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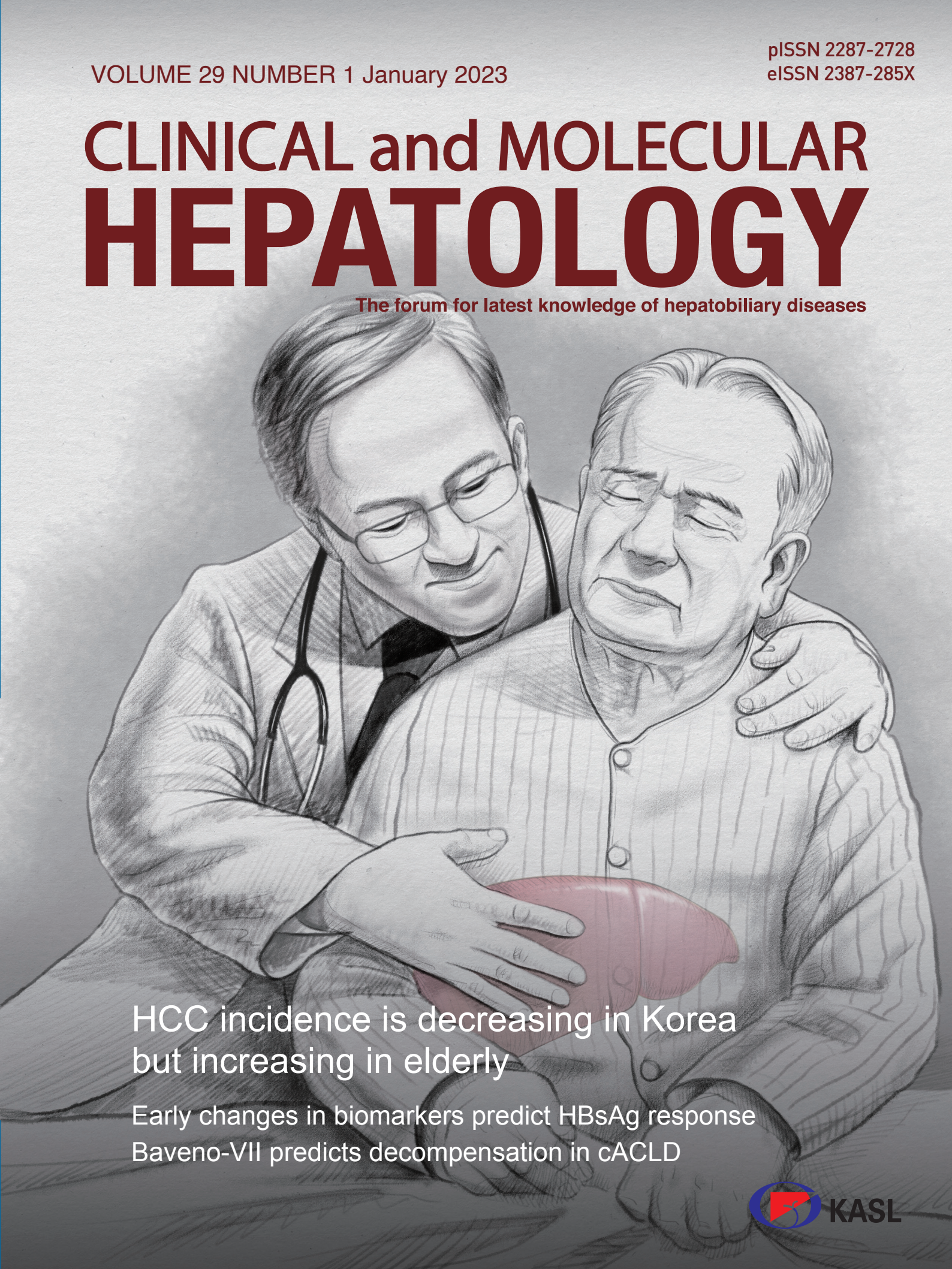

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Letter to the Editor

Letter regarding "The usefulness of metabolic score for insulin resistance for the prediction of incident non-alcoholic fatty liver disease in Korean adults"

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Keywords: Insulin resistance; Non-alcoholic fatty liver disease; Incidence

Dear Editor,

The euglycemic-hyperinsulinemic clamp (EHC) is the gold standard for assessing insulin sensitivity in peripheral tissues.[1] However, simpler metrics are needed to assess insulin resistance (IR). The metabolic score for the IR (METS-IR) index is a new metric for measuring IR that is simple, reliable, and reproducible.[1,2] Although Lee et al.[3] applied this score to Koreans, we would like to address some points regarding the associations between non-alcoholic fatty liver disease (NAFLD) and METS-IR.

First, is the METS-IR a reliable score? This score was first proposed by a Mexican research team.[1] The METS-IR discovery sample included 125 subjects who underwent the EHC. The study included subjects aged 20–79 years, with a wide range of body mass indices (18–34.9 kg/m^2), who were recruited from the outpatient diabetes clinic of a university hospital in Mexico City. Among the 125 subjects, 68 had type 2 diabetes mellitus (DM) and 57 did not. The subjects with DM were included if they met the following conditions: their glycated hemoglobin concentration was <8%; they did not take insulin; and they were treated with only metformin. However, the number of patients used to develop this score was too small. Furthermore, the composition of the discovery population was heterogeneous. No precise definition of how the METS-IR discovery population was recruited was provided. Although the factors included in the METS-IR score reflect IR, the question is, whether an appropriate patient population was recruited to develop the METS-IR.

Second, NAFLD progresses from simple steatosis, steatohepatitis, and fibrosis to cirrhosis.[4,5] The authors argued that METS-IR can be used to predict the incidence of NAFLD.[3] As mentioned in the editorial by Kim and Cheong,[6] METS-IR was inversely correlated with the prediction of fibrosis in patients with NAFLD in another study.[5] The same authors explained that a reduction in triglycerides with the progression of liver fibrosis was one hypothesis.[5] Serum triglyceride levels decrease as liver disease progresses to liver fibrosis.[7] As triglyc-

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Table 1. Formulas of METS-IR and HOMA-IR

	Formula
METS-IR	ln (2 × FPG [mg/dL] + fasting serum triglyceride [mg/dL]) × BMI (kg/m^2) / ln (HDL cholesterol [mg/dL])
HOMA-IR	(fasting serum insulin [μIU/mL] × FPG [mg/dL] / 405)

METS-IR, metabolic score for the insulin resistance; HOMA-IR, homeostatic model assessment for insulin resistance; FPG, fasting plasma glucose; BMI, body mass index; HDL, high-density lipoprotein.

erides are normally the principal source of lipids in the liver, the fat mass in the liver may decrease with fibrosis. Therefore, if METS-IR is strongly affected by triglycerides, this is a major limitation of the METS-IR index. Triglyceride levels can be affected by many factors, including uric acid, being overweight, arterial blood pressure, use of oral contraceptives, consumption of alcohol and tobacco, lack of physical exercise, thyroid disease, and medications, such as diuretics, hormones, corticosteroids, and beta blockers.[8] We can easily find patients with NAFLD, and there are patients with abnormally elevated triglycerides or already taking triglycerides lowering agents, which may limit the use of METS-IR. The authors should explain the mechanism for the contradictory results in predicting steatosis and liver fibrosis with the METS-IR index.

Third, the homeostatic model assessment for insulin resistance (HOMA-IR) contains insulin in the formula, while METS-IR does not include insulin in the formula (Table 1). Additionally, METS-IR includes the blood lipid profile in the formula, while HOMA-IR does not. The METS-IR is superior to the HOMA-IR for predicting incident NAFLD, and is not inferior to the HOMA-IR for predicting prevalent NAFLD. Then, the incidence of NAFLD can be easily detected by images or laboratory findings. If METS-IR is non-inferior for predicting the development of NAFLD, why do we need a more complex formula to predict NAFLD? Another question arises as to whether METS-IR is a more useful marker for early detection and prediction of insulin sensitivity than HOMA-IR. Therefore, it is necessary to consider the clinical use and application of METS-IR in fatty liver patients.

In conclusion, further studies are needed to determine whether METS-IR is an appropriate predictor for NAFLD incidence.

Conflicts of Interest

The author has no conflicts to disclose.

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Abbreviations:

DM, diabetes mellitus; EHC, euglycemic-hyperinsulinemic clamp; HOMA-IR, homeostatic model assessment for insulin resistance; IR, insulin resistance; METS-IR, metabolic score for the insulin resistance; NAFLD, non-alcoholic fatty liver disease

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