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EDITORIAL

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MAFLD vs NAFLD: Let the contest begin!

Fatty liver disease (FLD) arouses increasingly more attention in research and clinical practice, because of the increasing prevalence of the disease and the fact that nowadays it represents a leading cause of liver-related morbidity and mortality.[1]

The need of a change in the definition from a "non-condition" into a clearly defined disease has been suggested since the early 2000s.[2] Recently, a consensus of international experts proposed to overcome the current nomenclature "Non-Alcoholic Fatty Liver Disease" (NAFLD) and adopt the acronym MAFLD, or "Metabolic dysfunction-Associated Fatty Liver Disease", giving relevance to the underlying condition of systemic metabolic dysfunction.[3] Although a broader consensus by all stakeholders in the field is still needed before a definite change in FLD definition can be implemented, the publication of the first statement signed by a large international panel of experts represents an initial step in this process.

Briefly, according to the aforementioned proposal, MAFLD diagnosis would be based on the detection of hepatic steatosis (diagnosed by imaging, biomarkers, or histology) and at least one feature among overweight/obesity, type 2 diabetes and metabolic dysregulation. The last criterium is met when at least two features are present among: increased waist circumference, arterial hypertension, hypertriglyceridemia, low HDL-C, prediabetes, insulin resistance and subclinical inflammation. These criteria will identify a more homogenous condition than NAFLD, overcoming the difficulties and controversies in the definition of at-risk alcohol intake, thereby hopefully fostering new pathophysiological developments and facilitating clinical studies (as brilliantly reviewed by Fouad et al in this journal [4]). However, the impact of the new FLD classification in clinical practice is not yet known. Indeed, this does not represent a simple change in the nomenclature: differently from NAFLD, MAFLD will be diagnosed in individuals with fatty liver and dysmetabolism, even when at-risk alcohol intake is reported, but not in lean individuals with fatty liver without metabolic comorbidities (such as a fraction of those with lean NAFLD).[5]

In this issue of Liver International, Lin et al [6] compared the characteristics of individuals with MAFLD vs NAFLD in 13,083 subjects from the general population enrolled in the third National Health and Nutrition Examination Survey of the United States (NHANES III). The prevalence of MAFLD, as defined by the new criteria, was comparable to that of NAFLD (31.2% vs 33.2%) and only 4.7% of participants met the diagnostic criteria of NAFLD, but not those of MAFLD (Figure 1). Remarkably, MAFLD criteria were able to identify participants at higher risk of progressive liver and cardiovascular diseases. Indeed, individuals with MAFLD had higher body mass index (BMI), proportion of metabolic comorbidities and ALT levels than those with NAFLD (Figure 1). On the other hand, individuals with NAFLD without MAFLD had less frequently metabolic comorbidities and non-invasively assessed hepatic fibrosis, whereas MAFLD individuals reporting at-risk alcohol consumption were younger than the others, and had a more favourable metabolic profile, but more severe liver fibrosis.

The proposed nomenclature change can benefit FLD awareness campaigns. The implications of co-existing metabolic dysfunction are neglected by the NAFLD definition, whereas interventions that improve the diet and life-style are key to reduce not only the hepatic, but also the cardiovascular, metabolic and neoplastic complications of fatty liver disease. Therefore, changing the name to MAFLD and giving clear diagnostic criteria would be helpful to focus on the underlying trigger. Secondly, but not of secondary importance, one should consider the role of alcohol in FLD. Accepted NAFLD criteria may suggest the misleading idea that a certain amount of alcohol consumption is acceptable. However, there is currently no robust demonstration of the existence of a safe threshold for alcohol, especially in persons suffering from a liver condition.[8] Once more, the definition of a disease based on the exclusion of just one risk factor is at very least simplistic. The new MAFLD criteria focus on the role of dysmetabolism on hepatic fat accumulation that is the most frequent driver of FLD progression.[9,10] However, alcohol, together with dietary fructose, inherited factors and so on, represent other triggers of liver disease progression,[11] and even modest alcohol consumption contributes to FLD development.[12] Therefore, alcohol and dysmetabolism should rather be considered as co-risk factors than as opposites when defining and classifying FLD.

Recently however, Younossi et al on behalf of the American Association for the Study of Liver Disease (AASLD) pointed out that renaming NAFLD may be premature: indeed, most physicians who are not hepatologists still have difficulties recognizing the importance of FLD screening in their practice, and regulatory agencies and patient organizations should be included in the decision process.[7] Furthermore, it was suggested that increasing the public and general awareness on FLD has a greater priority than to improve the diagnostic algorithm. These important and shared concerns should be carefully weighed against the potential benefits of this nomenclature change. Therefore, it seems reasonable to retain the nomenclature nonalcoholic steatohepatitis (NASH) for awareness campaigns (eg "International NASH day") to define the most severe form of the

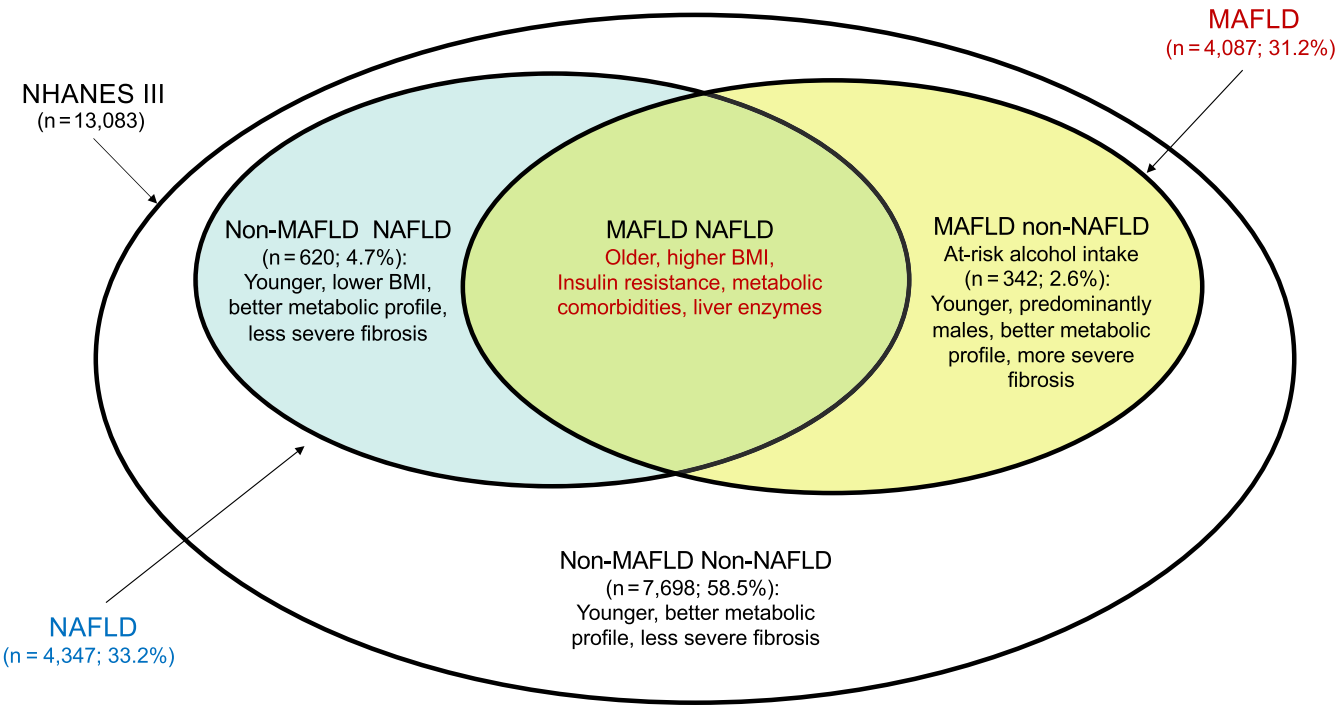

FIGURE 1 MAFLD vs NAFLD in the general population (NHANES III; n = 13,083). Prevalence of patients with the diagnosis of MAFLD (Metabolic associated fatty liver disease) was comparable to that of NAFLD (nonalcoholic fatty liver disease). MAFLD improved the detection of patients at higher risk of liver and cardiovascular comorbidities. New criteria of MAFLD include also at-risk alcohol users, who were younger males with a better metabolic profile but more severe liver fibrosis respect to non-alcohol users. NHANES III: third National Health and Nutrition Examination Survey of the United States. BMI: body mass index

disease as opposed to that caused by alcohol excess and at least, until a consensus is reached, in clinical trials.

For these reasons, and in order to contribute with more high-quality data to inform the current debate without supporting a priori either position, *Liver International* will keep publishing pathophysiological, genetic, clinical (eg comparing the natural history between MAFLD/NAFLD concerning both the hepatic and extra-hepatic complications), and public health research aimed at comparing MAFLD vs NAFLD. Let the contest begin then, and the best win!

KEYWORDS

fatty liver disease, insulin resistance, metabolism, obesity, steatosis

CONFLICT OF INTEREST

Authors declare that they do not have any conflict of interest relevant to this manuscript.

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