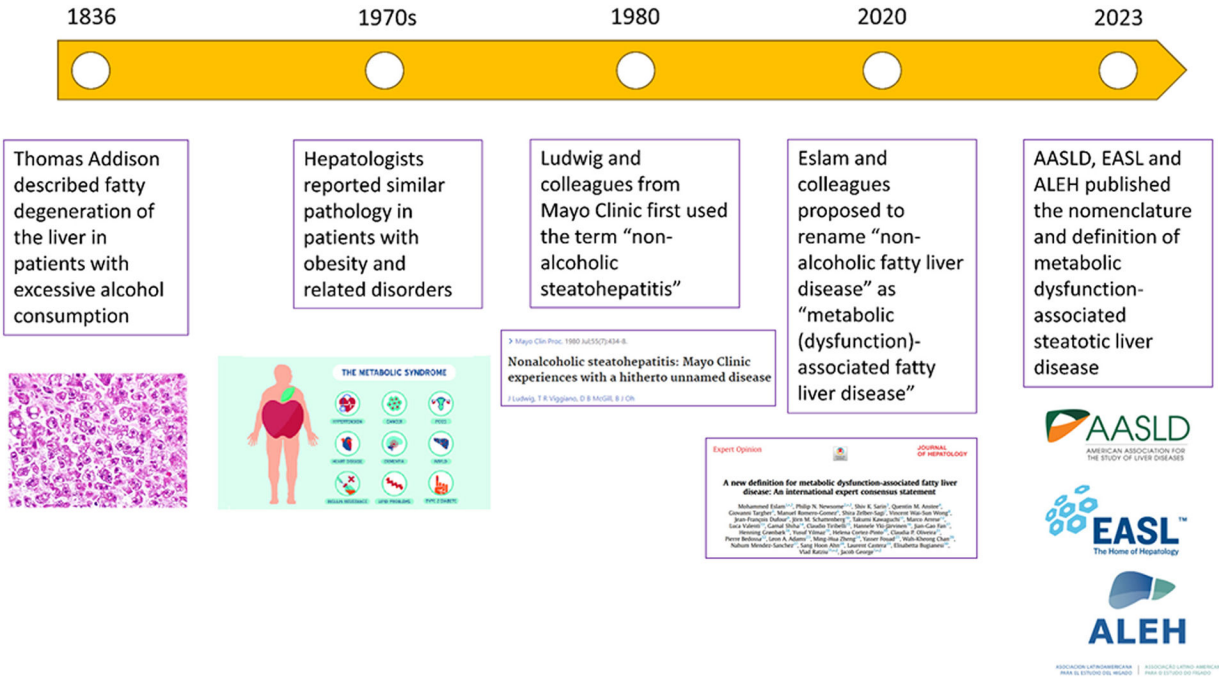

FIGURE 1.
A history of the nomenclature of steatotic liver disease.

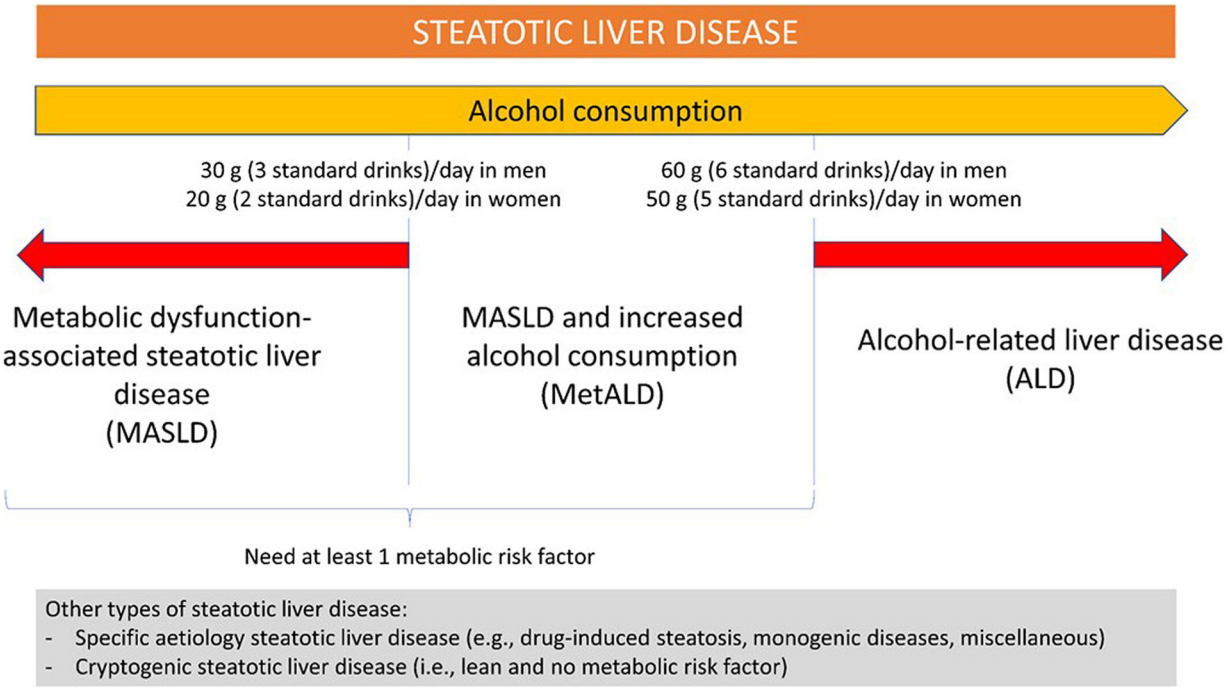

FIGURE 2.
Classification of steatotic liver disease.

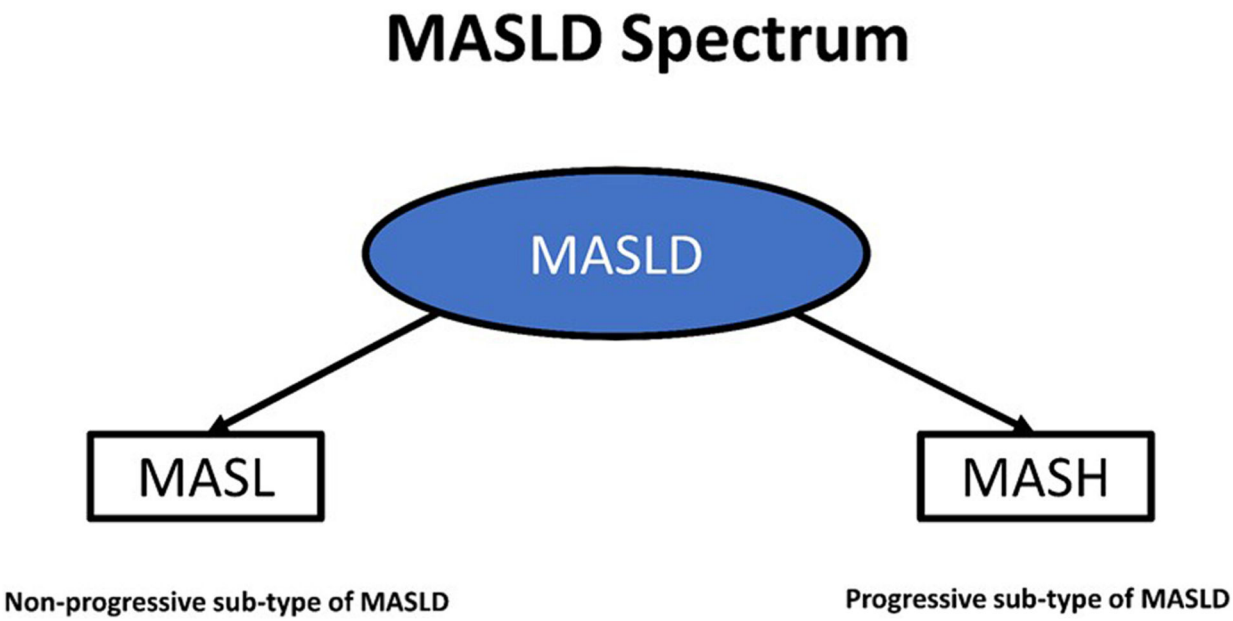

FIGURE 3.
Sub-types of MASLD.

TABLE 1.

Comparison of the definitions of non-alcoholic fatty liver disease (NAFLD), metabolic dysfunction-associated fatty liver disease (MAFLD) and metabolic dysfunction-associated steatotic liver disease (MASLD).

	NAFLD	MAFLD	MASLD
Demonstration of hepatic steatosis by imaging, histology or prediction scores	Required	Required	Required
Exclusion of excessive alcohol consumption	Required	Not required	Allow moderate-alcohol consumption (up to 60 g per day in men and 50 g per day in women) but not excessive alcohol consumption (classified as alcohol-related liver disease)
Exclusion of viral hepatitis and other liver diseases	Required	Not required	Not required
Exclusion of secondary causes of hepatic steatosis	Required	Not required	Required (classified as drug-induced liver injury and monogenic diseases)
Presence of metabolic risk factors	Not required	Need to have type 2 diabetes, overweight or obesity, or 2 other metabolic risk factors	Need to have 1 or more metabolic risk factors