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Reply to Correspondence

Reply to correspondence on "Prognosis of biopsy-confirmed metabolic dysfunction-associated steatotic liver disease: A sub-analysis of the CLIONE study"

Eileen Laurel Yoon[1,2] **and Dae Won Jun**[1,2]

[1]Department of Internal Medicine, Hanyang University Hospital, Hanyang University College of Medicine; [2]Hanyang Institute of Bioscience and Biotechnology, Hanyang University, Seoul, Korea

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Dear Editor,

I thank Fujii et al. for their correspondence to the letters.[1,2] Fujii et al. provided systematic and insightful comments on various recent issues related to metabolic dysfunction-associated steatotic liver disease (MASLD), along with the clinical characteristics of the Clinical Outcome Cohort Nonalcoholic Fatty Liver Disease (CLIONE) cohort.[3] The CLIONE and Nonalcoholic Steatohepatitis Clinical Research Network (NASH-CRN) cohorts are representative of Eastern and Western MASLD populations, respectively, and offer valuable information on the long-term outcomes of biopsy-proven MASLD patients.[4]

These two cohorts can offer insights into the differences in long-term outcomes that may occur between different races and the impact of each cardiometabolic risk factor (CMRF) on these outcomes.[5,6] We need more data to determine whether different cutoffs should be applied between regions and races for the other four CMRFs, aside from body mass index (and/or waist circumference), among those that constitute MASLD. As the impact of obesity (measured by waist circumference) on hard clinical outcomes varies by race, additional data are also needed to determine whether the four different CMRFs have distinct impacts on the occurrence and progression of MASLD according to race.

Despite the similarity of clinical characteristics of the CLIONE study and the NASH-CRN cohort regarding severity, there are notable differences in the risk of developing hepatocellular carcinoma (HCC) between these two cohorts, particularly among MASLD patients with advanced hepatic fibrosis. Future evaluations are necessary to determine the causes of these differences. A comprehensive evaluation is needed to ascertain whether the variation in HCC incidence between Eastern and Western cohorts is due to genetic traits—currently relatively undervalued in the new nomenclature—or to characteristics like lean MASLD or sarcopenia, which are more prevalent in Asian MASLD populations.

With the introduction of the new MASLD nomenclature,

Corresponding author : **Dae Won Jun**
Department of Internal Medicine, Hanyang Institute of Bioscience and Biotechnology Gastroenterology, Hanyang University College of Medicine, 222 Wangsimni-ro, Seongdong-gu, Seoul 04763, Korea
Tel: +82-2-2290-8338, Fax: +82-2-972-0068, E-mail: noshin@hanyang.ac.kr
https://orcid.org/0000-0002-2875-6139

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one of the most unmet needs pertains to the long-term outcomes of the newly proposed MetALD subgroup.[7] MetALD, recently defined, includes moderate alcohol drinkers among existing nonalcoholic fatty liver disease patients, but there is currently no large-scale biopsy-proven cohort for this group. Many large-scale studies report the prevalence and long-term outcomes of MetALD using non-invasive tests such as the hepatic steatosis index (HSI) or fatty liver index (FLI). However, when MetALD is identified based on serological non-invasive tests (HSI and FLI), there is a bias due to overlapping evaluations of CMRFs, leading to overestimation of cardiovascular events. Therefore, there is a need for an international biopsy-proven MetALD cohort to address these gaps.

Authors' contribution

EY: Drafting the manuscript; DWJ: Revision and Supervision of the manuscript.

Conflicts of Interest

The authors have no conflicts to disclose.

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Abbreviations:

MASLD, metabolic dysfunction-associated steatotic liver disease; CLIONE, Clinical Outcome Nonalcoholic Fatty Liver Disease; NASH-CRN, Nonalcoholic Steatohepatitis Clinical Research Network; CMRF, cardiometabolic risk factor; HSI, hepatic steatosis index; FLI, fatty liver index

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