COMMENTS AND RESPONSES

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

Response to Boyko

We appreciate the thoughtful comments by Boyko (1). The premise of our study (2) was to understand whether homeostasis model assessment (HOMA) of β-cell function (HOMA-β) had utility in predicting diabetes development above and beyond glucose concentration in a large sample of individuals. We concluded that it did not. Even in narrowly defined glucose categories (normal fasting glucose [NFG], <5.6 mmol/l; impaired fasting glucose [IFG]-100, 5.6–6.0 mmol/l; and IFG-110, 6.1–6.9 mmol/l), baseline glucose concentrations were significantly higher in those who eventually developed diabetes; however, HOMA-β was either significantly higher or similar in those who developed diabetes. Although we adjusted our model for age, sex, and BMI, Boyko notes that we failed to adjust for "insulin resistance" (HOMA of insulin sensitivity [HOMA-S]) and our results are therefore biased. While we agree that there is a relationship between insulin resistance and secretion (3), what does it mean to adjust for HOMA-S using the HOMA calculation? Both HOMA-β and HOMA-S calculations involve inputting two variables—fasting glucose and insulin concentration. HOMA-S is nearly perfectly correlated with fasting insulin concentration; in our study, the *r* value was −0.99. Therefore, when one adjusts for HOMA-S or insulin concentration, glucose is the only value that varies in the HOMA-β calculation. When we adjusted HOMA-β for age, sex, BMI, and HOMA-S, indeed, HOMA-β was lower in individuals who developed diabetes: NFG group, 95 vs. 99 ($P = 0.09$); IFG-100, 75 vs. 80 ($P < 0.001$); and IFG-110, 67 vs. 69 ($P < 0.001$). However, this information merely reiterates the fact that fasting glucose was different in the population that developed diabetes. Other more "sophisticated" measures of insulin secretion have the same issue. For example, Boyko notes the decline in acute insulin response (AIR) with worsening glucose tolerance that is more pronounced after adjusting for insulin sensitivity using the minimal model. As with HOMA-β, AIR varies closely with fasting glucose concentration and is essentially abolished when fasting glucose concentration is <6.4 mmol/l (4). Because HOMA-β and AIR are in frequent use, it is important to recognize their limitations.

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