

Metabolic Muddle. MASLD and MASH on the Horizon

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NAFLD (non-alcoholic fatty liver disease) and NASH (non-alcoholic steatohepatitis) are time-honored acronyms, with widely popular acceptance. Experts now recommend discarding them in favor of MASLD for “metabolic dysfunction-associated steatotic liver disease” and MASH for “metabolic dysfunction-associated steatohepatitis.” The reasons for this change are explored and an argument about why the change is confusing, is advanced. Should these acronyms become clinically popular, risk assessment manuals will require updates.

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WHY THE CHANGE?

Non-alcoholic fatty liver disease (NAFLD) and its subset, non-alcoholic steatohepatitis (NASH), are descriptors that were coined in the 1980s.¹ They are widely used in the field of hepatology and listed in both the international coding of diseases (ICD) and SNOMED systems, underscoring their legitimacy. However, expert groups now propose to abandon both. The rubs against the names are three-fold: first, they are considered exclusionary, ie, they define a condition by virtue of not being something else, an unsatisfactory

taxonomic approach. Second, they contain stigmatizing language—both the words “alcoholic” and “fatty” are considered at fault. Thirdly, they do not capture the underlying pathogenetic mechanism at play – metabolic dysfunction.

Dissatisfaction with NAFLD and NASH has been recorded for many years. In 2020, an expert group proposed MAFLD for “metabolic dysfunction-associated fatty liver disease.”^{2,3} This underscored the importance of metabolic dysfunction, registered a dislike of “non-alcoholic” but an acceptance of “fatty.” The more recent expert proposal was impressive in its industry—a 34-person steering

committee convened 236 panellists from 56 countries in a modified Delphi process, involving 4 online surveys, and 2 hybrid meetings.⁴ An *a priori* agreement required a supermajority consensus of >67% to merit a nomenclature change. (Interestingly, this requirement was waived for the question of stigmatizing language, somewhat devaluing the otherwise careful design). The outcome of this exercise was “metabolic dysfunction-associated steatotic liver disease,” or MASLD, and “metabolic dysfunction-associated steatohepatitis” or MASH.

OUT OF THE FRYING PAN....?

One can find sympathy with all 3 complaints about NAFLD and NASH. True, diseases should be defined by what they are, rather than by what they aren't, particularly if you know the “are.” But this is far from an absolute. Witness non-Hodgkin's lymphoma (NHL), which does not seem to bother the hematologists, or non-small cell lung cancer, (NSCLC) which doesn't exercise the oncologists. To the second truth: stigmatizing language in a disease name should be avoided. “Non-alcoholic” and “fatty” may be stigmatizing, and if that opinion reaches some sort of informed consensus, it should be deleted. However, it is the addition of the term “metabolic dysfunction” that is more problematic.

WHAT IS METABOLIC DYSFUNCTION?

The expert group defined “metabolic dysfunction” as the presence of any 1 of 5 cardio-metabolic criteria: elevated BMI, hypertension, hyperglycemia, elevated triglycerides and/or low HDL-cholesterol. This is puzzling. While an argument can be made that hyperglycemia and hyperlipidemia are dysfunctions of glucose and lipid metabolism, a BMI of 26 or a blood pressure of 130/90 hardly amount to metabolic dysfunction, either singly or together. Yet, in the presence of fat in the liver, either would be adequate to establish MASLD.

Whatever the diagnostic merit of these criteria, the construct of metabolic *dysfunction* is a new arrival. It is almost identical to metabolic *syndrome*; both share the same diagnostic criteria. However, metabolic *syndrome* requires 2 or more criteria to confirm the syndrome, whereas metabolic *dysfunction* only requires 1. Thus, those diagnosed with metabolic syndrome may also be diagnosed with MAFLD, but those with the metabolic dysfunction of MAFLD need not have the metabolic syndrome, a confusing outcome. So, metabolic *syndrome*, still a debated entity^{5,6}—there are presently 5 different definitions—is now joined by metabolic *dysfunction*. The debate may well intensify.

ALL THINGS METABOLIC?

The term *metabolic* may also be part of the problem. It works well when describing established metabolic diseases such as phenylketonuria and porphyria. But when used to describe a collection of anthropometric and blood measures, rather than a disrupted biochemical pathway, it may be less appropriate. Further, as these measures are well-established cardiovascular risk factors, one might ask why they should also be labeled “metabolic.”

ARE MASLD AND MASH WELCOME ARRIVALS?

Taxonomy aside, are MASLD and MASH useful new descriptors? To a non-hepatologist, the changes are not substantive, and the new terminology is confusing. While it emphasizes a context in which steatotic liver disease may occur, it does not clarify pathogenesis, and it introduces a new construct, which will be confused with an existing one. More importantly, it is not clear how it will improve diagnosis and treatment. At present, this change will have no underwriting implications, but should it enter clinical practice, nomenclature updates to manuals and risk calculators will become necessary.

CONCLUSION

There is momentum to abandon the disease names non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) and replace them with “metabolic dysfunction-associated steatotic liver disease (MASLD)” and “metabolic dysfunction-associated steatohepatitis (MASH).” The benefits are unclear. More accurate names would be welcome. However, they await a better understanding of the pathogenesis of hepatic fat accumulation and its clinical variants. In the meantime, the proposed changes lack obvious merit. And the taxonomy challenge they present is taxing.

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