Reply to correspondence: “Prognosis of biopsy-confirmed MASLD: A sub-analysis of the CLIONE study”

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I thank Fujii et al. for their correspondence to the letters. Fujii et al. provided systematic and insightful comments on various recent issues related to MASLD, along with the clinical characteristics of the Clinical Outcome Cohort Nonalcoholic Fatty Liver Disease (CLIONE) cohort. 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.

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. We need more data 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 clinical hard 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 similarity of two clinical characteristics of the CLIONE study and the NASH-CRN cohort regarding to severity, there are notable differences in the risk of developing hepatocellular carcinoma between these two cohorts, particularly among MASLD with advanced hepatic fibrosis patients. Future evaluations are necessary to determine the causes of these differences. A comprehensive evaluation is needed to ascertain whether the variation in hepatocellular carcinoma 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, one of the most unmet needs pertains to the long-term outcomes of the newly proposed MetALD subgroup. MetALD, recently defined, includes moderate alcohol drinkers among existing non-alcoholic 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 overestimate cardiovascular events. Therefore, there is a need for an international biopsy proven MetALD cohort to address these gaps.

Reference


4. Yoon EL, Jun DW. Correspondence on Letter regarding "Risk factors in nonalcoholic fatty liver disease". Clin Mol Hepatol 2023;29:1050-1051.
