Response

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Differences in Clinical Outcomes between Patients with and without Hypoglycemia during Hospitalization: A Retrospective Study Using Real-World Evidence (*Diabetes Metab J* 2020;44:555-65)

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We appreciate Professor Sung-Woo Kim for his interest and valuable comments regarding our recently published article, entitled, "Differences in clinical outcomes between patients with and without hypoglycemia during hospitalization: a retrospective study using real-world evidence," which was published in *Diabetes & Metabolism Journal* [1].

Regarding the comment about matching of covariates for analyzing complications after hypoglycemia, we aimed to analyze the risk factors for hypoglycemia between patients who experienced and those who did not experience hypoglycemia during hospitalization and the effect of hypoglycemia on complications. Therefore, we could not match age and sex despite the large number of observations in the control group compared to the hypoglycemic group. Old age, female sex, and prevalence of type 1 diabetes mellitus (DM) were risk factors for hypoglycemia in our study and there were no significantly different complications after hypoglycemia. Nonetheless, we agreed with your opinion. We should match some covariates which could affect complications after hypoglycemia. As the occurrence and role of hypoglycemia in cardiovascular complications differed between type 1 DM and type 2 DM patients [2-4], our results would be more meaningful if we compared complication rates after matching for confounders.

Second, the length of the hospital stay was significantly longer in the hypoglycemia group than in the group without hypoglycemia. Patients who were admitted only for glycemic control were reviewed and patients with frequent hypoglycemia were excluded from this study. As Professor Kim suggested, there were no differences in baseline glycosylated hemoglobin (HbA1c) among the patients and we assume that hypoglycemia was the primary cause of longer hospitalizations. Most importantly, our study is an electronic medical record-based retrospective cohort study. In retrospective cohort studies, it is not possible to determine the causality with respect to study results [5,6]. It can only identify correlations or associations. For this reason, we can only speculate that hypoglycemia is the main cause of these outcomes. Efforts have been made to include variables to examine various causes, but this is a clear limitation of retrospective cohort studies. We are simply measuring the status of hypoglycemia in clinical practice. Hypoglycemia affects several factors that influence length of hospitalization, such as adjustment of treatment regimen and hypoglycemic outcomes. We analyzed patients without severe morbidity in a general ward so that there were no significant factors

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that could extend the hospital stay except for blood glucose control.

To respond to the third point, de-intensified antidiabetic therapy and modification of the insulin regimen after hypoglycemia leads to higher HbA1c levels during follow-up. As Professor Kim mentioned, comparing the proportion of patients achieving their glucose target in each group or glycemic variability after 2 years would be valuable for analyzing complications. However, due to the nature of retrospective cohort research, it is necessary to consider the limitation that the dropout rate for the research subjects increases as the research period increases.

CONFLICTS OF INTEREST

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

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