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Cardiovascular Disease Predicts Severe Hypoglycemia in Patients with Type 2 Diabetes (*Diabetes Metab J* 2015; 39:498-506)

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We sincerely appreciate the interests and comments on our study, "Cardiovascular disease predicts severe hypoglycemia in patients with type 2 diabetes" which was published in *Diabetes & Metabolism Journal* [1].

Recent guidelines emphasize that glycemic management should be individualized according to multiple patients factors [2]. Hypoglycemia is regarded as one of the major barriers to achieve glycemic targets, and early detection of hypoglycemia risk is clinically important [3]. In this study, we have found that a history of cardiovascular disease was an independent risk factor for the development of severe hypoglycemia (SH) after adjusting for other SH-related factors (including cardiovascular autonomic dysfunction) in type 2 diabetes patients without renal dysfunction.

We agree with Dr. Kim's opinion that glycemic variability is one of the important factors that may influence the development of SH. In this study, 62 patients experienced a total of 78 SH episodes during the 10-year follow-up period. Two SH events occurred in eight patients, and three SH events occurred in four patients. We routinely checked the patients' glycosylated hemoglobin (HbA1c) level every 6 months and calculated the mean and standard deviation (SD) of HbA1c during the follow-up period. As a result, we found that there were no differences in the mean HbA1c (8.34%±1.31% vs. 8.52%±1.47%, P=0.684) and SD of HbA1c (1.10±0.58 vs. 1.14±0.61, P=0.855) between the group that experienced one SH event and those that experienced recurrent SH events. Also, there were no differences in mean HbA1c (8.37%±1.34% vs. 8.24%±1.35%, P=0.460) and SD of HbA1c (1.11±0.58 vs. 1.23±0.75, P=0.228) between the group who experienced SH and those who did not experienced SH, although the group with SH showed borderline significant difference in baseline HbA1c when compared with the group without SH. Further regression model adjusted for SD of HbA1c did not affect the outcome (hazard ratio, 2.40; 95% confidence interval, 1.11 to 5.21; P=0.027). Thus, we confirmed that long-term glycemic variability did not influence the main result of this study.

In addition, there were some studies that evaluated peripheral neuropathy as a risk factor for SH. In Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, peripheral neuropathy conferred a modest but significantly increased risk of SH [4]. Other studies showed that peripheral neuropathy was related to the risk of recurrent SH [5-7], as Dr. Kim pointed out. The precise mechanism for the relationship between peripheral neuropathy and SH remained obscure. Unfortunately, baseline examinations of peripheral neuropathy were not performed in all patients in this study. Future analyses will include factors such as nerve conduction study [8] as well as additional data.

We would like to appreciate Dr. Kim for the interest in our study and the thoughtful comments.

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CONFLICTS OF INTEREST

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

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