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Response

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Response: Triglyceride–Glucose Index Predicts Cardiovascular Outcome in Metabolically Unhealthy Obese Population: A Nationwide Population-Based Cohort Study (J Obes Metab Syndr 2022;31:178-86)

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The triglyceride glucose (TyG) index is considered a surrogate marker of cardiovascular disease (CVD) and mortality using the parameter of insulin resistance. Numerous studies have investigated the associations between the TyG index and cardiovascular outcomes, including cardiovascular mortality. A recent meta-analysis and systematic review evaluated associations between the TyG index and the risks of CVD and mortality in the general population.[1] Twelve cohort studies involving 6,354,990 participants were analyzed. Higher TyG index values were significantly associated with an increased incidence of CVD; however, the TyG index was not correlated with mortality, including cardiovascular mortality in analyses.[1] A subgroup analysis of the population without diabetes revealed no significant association between myocardial infarction incidence and the TyG index, indicating the heterogeneous implications of this index across populations.[2] The present study contributes to the literature because we focused on the specific population in which the TyG index could be a useful surrogate marker for an elevated CVD risk.[3] Our results demonstrated that the TyG index could predict CVD mortality only in participants with metabolically unhealthy obesity (MUO), and that the index is substantially and consistently associated with CVD regardless of the metabolic health phenotype or presence of obesity.[3]

In a letter to the editor, the author stated that assessing the predictive value of the TyG index for CVD outcomes would provide greater benefit if we considered changes in the TyG index as well as the obese metabolic health phenotype. Several recent studies have reported the significant effect of longitudinal changes in the TyG index on CVD risk. We appreciate the letter author for highlighting these important points. A study involving 62,443 healthy Chinese people found that CVD risk increased with quartile of change in the TyG index during a median follow-up of 7.01 years, and that adding change in the TyG index to a baseline risk model for CVD improved its predictive power.[4] Another prospective cohort study involving 36,359 participants with a median observation period of

8 years similarly reported that, compared to a stable TyG level, both loss and gain were associated with increased risks of cardiometabolic diseases.[5]

Recently, cumulative exposure to particular risk factors has garnered considerable attention. Cui et al.[6] calculated the cumulative TyG index by multiplying the average TyG index and the time between two consecutive examinations. They discovered that the CVD risk increased with each quartile of the cumulative TyG index, and that a longer duration of exposure to a higher TyG index was significantly correlated with increased CVD risk.[6] The *post hoc* analysis of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial revealed that, in patients with type 2 diabetes mellitus, the cumulative TyG index independently predicts the incidence of major adverse cardiovascular events.[7] Consequently, incorporating cumulative exposure to insulin resistance may improve the estimation of future CVD risk and assist physicians and patients in determining therapeutic and preventative strategies for CVD.

Moreover, as the letter author noted, the metabolically healthy phenotype and obesity status may change over time, and these changes may influence CVD risk. Our research team has reported that metabolically healthy obesity (MHO) phenotypes represent a heterogeneous group that is subject to change over time, and such change has substantial impacts on cardiovascular outcomes.[8] Compared to individuals with stable MHO, the risk of cardiovascular events was 1.24-fold higher in individuals who transitioned to MUO.[8]

Collectively, incorporating the dynamic changes of the obese metabolic health phenotype and TyG index and evaluating their implications for the CVD risk would be intriguing. We anticipate that further research with longer follow-up and larger numbers of participants would reveal these intriguing associations.

CONFLICTS OF INTEREST

Chang Hee Jung is an editorial board member of this journal; however, he was not involved in the peer reviewer selection, evaluation, or decision process for this article. No other potential conflicts of interest relevant to this article were reported.

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