Reply: Is the METS-IR index an appropriate predictor for nonalcoholic fatty liver disease?

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We appreciate Dr. Lee’s interest in this study. As Dr. Lee commented in the letter, the metabolic score for insulin resistance (METS-IR) has been used as a simple, reliable, and reproducible surrogate insulin resistance (IR) marker in the South American population.\textsuperscript{1,2} However, several Korean epidemiological studies using METS-IR\textsuperscript{3-5} lack validation and cut-off points that would help to identify IR in Koreans. A follow-up study is needed to compare METS-IR with the hyperinsulinemic-euglycemic index in order to determine whether reflects it insulin sensitivity well and if it is more reliable than the homeostatic model assessment for IR (HOMA-IR) used in the general Korean population.

The formula that constitutes METS-IR uses triglyceride levels, which are affected by multiple factors, including arterial blood pressure, alcohol use, carbohydrate intake, and use of medications such as diuretics and oral contraceptives.\textsuperscript{6} We adjusted for hypertension, alcohol use, and energy intake because such factors also contribute to nonalcoholic fatty liver disease (NAFLD).\textsuperscript{7,8} However, the lack of information in the Korean Genome and Epidemiological Study dataset about specific medication use could serve as a potential confounder in our study.\textsuperscript{10} Despite this limitation, there is also the possibility that the potential effect of the confounder was attenuated because we used community-based cohort data to analyze a large population. Further clinical trials should be performed with controlling for potential confounding variables to verify the association between METS-IR and NAFLD.

Current guidelines for management of NAFLD state that radiologic methods, such as abdominal ultrasonography, controlled-attenuated parameter, or unenhanced abdominal computed tomography, are acceptable to diagnose hepatic steatosis.\textsuperscript{8} Serologic surrogate markers, such as NAFLD-liver fat score, hepatic steatosis index, or fatty liver index, can be used to assess hepatic steatosis if radiological examinations are infeasible.\textsuperscript{9} We believe that METS-IR will be less accurate for diagnosis of hepatic steatosis than radiologic tests or serologic surrogate markers for hepatic steatosis. This is because METS-IR was developed as a surrogate marker for IR. We do not claim to use METS-IR as a single predictive model for NAFLD; if fatty liver disease has not yet developed, abdominal ultrasonography or abdominal computed tomography will not provide additional information about the risk of developing NAFLD. As IR is closely related to NAFLD, we believe that the assessment and management of IR are important strategies for the early prevention and management of NAFLD. In clinical practice, HOMA-IR is the most commonly used surrogate marker for IR. However, serum insulin level is not routinely measured in the general clinical field, so MET-IR can be applied more easily than HOMA-IR even though METS-IR uses a more complex formula. In our study, METS-IR was not inferior to HOMA-IR in
predicting the prevalence of NAFLD, and it was superior to HOMA-IR in predicting the incidence of NAFLD. Therefore, our findings suggest that METS-IR can be used as an IR marker in patients with or who are at risk of developing NAFLD. Further experimental studies and clinical trials should be performed to elucidate the mechanism by which METS-IR is positively related to NAFLD and negatively related to advanced liver fibrosis, considering the changes in METS-IR values over time. Further studies on the genetic variations affecting METS-IR values, hepatic steatosis, and liver fibrosis are also necessary.

References

10. Kim Y, Han BG. Cohort Profile: The Korean Genome and Epidemiology Study (KoGES)