

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

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Hypoglycemia is a common adverse event and one of the main obstacles to achieving good glycemic control to minimize the risk of diabetic complications in patients with diabetes [1]. Numerous studies reported that hypoglycemia increases cardiovascular risk and mortality [2]. It is currently unclear how hypoglycemia influences the risk of cardiovascular disease, but several mechanisms have been suggested, such as its link to increased catecholamine levels, thrombocytosis, and inflammation [2]. Therefore, most physicians have attempted to control hypoglycemia with the aim of reducing cardiovascular risk. Yun et al. [3] reported that cardiovascular disease is an independent risk factor for severe hypoglycemia in patients with type 2 diabetes mellitus. Patients with severe hypoglycemia were older, used insulin more often, had a longer cardiovascular history, and were diagnosed more often with cardiovascular autonomic neuropathy than those without severe hypoglycemia. These results are similar to those of other studies [1,4]. Interestingly, cardiovascular disease remained as a risk factor for hypoglycemia even after adjusting for cardiac autonomic neuropathy, which is a known prognostic factor [3]. However, there are some concerns about this study.

First, some studies showed that patients with severe hypoglycemia have higher hemoglobin A1c levels [5,6]. Davis et al. [4] suggested that recurrent severe hypoglycemia might result in poor glycemic control, including unpredictable swings between high and low levels of glucose. A study that continuously monitored the glucose level of patients with type 2 diabetes

showed that variability in interstitial glucose level is an independent predictor for severe hypoglycemia, suggesting that poor glycemic control is a major risk factor for hypoglycemia [6]. In this study, patients with severe hypoglycemia tended to have higher hemoglobin A1c levels. Therefore, it is questionable whether or not the authors collected enough data about the frequency of severe hypoglycemia.

Second, diabetic peripheral neuropathy is the most common complication of diabetes. According to a report of Diabetic Neuropathy Study Group of the Korean Diabetes Association, 33.5% patients with diabetes had peripheral neuropathy that is associated with a history of cerebrovascular accident or peripheral artery disease [7]. In addition, about 80% of patients with peripheral neuropathy had abnormal cardiac autonomic neuropathy test results [8]. Davis et al. [4] reported that peripheral neuropathy is an independent predictor of severe hypoglycemia, and that it could be a surrogate for compromised autonomic/neuroendocrine defenses that also predisposes patients to hypoglycemia. Therefore, peripheral neuropathy could have been a confounding factor as well as a predictive factor of severe hypoglycemia in this study.

It is unclear whether hypoglycemia precedes cardiovascular disease or vice-versa, but it is generally accepted that hypoglycemia is associated with cardiovascular disease. Further studies are needed to find ways of reducing hypoglycemia and cardiovascular risk, and to uncover new predictive factors.

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CONFLICTS OF INTEREST

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

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