Metabolic steatosis: recent scientific data also support a change in nomenclature

N. Lanthier[1-2], M.J. Armstrong[3-4]

(1) Service d'Hépato-Gastroentérologie, Cliniques universitaires Saint-Luc, UCLouvain, 1200 Brussels, Belgium; (2) Laboratory of Gastroenterology and Hepatology, Institut de Recherche Expérimentale et Clinique, UCLouvain, 1200 Brussels, Belgium; (3) Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, United Kingdom; (4) Liver Unit, Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom.

Keywords: MAFLD, steatosis, ethanol, microbiome, ethylglucuronide, alcohol.

To the Editor,

Two years ago, many experts spoke out in favour of changing the nomenclature of the most common liver disease in the world, non-alcoholic fatty liver disease (NAFLD) (1). This was the subject of an editorial in the *Acta Gastroenterologica Belgica* Journal (1). Even though many researchers still mention that its pathophysiology remains poorly understood or that the exact mechanisms remain to be elucidated, it would be dishonest not to recognise a common factor, namely the metabolic context (metabolic syndrome, insulin resistance and possibly type 2 diabetes, overweight or obesity) in the pathogenesis of this liver disease (1). The term "MAFLD" for "metabolic dysfunction-associated fatty liver disease" therefore makes sense. It is indeed more logical to call something by what it is than by what it is not (1). The perceived stigma of patients using the term "alcoholic" in naming their disease also supports an adaptation of the nomenclature (2). Recently, the term "fatty" has also been suggested as potentially stigmatizing. However, it seems more common than the term "steatotic" which should be explained to the majority of patients by using the term "fatty liver" (2). We do not deny the history of the disease, which was first described in 1980 in patients with hepatocyte steatosis and cirrhosis, resembling alcohol-related liver disease (ALD), with little or no consumption of alcohol (for this reason, the disease was initially called "non-alcoholic") (1), but we think it's time to move forward and would like to draw attention to data from two recent interesting scientific articles (3,4), which, in our view, indirectly support the use of "MAFLD" nomenclature.

Firstly, in real life, many people are "bon vivants" and have a metabolic syndrome and regular consumption of beer, wine etc. The only exclusion criterion concerning excessive consumption of alcohol is based on the patient's medical history... which can be questioned (5). Researchers have correctly demonstrated this by showing that 29% of "NAFLD" patients actually had a moderate to excessive alcohol consumption (3). This was demonstrated by analysing the patients' ethylglucuronide in hair (a metabolite of alcohol) and then confirmed by the patients themselves. This consumption of alcohol can of course have an impact on the evolution of the liver disease (3). Far be it from us to want to abandon the "ALD" designation, which remains entirely justified for a lot of patients. In current practice, the anamnesis can help us, but also the mean corpuscular volume or the aspartate aminotransferase (AST)/alanine aminotransferase (ALT) ratio. These data are included in an ALD/NAFLD index (ANI) which also takes into account the patient's body mass index and gender, and which is designed to separate patients with ALD from NAFLD (6). However, there are also mixed "ALD + MAFLD" diseases (1).

Secondly, the role of the gut microbiota and more precisely the gut microbiome (a term that includes not only the microorganisms but also the metabolites it produces) is increasingly being recognized as a contributor to metabolic fatty liver disease (7). In summary, an increase in Gram-negative bacteria and a decrease in Gram-positive bacteria is evidenced in MAFLD patients. Some bacterial metabolites can be considered beneficial (short-chain fatty acids, indole derivatives,...) or deleterious (ethanol, phenylacetic acid,...) for the liver (7). Other possible mechanisms are changes in intestinal permeability, bacterial translocation and bile acid modulation (7). Researchers have elegantly shown that the gut microbiota of obese NAFLD patients produced significantly more ethanol than those of slim patients and that ethanol levels reaching the liver via the portal vein were up to 187 times higher than in the circulating blood (4). This endogenous ethanol production is therefore considered to be a potential player in the disease that can drive liver inflammation (4), although the exact role of this endogenous ethanol on the severity of liver disease remains to be determined.

In conclusion, for both semantic, practical and recent scientific reasons based on cohort data and translational data on new pathophysiological mechanisms, it seems logical to move towards a nomenclature that better reflects the patients and the disease. Fortunately, despite

Correspondence to: Pr. Nicolas Lanthier, Service d'Hépato-Gastroentérologie, Cliniques universitaires Saint-Luc, UCLouvain, Avenue Hippocrate, 10, 1200 Brussels, Belgium. Phone: +32.2.764.28.22. Fax: +32.2.764.89.27.
Email: nicolas.lanthier@saintluc.uclouvain.be

Submission date: 10/12/2022
Acceptance date: 14/12/2022

the reluctance of some, the new term "MAFLD" is now supported by many hepatologists but also endocrinologists, pathologists, nutritionists,... worldwide (8).

References

1. Lanthier N, Vanuytsel T. Metabolic dysfunction-associated fatty liver disease: A new clearer nomenclature with positive diagnostic criteria. *Acta Gastroenterol Belg.* 2020;**83**(4):513-5.
2. Shiha G, Korenjak M, Casanovas T, Mooney V, Sigurðardóttir S, Koulla Y, *et al*. MAFLD 2022: An ELPA/ALPA/EASO-ECPO joint statement on disease stigma. *J Hepatol.* 2022 Dec;**77**(6):1717-9.
3. Staufer K, Huber-Schönauer U, Strebinger G, Pimingstorfer P, Suesse S, Scherzer TM, *et al*. Ethyl glucuronide in hair detects a high rate of harmful alcohol consumption in presumed non-alcoholic fatty liver disease. *J Hepatol.* 2022 Oct;**77**(4):918-30.
4. Meijnikman AS, Davids M, Herrema H, Aydin O, Tremaroli V, Rios-Morales M, *et al*. Microbiome-derived ethanol in nonalcoholic fatty liver disease. *Nat Med*. 2022 Oct;**28**(10):2100-6.
5. Armstrong MJ, Mellinger JL, Trivedi PJ. Alcohol Consumption in Patients with Non-alcoholic Fatty Liver Disease: Convenient vs. Inconvenient Truths. *Am J Gastroenterol.* 2018 Oct;**113**(10):1437-9.
6. Dunn W, Angulo P, Sanderson S, Jamil LH, Stadheim L, Rosen C, *et al*. Utility of a New Model to Diagnose an Alcohol Basis for Steatohepatitis. *Gastroenterology*. 2006;**131**(4):1057-63.
7. Lanthier N, Delzenne N. Targeting the Gut Microbiome to Treat Metabolic Dysfunction-Associated Fatty Liver Disease: Ready for Prime Time? *Cells*. 2022 Aug;**11**(17):2718.
8. Méndez-Sánchez N, Bugianesi E, Gish RG, Lammert F, Tilg H, Nguyen MH, *et al*. Global multi-stakeholder endorsement of the MAFLD definition. *Lancet Gastroenterol Hepatol.* 2022 May;**7**(5):388-90.