COMMENTS AND RESPONSES

Response to Comment on: Calleja et al. Insulin Resistance Is Associated With a Poor Response to Intravenous Thrombolysis in Acute Ischemic Stroke. Diabetes Care 2011;34:2413–2417

We have read with interest the letter by Natarajan et al. (1) about our original article published in *Diabetes Care* (2). Our aim was to evaluate the prognostic effect of insulin resistance on the response to acute stroke thrombolysis. Insulin resistance was quantified with the homeostasis model assessment of insulin resistance (HOMA-IR) using fasting blood samples drawn 24–48 h after admission. We tried to design the study in a way that would minimize the potential confounding effect of hyperglycemia. First, on the basis of the results of the Glycemia in Acute Stroke study demonstrating that glycemia >155 mg/dL is an independent predictor of poor outcome in acute stroke patients (3), we excluded those patients with glucose concentration above this value on admission. Second, the logistic regression models were adjusted by admission glycemia. Previous literature on ischemic stroke had focused mainly on admission glycemia as one of the most robust predictors of poor outcome, and therefore we relied on this parameter to rule out this potential confounding effect. However, in agreement with the observation by Natarajan et al., the Glycemia in Acute Stroke study pointed to 155 mg/dL at any time within the first 48 h from stroke onset as the optimal glycemia cutoff level for good outcome at 3 month.

Attending the authors' criticism, we checked the concentrations of glucose and insulin at 24–48 h in the groups of patients with good versus poor outcome. Both parameters were higher in the group of patients with a poor response to thrombolysis. Of note, mean glucose level in the poor outcome group was only modestly raised (124 mg/dL), in line with the idea that even mild increments of glycemia could be deleterious. We then conducted independent logistic regression models in which we included HOMA-IR, fasting glycemia, or insulin alone, and the association of HOMA-IR with poor outcome appeared to be more robust than the associations of HOMA-IR individual components. Thus, our results support the notion that insulin resistance itself may exert a deleterious effect in acute ischemic stroke. Nevertheless, from a methodological standpoint, it may be tremendously arduous to isolate the effects of insulin resistance and completely exclude a potential interference of glycemia. Trying to reconcile the observations of Natarajan et al. with our findings, one could argue that insulin resistance is a crucial factor contributing to more lasting and persistent high glucose levels during the acute phase of ischemic stroke. Finally, as stated in the limitations section, the results of our exploratory study warrant confirmation in a larger series.

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