COMMENTS AND RESPONSES

# New Insights on the Simultaneous Assessment of Insulin Sensitivity and β-Cell Function With the HOMA2 Method

Response to Caumo et al.

We read the article by Caumo et al. (1) with great interest. Using homeostasis model assessment (HOMA), they have simultaneously assessed insulin sensitivity (HOMA-S%) and β-cell function (HOMA-B%) by using the HOMA2 method (2) in a group of 76 normoglycemic subjects with or without obesity. They found the HOMA scatter plot to be reminiscent of the hyperbolic relationship previously reported using acute insulin response and insulin sensitivity index calculated by minimal model analysis of intravenous glucose tolerance testing (3). From their HOMA scatter plot, they also proposed the unique disposition index (DI), which is the product of HOMA-B% and HOMA-S% determined using the HOMA2 method. In fact, the DI was decreased in diabetic subjects and improved by rosiglitazone treatment in obese subjects (1).

We have also analyzed HOMA-S% and HOMA-B% using the HOMA2 method in 295 Japanese healthy men who underwent a 75-g oral glucose tolerance test and who were proven to have normal glucose tolerance by Japan Diabetes Society criteria, i.e., fasting glucose <6.11 mmol/l and 2-h glucose <7.77 mmol/l (4). They were aged (mean ± SD) 23 ± 3 years (range 21–57), and their BMI was 22.4 ± 2.9 kg/m$^2$ (17.5–41.7). According to the wide range of the degree of obesity, HOMA-S% ranged from 22 to 756% (151 ± 91) and HOMA-B% from 22 to 327% (91 ± 36). Since both HOMA-S% and HOMA-B% were not normally distributed, both were log transformed to explore the relationship between the two indexes. A simple linear regression analysis was used: ln(HOMA-B%) = 7.33 − 0.592 × ln(HOMA-S%) ($r = -0.846$, $P < 0.0001$). Since the 95% CI of the slope of the regression line was between −0.549 and 0.635 (not reaching −1), the relationship between HOMA-S% and HOMA-B% was considered to be not hyperbolic but rather linear. Therefore, the product of HOMA-S% and HOMA-B%, the DI proposed by Caumo et al., was not constant in our samples of the healthy Japanese population and cannot be directly applicable to our population.

There may be an ethnic difference between the insulin sensitivity and β-cell function relationship that should be thoroughly explored in healthy population samples to correctly establish the formula to calculate DI. It is generally considered that insulin secretory capacity is without much reserve in the Japanese population (5). Therefore, the β-cell compensation for increasing insulin resistance may not be fully accomplished, and as a result the relationship could be not hyperbolic but linear in the Japanese population. In addition, some doubt has been raised recently as to the hyperbolic relationship between insulin sensitivity and β-cell function (6). Since Caumo et al. did not kindly provide exact relationships between HOMA-S% and HOMA-B% in their samples (1), we would like to know whether their relationship would differ from ours.

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DOI: 10.2337/dc07-0016

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