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Correspondence on Letter regarding “Waiting for the changes after the adoption of steatotic liver disease”

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Dear Editor,

We have carefully reviewed the Letter to the editor by Yew et al. and find their discussion on the implementation of the new nomenclature, steatotic liver disease (SLD), to be highly insightful.^{1,2} Yew et al.² raised crucial issues, with a particular emphasis on the insufficient consideration of differences between Western and Asian countries regarding the new definition of SLD. Additionally, they highlighted the need for extensive discussions in the future regarding whether individuals with alcohol-related liver disease (ALD) should be included in the SLD category or another distinct disease framework. These discussions and research endeavors will undoubtedly contribute to a more comprehensive and refined understanding of liver diseases across diverse populations.

Effect size of cardiometabolic risk factors in Western and Asian patients

It is widely accepted that the impact of individual cardiometabolic risk factors and their respective cut-offs on individuals may differ between Asian and Western populations. First, the new SLD nomenclature applies different cut-offs for the body mass index (BMI) and waist circumference for Western and Eastern populations, other various cardiometabolic risk factors beyond the BMI require Asian-specific cut-offs. Second, the influence of each cardiometabolic risk factor on the progression of SLD and its correlation with adverse cardiovascular outcomes remains unclear. For example, there is a lack of data regarding whether equivalent consideration should be given to SLD individuals with diabetes or those with lower high-density lipoprotein cholesterolemia. Third, there is a need for additional data to validate whether the definition of metabolic dysfunction, comprising one or more abnormal cardiometabolic risk factors, is clinically reasonable and has a similar impact on Western and Eastern popula-

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tions. The scientific rationale for defining metabolic dysfunction as one or more abnormal cardiometabolic risk factors is not entirely clear. Future research is warranted to comprehensively investigate the impact of each cardiometabolic risk factor and its cut-off values on Eastern and Western populations. This validation is crucial for ensuring the clinical relevance and applicability of the defined metabolic dysfunction criteria across diverse populations.

Binary framework for metabolic liver disease and alcohol-related liver disease

Metabolic dysfunction-associated steatotic liver disease (MASLD) and ALD share several commonalities in their pathogenesis, including the genetic polymorphisms PNPLA3, TM6SF2, and MBOAT7.³ Accurately determining alcohol intake is a realistic challenge, and it is difficult to clearly distinguish between these two disease entities in the real world. Therefore, adopting a binary framework that strictly separates metabolic liver disease from alcohol-related liver disease may not be entirely realistic or reflective of the underlying pathophysiology in some aspects. Nevertheless, the data on whether the effect of alcohol consumption on MASLD has additive synergistic effects remain inconclusive.^{4,5} This underscores the complexity of the interactions between metabolic factors and alcohol intake in the development and progression of liver diseases, necessitating further research to elucidate the nuanced relationships between these factors.^{6,7}

Adopting a pathogenesis-based approach

The new SLD nomenclature represents a crucial advance that has the potential to enhance disease awareness and facilitate increased access to appropriate treatments. By aligning with the pathophysiology of the disease, this classification system promotes accurate identification and facilitates timely linkage to care within primary care settings.⁸ The subdivision of SLD into distinct subgroups based on factors such as hepatitis C and alcohol consumption is a judicious ap-

proach that acknowledges the diverse etiological factors contributing to fatty liver.

In summary, the new SLD classification, built on a pathogenesis-based model, is well-suited to replace the existing nomenclature of non-alcoholic fatty liver disease. It not only eliminates stigmatization associated with the disease name but also fosters heightened awareness and encourages better linkage to care.⁹ Nevertheless, challenges persist in understanding MASLD. More in-depth research is warranted to explore regional and racial variations related to the extent and impact of cardiometabolic risk factors on the occurrence of liver and cardiovascular diseases. Additionally, investigating whether alcohol consumption has an additive or synergistic effect on MASLD requires further exploration. Addressing these unresolved issues will contribute to a more comprehensive understanding of MASLD and guide effective management strategies.

Authors' contribution

First draft: Eileen L. Yoon. Theoretical framework, revision, and supervision: Dae Won Jun.

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Conflicts of Interest

The authors have no conflicts to disclose.

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Abbreviations:

SLD, steatotic liver disease; ALD, alcohol-related liver disease; BMI, body mass index; MASLD, metabolic dysfunction-associated steatotic liver disease; NAFLD, nomenclature of non-alcoholic fatty liver disease

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