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Association between Metabolic Syndrome and Microvascular Complications in Chinese Adults with Type 1 Diabetes Mellitus (*Diabetes Metab J* 2022;46:93-103)

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We sincerely thank Dr. Kim for his interest in our article entitled "Association between metabolic syndrome and microvascular complications in Chinese adults with type 1 diabetes mellitus" [1]. We also thank the editor for providing us the opportunity to discuss further the issues related to our article.

We agree with Dr. Kim that insulin dose could contribute to insulin resistance among patients with type 1 diabetes mellitus (T1DM) and potentially be relative to the presence of metabolic syndrome (MetS). We have to acknowledge that the lack of data on insulin dose and medications for hypertension and dyslipidemia is one of the major limitations of our study. As was mentioned in our article, because the data in our study was based on the retrospective collection, it was inevitable that some data was missing. Instead, we tried to assess the insulin resistance (IR) level using an estimated glucose disposal rate (as in our article, lnGDR) derived from a previous study using euglycemic-hyperinsulinemic clamp to establish a model between clinically accessible variables and IR [2]. As expected, our study found that the patients with T1DM and MetS presented lower lnGDR (1.7 vs. 1.9, $P<0.001$) than the T1DM participants without MetS. It suggests that lower GDR and more severe IR are associated with MetS in T1DM, consistent with previous studies [3].

As for the relationship between MetS and microvascular complications, we also agree with Dr. Kim that it was important to consider the influence of glycemic control on blood lipid profile. We tried to minimize such effect by adjusting for glycosylated hemoglobin (HbA1c) in the logistic models, and the association between MetS and the risk of diabetic kidney disease (DKD) or diabetic retinopathy (DR) remained significant. According to Dr. Kim's advice, we further adjusted for boy mass index in addition to the variables in model 1 to 4. The results showed that MetS was positively associated with DKD (odds ratio [OR], 2.53; 95% confidence interval [CI], 1.28 to 5.00) and DR (OR, 4.12; 95% CI, 1.71 to 9.90). To perform subgroup analysis, we divided all the participants into two groups: optimal glycemic control (HbA1c <7%, $n=114$) and suboptimal glycemic control (HbA1c ≥7%, $n=433$). We can see a differences in the unadjusted ORs in both DKD and DR between the optimal glycemic control group (DKD [OR, 1.89; 95% CI, 0.53 to 6.67], DR [OR, 3.24; 95% CI, 0.87 to 12.04]) and the suboptimal control group (DKD [OR, 2.55; 95% CI, 1.47 to 4.40], DR [OR, 2.73; 95% CI, 1.34 to 5.58]). However, both *P* values for interaction were over 0.05. Further study with a larger sample size would be beneficial to interpret the effect of controlling glucose to target on the relationship

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between MetS and microvascular complications.

As Dr. Kim mentioned, metformin, medications for hypertension and dyslipidemia, such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and sodium-glucose co-transporter 2 inhibitors (SGLT2i), may have an influence on the risk of DKD or DR. However, information on the usage of these drugs were not available in our database; thus, we are not able to eliminate the effect of the these drugs on the outcome of microvascular complications in T1DM patients. Notably, SGLT2is have not been approved by the Chinese National Medical Product Administry for treating T1DM, and thus we do not have patients using SGLT2i in our cohort. We acknowledge this as one of our limitations in our study. Inclusion of data on medication use in future studies would be beneficial to fully elucidate this issue.

We would like to thank Dr. Kim for his comments on the importance of comprehensive management of T1DM. Our article acquired the information using a standardized questionnaire on receiving diabetic education, receiving nutrition therapy education, and adherence to a diabetic diet. In other words, this information was self-report and may be subjective to bias. We also noticed that the different impact on MetS of these educational and behavioral elements, and the potential clinical importance in guiding future diabetic eduction. Therefore, a more objective approach, such as video logs, should be applied in future studies to offer more accurate evaluation and richer information on this issue. Lastly, we agree with Dr. Kim that longitudinal studies would better address the potential causal effect of MetS on microvascular complications, which is what we are currently endeavoring to do in a larger population of T1DM in China.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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