COMMENTS AND RESPONSES

Utility of Homeostasis Model Assessment of β-Cell Function in Predicting Diabetes in 12,924 Healthy Koreans

Response to Sung, Reaven, and Kim

Sung et al. (1) are to be commended for their efforts in reporting on the utility of a homeostasis model assessment (HOMA) of β-cell function (HOMA-β) as a measure of insulin secretion to predict the development of diabetes in a large population (n = 12,924) followed through retrospective medical record review. They conclude by questioning the utility of HOMA-β in predicting the development of diabetes. This conclusion is problematic, though, and likely to be biased. Sung et al. do not adequately address the physiological relationship between insulin sensitivity and secretion in their analysis. It is well know that a hyperbolic association exists between these two measures, and this has been demonstrated not only from direct measurements of insulin sensitivity and secretion but also surrogate measures from the oral glucose tolerance test (2). Given this association, a measure of insulin secretion is not interpretable without taking into account the prevailing level of insulin sensitivity, as higher secretion may reflect greater resistance (3,4). Thus, greater insulin secretion may serve as a marker for insulin resistance, a known risk factor for diabetes, and to properly assess its association with diabetes risk, one must adjust for this confounding (4).

One of the originators of the HOMA model has recently written that it is not appropriate to report HOMA-β in isolation (3). There is no doubt that HOMA of insulin sensitivity (HOMA-S) and HOMA-β inaccurately capture what they were designed to measure, but nevertheless these and other measures with less than perfect accuracy (such as BMI to reflect body adiposity) have shown their usefulness in estimating risk for the development of type 2 diabetes. Some residual confounding remains after adjustment for a misclassified confounder, but the result obtained is generally less biased compared to no adjustment at all. This is demonstrated in an article cited by Sung et al. comparing HOMA-β with the acute insulin response (AIR) to intravenous glucose by glucose tolerance status (5). A decline in AIR is seen across categories of glucose tolerance from normal to diabetes defined by high 2-h glucose that becomes more pronounced after adjustment for insulin sensitivity assessed using the minimal model. No differences are observed in comparing HOMA-β across normal glucose tolerance, impaired glucose tolerance, and diabetes defined by high 2-h glucose categories until adjustment for HOMA-S is performed. Thus, adjustment for HOMA-S leads to results in generally the same direction but of lesser magnitude than those seen with more direct and accurate measures of insulin sensitivity and secretion. The unadjusted HOMA-β analysis though is biased and would lead to the incorrect conclusion of no differences in insulin secretion by these categories of glucose tolerance. By not adjusting for a measure of insulin sensitivity, the result reported by Sung et al. regarding the association between HOMA-β and diabetes risk is probably biased. It would be beneficial to see the results of a reanalysis of their data adjusted for HOMA-S to permit readers to draw their own conclusion about the value of HOMA-β in the prediction of future diabetes in this Korean population.

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