Metabolic dysfunction-associated fatty liver disease : a new clearer nomenclature with positive diagnostic criteria

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Key words : MAFLD, NASH, steatosis, ALD, histology, diagnosis.

Abbreviations : MAFLD : metabolic dysfunction-associated fatty liver disease ; NAFLD : non-alcoholic fatty liver disease ; NASH : non-alcoholic steatohepatitis ; MASH : metabolic dysfunction-associated steatohepatitis ; ALD : alcoholic liver disease.

Don't say NAFLD anymore but MAFLD ("metabolic" instead of "non-alcoholic") (1,2) !

This liver disease, which is the most frequent cause of elevated liver tests in our country, finally has an appropriate name.

Until recently, MAFLD was a diagnosis of exclusion, in a patient with more than 5% steatotic hepatocytes at the liver histology and after having ruled out the consumption of alcoholic beverages but also other rarer causes (such as viral hepatitis infection, drugs, auto-immune disorders...). The different non-invasive techniques for the detection of steatosis described in our guidance document (3) are now possible for this new positive diagnosis of MAFLD (Table).

Table : **Diagnostic criteria for metabolic dysfunction-associated fatty liver disease (MAFLD)**

1. Evidence of **liver steatosis**:
   – by an imaging technique
   – and/or by the positivity of one score based on laboratory and anthropometric parameters (such as the Fatty Liver Index)
   – and/or by liver histology

+

2. Presence of a **metabolic** risk **condition**:
   – overweight/obesity
   – and/or metabolic syndrome
   – and/or type 2 diabetes mellitus

Several sporadic reports already existed in the 19th and early 20th centuries on the potential association between liver steatosis, obesity or diabetes and risk of cirrhosis. However, the terms "NAFLD" and "NASH" only appeared in 1980 with the Jurgen Ludwig's series of patients (4). In our *Acta Gastro-Enterologica Belgica* Journal, the first manuscript on NAFLD was published in 2002 (!) and written by Oliver James (University of Newcastle), following an invited lecture at the Winter meeting of the *Belgian Association for the Study Liver* held in Charleroi in 2001 (5). It was not until 2006 that a second publication (from the Hacettepe University) on the subject appeared, reporting low vitamin E levels in a subgroup of severe NAFLD patients (6). Interestingly, vitamin E supplementation is currently one of the available treatments for MAFLD in some conditions (3,7). The third publication on MAFLD published in our Journal is a synthesis of Isabelle Leclercq's experimental work (UCLouvain) on disease pathophysiology (2007), which was awarded the Brohée prize (8).

Many other interesting articles dedicated to MAFLD have been published since then in our Journal (3,9-13). In this issue, three important publications are present (14-16). The first one analyzes the characteristics of cirrhotic patients over two distinct periods (1995-1999 and 2010-2014) in a Belgian hospital center (16). Edeline Kaze et al. (Hôpital de Jolimont) report that MAFLD is indeed a severe disease because it is now a frequent cause of cirrhosis (16% of all causes of cirrhosis in their recent series *versus* 3% in the older one). Even in the case of cirrhosis, the histological diagnosis confirmation is provided in less than half of the cases in the daily practice (46 % in their series). Precisely, the second publication on MAFLD in this issue focuses on the histological diagnosis of the inflammatory form of the disease, called NASH (15). Performing a biopsy remains important in order to know the activity of the disease and to characterize the disease process. While it is considered the gold standard, this histological diagnosis is difficult, subject to inter-observer variations and based on the presence of suffering or "ballooned" hepatocyte cells, in addition to steatosis and inflammatory infiltrate. The authors (from the Balikesir University Medical School) analyzed the presence of microvesicular steatosis that so far is not part of the NASH histological severity score performed in our daily practice (3) or evaluated in clinical trials (7). Confirming already available data (17), the authors highlighted that microvesicular steatosis is associated with the presence of hepatocyte ballooning, and therefore with the severity of the disease. The third

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Submission date : 15/10/2020
Acceptance date : 15/10/2020

publication on MAFLD in our Journal presents the mechanisms of steatosis development as well as different proteins/enzymes playing a key role in this process (14). These mechanisms can be diverse (*de novo* lipogenesis, reduced fatty acid oxidation, increased fatty acid uptake or export defect). The authors (from the Universidad Popular Autónoma del Estado de Puebla) present how these proteins can possibly serve as a disease marker or a therapeutic target.

With the new nomenclature, MAFLD can now also co-exist without contradiction with alcoholic liver disease (ALD). Indeed, alcohol use disorder patients could also be overweight or obese with a dual liver disease etiology (superimposed nutritional or metabolic steatosis in addition to ALD). It is important to be able to insist on this fact because this association (MAFLD + ALD) can be particularly deleterious (18,19). MAFLD and ALD share a common point : that of changes in the gut microbiota (18). These disturbances of the microbiota could participate to MAFLD, then deserving to be called "dysbiosis", and constitute therefore a current perspective of research and treatment (20). In a captivating manuscript of this issue, Sophie Leclercq (UCLouvain) gives an update on the microbiota changes occurring in ALD patients (with the certainties, doubts and limitations related to the methodology used for observations) and describes how this dysbiosis can be targeted (in particular by prebiotics) to potentially treat ALD (21).

Finally, we take the opportunity of this editorial focused on liver "nutritional" diseases to announce the arrival of a new scientific society : the *Belgian Society of Clinical Nutrition* (SBNC) within the Editorial Board of *Acta Gastro-Enterologica Belgica*. After the *Belgian Liver and Intestine Advisory Committee* (BeLIAC) (22), the SBNC is the second scientific society to join the *Acta Gastro-Enterologica Belgica* editorial board this year. We are delighted with the multi-disciplinary nature of the *Acta Gastro-Enterologica Belgica* and we would like to thank Vincent Fraipont (president of the SBNC) and Anne-Françoise Rousseau (new associate editor) for this important collaboration. Indeed, the implication of national scientific societies is crucial. Our Journal allows the dissemination of their scientific knowledge and points of view (23). It is in this context that two high quality manuscripts, resulting from a survey according to the Delphi method, were accepted for publication. The first one, published in this issue, from the *Belgian Group of Digestive Oncology*, focuses on the diagnostic and therapeutic management of neuroendocrine neoplasms (24). The second one, entitled "*Belgian consensus on the management of hemorrhoidal disease*", is written by the *Belgian Working Group on Proctology* and will be published in the next issue (25).

In conclusion, as explained in the previous issue, the world of hepatology and gastroenterology is evolving (26). New definitions for common diseases are proposed, such as the term "metabolic dysfunction-associated fatty liver disease". However, a formal consensus between experts has yet to be reached. For us, the only gap in those points of view is the disappearance of the term "NASH", designated to define the inflammatory form of the disease characterized by hepatocyte inflammation and ballooning. It seems essential to keep a specific name to characterize this subtype of disease/patient profile, linked to a poorer prognosis (27). The term "MASH" (for metabolic dysfunction-associated steatohepatitis) could therefore become part of the standard nomenclature. Pending a formal consensus, the terms NAFLD, MAFLD, NASH will co-exist in our Journal... and *Acta Gastro-Enterologica Belgica* will continue to publish both original articles and expert points of view to synthesize recent advances in many hepato-gastroenterology fields.

We wish you an excellent reading.

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