Estimation of \( \beta \)-cell function from the data of the oral glucose tolerance test

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Sakaue S, Ishimaru S, Ikeda D, Ohtsuka Y, Honda T, Suzuki J, Kawakami Y, Ishii J, Nishimura M. Estimation of \( \beta \)-cell function from the data of the oral glucose tolerance test. Am J Physiol Endocrinol Metab 292: E1575–E1580, 2007. First published February 6, 2007; doi:10.1152/ajpendo.00341.2006.—Although a hyperbolic relationship between insulin secretion and insulin sensitivity has been shown, the relationship has been often questioned. We examined the relationship using oral glucose tolerance test (OGTT)-derived indexes. A total of 374 Japanese subjects who had never been given a diagnosis of diabetes underwent a 75-g OGTT. In subjects with normal glucose tolerance (NGT), the \( \ln \) [insulinogenic index (IGI)] was described by a linear function of \( \ln (x) \) (x, insulin sensitivity index) in regression analysis when the reciprocal of the insulin resistance index in homeostasis model assessment, Matsuda’s index, and oral glucose insulin sensitivity index were used as \( x \). Because the 95% confidence interval of the slope of the regression line did not necessarily include \(-1\), the relationships between IGI and \( x \) were not always hyperbolic, but power functions \( \text{IGI} \times \text{x}^n \) were a constant. We thought that \( \text{IGI} \times \text{x}^n \) was an appropriate \( \beta \)-cell function estimate adjusted by insulin sensitivity and referred to it as \( \beta \)-cell function index (BI). When Matsuda’s index was employed as \( x \), the BI values were decreased in subjects without NGT. Log BI had a better correlation with fasting plasma glucose (PG; FPG) and 2-h PG in non-NGT subjects than in NGT subjects. In subjects with any glucose tolerance, log BI was linearly correlated with 1-h PG and glucose spike (the difference between maximum PG and FPG). In conclusion, the relationship between insulin secretion and insulin sensitivity was not always hyperbolic. The BI is a useful tool in the estimation of \( \beta \)-cell function with a mathematical basis.

\( \beta \)-cell function index; insulinogenic index; Japanese

INSULIN SECRETION CAPACITY has been often assessed using the acute insulin response (AIR), which is the increment of plasma insulin concentration several minutes after intravenous glucose load and is an index of first-phase insulin secretion. As a surrogate of AIR, the insulinogenic index [IGI, the increment of serum insulin level divided by the increment of plasma glucose (PG) level for the first 30 min of the oral glucose tolerance test (OGTT)] (19) has been also used, because the IGI is correlated with AIR (10, 17).

However, we should note that insulin secretion is influenced by insulin sensitivity (8). There is a hyperbolic relationship between AIR and the insulin sensitivity index estimated by minimal model analysis (\( S_t \)) (9). This relationship implies a feedback system of insulin action to the \( \beta \)-cell. Therefore, \( \beta \)-cell function must be estimated in consideration of insulin sensitivity (2). The product of AIR and \( S_t \), called the disposition index (DI), has been used for an evaluation of \( \beta \)-cell function based on the constancy of their product due to the hyperbolic relationship (2). This index has been thought to express \( \beta \)-cell’s capacity to compensate for decreased insulin sensitivity.

For the same purpose of adjustment for the degree of insulin sensitivity, the other variables for insulin secretion and insulin sensitivity have been also used. In recent studies, the product of IGI and the reciprocal of the insulin resistance index in homeostasis model assessment (HOMA-IR) (16) was used for the estimation of \( \beta \)-cell function (7, 12). In addition, the feedback curve between the IGI and Matsuda’s insulin sensitivity index [ISI composite (ISIc), the index calculated from OGTT data and expressed insulin sensitivity] (15) was shown in obese children and adolescents (25), and the product was used for the estimation of \( \beta \)-cell function (24). Such OGTT-derived indexes may be useful for easier estimation of \( \beta \)-cell function for clinical or large-scale epidemiological applications because OGTT can be performed as a routine clinical test. However, the validity of using those indexes has not been adequately verified mathematically, although the use of the product of insulin secretion index and insulin sensitivity index must be based on the hyperbolic relationship between those indexes. Indeed, not all studies have shown the hyperbolic relationship between insulin secretion capacity and insulin sensitivity (4, 5). Thus the hyperbolic relationship between insulin secretion and insulin sensitivity is sometimes questioned (13).

The purpose of this study was to check the nature of the relationship between insulin secretion and insulin sensitivity by using indexes calculated from OGTT data. On the basis of the results, we proposed a method for the estimation of \( \beta \)-cell function from OGTT data. Using this method, we investigated the importance of \( \beta \)-cell function for determinants of fasting PG (FPG) levels and postchallenge PG levels in Japanese subjects.

METHODS

Subjects. Subjects recruited were individuals who had requested annual medical checkups (\( n = 134 \)) or those who agreed to be volunteers (\( n = 69 \)). Obese students of Hokkaido University who were called for a physical examination were also included in the study (\( n = 10 \)). Individuals who visited Hokkaido Hospital for Social Health Insurance to take further examinations due to high PG levels were also included (\( n = 161 \)). All of the participants had never been given a diagnosis of diabetes mellitus (DM). A total of 374 subjects under-
went a standard 75-g OGTT. Blood samplings were taken every 30 min to measure PG and serum insulin levels. Subjects were classified based on American Diabetes Association definitions (3, 21) as follows: normal glucose tolerance (NGT; FPG < 5.6 mmol/l and 2-h PG < 7.8 mmol/l), isolated impaired fasting glucose (iIFG; 5.6 ≤ FPG < 7.0 mmol/l and 2-h PG < 7.8 mmol/l), isolated impaired glucose tolerance (iIGT; FPG < 5.6 mmol/l and 7.8 ≤ 2-h PG < 11.1 mmol/l), IFG/IGT (5.6 ≤ FPG < 7.0 mmol/l and 7.8 ≤ 2-h PG < 11.1 mmol/l), and DM (FPG ≥ 7.0 mmol/l or 2-h PG ≥ 11.1 mmol/l). This study was approved by the Ethics Committee of Hokkaido University School of Medicine and carried out according to the Declaration of Helsinki. Written informed consent was obtained from the subjects.

Calculations. Glucose spike was defined as the difference between FPG and the maximum PG level during OGTT. As indexes of insulin sensitivity, we used the 1/HOMA-IR (16, 18), ISIc (15), ISIest (20), and oral glucose insulin sensitivity (OGIS) index (14). They were calculated using insulin and glucose values during OGTT, as follows: 1/HOMA-IR = 405/(FPG × fasting insulin; ISIc = 10,000/√[(fasting glucose) (fasting insulin); and ISIest = 0.226 – 0.0032 × BMI – 0.000645 × 2-h insulin – 0.0037 × 90-min PG, where BMI is body mass index (body weight/height, kg/m²). We used different units for glucose level and insulin level (mg/dl and μU/ml, respectively) for the calculation of HOMA-IR and ISIc than for ISIest (mmol/l and pmol/l, respectively). OGIS index was obtained using a spreadsheet downloadable from the web site (http://www.ladseb.pd.cnr.it/bioing/ogis.home.html). The IGI was calculated from OGTT data as IGI = (increment of insulin from 0 to 30 min)/(increment of glucose from 0 to 30 min). The units used for the calculation were same as those of HOMA-IR and ISIc. Eight subjects whose changes in PG or insulin level from 0 to 30 min during OGTT were 0 or below were deleted from the analysis.

Statistical analysis. Age, BMI, FPG, and 2-h PG were compared among the groups divided according to OGTT using ANOVA. Because IGI, each index of insulin sensitivity, and the index used for β-cell function in the present study had no normal distribution, the indexes were log-transformed to use ANOVA and the Tukey-Kramer method for comparison among the groups. Sex distribution was compared with the χ² test. The relationships between IGI and insulin sensitivity indexes were investigated using Pearson’s correlation coefficients and partial correlation coefficients. The values are expressed as means ± SD if not described. P < 0.05 was considered significant.

Table 1. Characteristics of subjects

<table>
<thead>
<tr>
<th></th>
<th>NGT</th>
<th>iIFG</th>
<th>iIGT</th>
<th>IFG/IGT</th>
<th>DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>149</td>
<td>52</td>
<td>18</td>
<td>62</td>
<td>85</td>
</tr>
<tr>
<td>Male/female</td>
<td>114/35</td>
<td>40/12</td>
<td>47/13</td>
<td>55/7</td>
<td>70/15</td>
</tr>
<tr>
<td>Age, yr</td>
<td>43 ± 14</td>
<td>50 ± 13*</td>
<td>47 ± 13</td>
<td>55 ± 9*</td>
<td>55 ± 9*</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>23.9 ± 4.3</td>
<td>25.1 ± 3.4</td>
<td>25.2 ± 6.0</td>
<td>26.4 ± 3.9*</td>
<td>25.8 ± 3.5*</td>
</tr>
<tr>
<td>FPG, mmol/l</td>
<td>4.9 ± 0.3*</td>
<td>5.9 ± 0.4†</td>
<td>5.1 ± 0.3†</td>
<td>6.2 ± 0.4†</td>
<td>7.7 ± 1.8*</td>
</tr>
<tr>
<td>2-h PG, mmol/l</td>
<td>5.9 ± 1.0†</td>
<td>6.3 ± 1.2†</td>
<td>9.1 ± 1.0†</td>
<td>9.3 ± 1.0†</td>
<td>14.6 ± 3.6*</td>
</tr>
<tr>
<td>I/HOMA-IR</td>
<td>1.03 ± 0.64†</td>
<td>0.69 ± 0.30†</td>
<td>0.90 ± 0.61†</td>
<td>0.53 ± 0.34*</td>
<td>0.44 ± 0.29*</td>
</tr>
<tr>
<td>ISIc</td>
<td>8.4 ± 4.4</td>
<td>5.8 ± 3.0*</td>
<td>5.8 ± 3.1</td>
<td>4.2 ± 2.6*</td>
<td>3.8 ± 2.1*</td>
</tr>
<tr>
<td>ISIest</td>
<td>0.13 ± 0.02†</td>
<td>0.12 ± 0.01†</td>
<td>0.11 ± 0.02†</td>
<td>0.10 ± 0.02†</td>
<td>0.09 ± 0.02*</td>
</tr>
<tr>
<td>OGIS</td>
<td>448 ± 49*</td>
<td>373 ± 42†</td>
<td>397 ± 46†</td>
<td>335 ± 42†</td>
<td>306 ± 41*</td>
</tr>
<tr>
<td>IGI</td>
<td>1.06 ± 1.01*</td>
<td>0.74 ± 0.70*</td>
<td>0.64 ± 0.36†</td>
<td>0.46 ± 0.32†</td>
<td>0.27 ± 0.27*</td>
</tr>
</tbody>
</table>

Values are means ± SD. The comparisons of age, body mass index (BMI), fasting plasma glucose (FPG), 2-h PG insulin sensitivity index composite (ISIc), and insulinogenic index (IGI) among the groups (NGT, normal glucose tolerance; iIFG, isolated impaired fasting glucose; iIGT, isolated impaired glucose tolerance; DM, diabetes mellitus) were performed using ANOVA and Tukey-Kramer tests. The sex-related rate was compared using the χ² test. The values of the reciprocal of the insulin resistance index in homeostasis model assessment (1/HOMA-IR), ISIc, ISIest, oral glucose insulin sensitivity (OGIS), and IGI were log-transformed at the analysis. *P < 0.05 compared with NGT, †P < 0.05 compared with DM.
data from the NGT subjects (n = 149). To check whether their relationship was hyperbolic, we performed linear regression analysis with ln (IGI) as the dependent variable and ln (x) as the independent variable. The results are summarized in Table 2. The relationship of ln (1/HOMA-IR) and ln (ISIc) with ln (IGI) fitted to a linear equation. The relationship of ln (OGIS) with ln (IGI) was also significant, but much weaker. The relationship between ln (ISIc) and ln (IGI) failed to have a significant correlation. Although the relationship between IGI and 1/HOMA-IR was statistically significant, the cause of this result may involve the possibility of a higher degree of an autocorrelation, because in both HOMA-IR and IGI, a main component is fasting insulin level. Accordingly, we used ISIc as an insulin sensitivity index for further analyses. The relationship was described by the equation ln (IGI) = −0.586 × ln (ISIc) + 0.881 (R² = 0.160, P < 0.001). The 95% confidence interval (CI) of the regression coefficient was −0.805 to −0.368; it did not include −1. Therefore, the relationship was not hyperbolic and was instead expressed by the equation IGI × (ISIc)0.586 = e0.881. This relationship is demonstrated in Fig. 1A.

Relationship between the results of OGTT and β-cell function. The relationship between IGI and ISIc of the non-NGT subjects is shown in Fig. 1B. The plotted points of the non-NGT subjects were placed at the lower left relative to those of NGT subjects. Even when plotted using 1/HOMA-IR and OGIS, the data revealed similar findings (data not shown). The shift of the plotted points indicates an impaired feedback system of insulin sensitivity to β-cells. We thought that those defects could be expressed by the decrease in the IGI × (ISIc)0.586. We defined these values, representing β-cell function as the β-cell function index (BI). The BI was compared among the groups classed by the results of OGTT (Fig. 2). The BI of the NGT group was 3.244 ± 3.262. The BI values were significantly decreased in all the groups with IFG (1.911 ± 2.118), iIGT (1.604 ± 0.711), and IFG/IGT (0.865 ± 0.450). There were significant differences in BI between groups with IFG and IFG/IGT. The BI of the DM group was significantly smaller than that of any other groups (0.491 ± 0.369).

Relationship between BI and PG levels and glucose spike. We further examined the association between PG levels during the OGTT and BI. Log-transformed BI was linearly correlated with FPG (r = −0.702, P < 0.001), 1-h PG (r = −0.860, P < 0.001), 2-h PG (r = −0.737, P < 0.001), and glucose spike (r = −0.834, P < 0.001) (Fig. 3). Although log IGI and log ISIc were also correlated with FPG, 1-h PG, 2-h PG, and glucose spike, the relationships were weaker than those between log BI and each PG level (Fig. 3).

Log BI had a better linear correlation with 1-h PG and glucose spike than with FPG and 2-h PG. This seemed to be because FPG and 2-h PG were almost unchanged visually as log BI fell in the range of high log BI values (Fig. 3). Accordingly, the same analysis was performed in subjects divided into NGT and non-NGT groups. In individuals with and without NGT, log BI had significant relationships with 1-h PG (NGT, r = −0.715; non-NGT, r = −0.804; both P < 0.001) and glucose spike (NGT, r = −0.629; non-NGT, r = −0.795; both P < 0.001). Although the correlation coefficients of log BI with FPG (r = −0.246, P = 0.002) and 2-h PG (r = −0.247, P = 0.002) were smaller in NGT subjects compared with those of log BI with 1-h PG or glucose spike, log BI had better correlations with FPG (r = −0.634, P < 0.001) and 2-h PG (r = −0.708, P < 0.001) in individuals without NGT (Fig. 4). Moreover, larger changes in FPG and 2-h PG were

![Fig. 1. A: relationship between insulin sensitivity and insulin secretion quantified as composite insulin sensitivity index (ISIc) and insulinogenic index (IGI), respectively, in subjects with normal glucose tolerance (NGT). The line shows the equation obtained from linear regression analysis of natural logarithm-transformed ISIc and IGI [IGI × (ISIc)0.586 = e0.881]. B: relationship between ISIc and IGI in non-NGT subjects. The lines show the same equations as in A; ○, isolated impaired fasting glucose (iIFG); △, isolated impaired glucose tolerance (iGTG); ×, IFG/IGT; ■, diabetes mellitus (DM).](http://ajpendo.physiology.org/)

![Fig. 2. The β-cell function index (BI) of the groups classed according to oral glucose tolerance test (OGTT). Each box expresses a range from the 25th to 75th percentiles, and the line in the box expresses a median. The error bar indicates a range from the 10th to 90th percentiles. The BI values were log-transformed to be compared using ANOVA followed by the Tukey-Kramer test. *P < 0.05 compared with the NGT group. †P < 0.05 compared with the DM group. The BI of the IFG/IGT group were also significantly smaller than those of the iIFG group.](http://ajpendo.physiology.org/)

Table 2. Relationship between IGI and each index of insulin sensitivity

<table>
<thead>
<tr>
<th></th>
<th>Slope (95% CI)</th>
<th>Intercept</th>
<th>R²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>I/HOMA-IR</td>
<td>−0.545 (−0.746, −0.344)</td>
<td>−0.366</td>
<td>0.163</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ISIc</td>
<td>−0.586 (−0.805, −0.368)</td>
<td>0.881</td>
<td>0.160</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ISIest</td>
<td>−0.791 (−1.715, 0.133)</td>
<td>−1.930</td>
<td>0.019</td>
<td>0.093</td>
</tr>
<tr>
<td>OGIS</td>
<td>−1.316 (−2.444, −0.188)</td>
<td>7.738</td>
<td>0.055</td>
<td>0.023</td>
</tr>
</tbody>
</table>

IGI and each index of insulin sensitivity were natural log-transformed and applied to linear regression analysis.
observed as the log BI decreased in non-NGT subjects more than in NGT subjects.

To confirm the association of β-cell function or insulin sensitivity with each PG level, we obtained partial correlation coefficients (Table 3). Log BI and log ISIc were significantly associated with FPG and 2-h PG in NGT subjects to a similar extent. However, in individuals without NGT, log BI had a robust association with FPG and 2-h PG, unlike log ISIc. Log BI was well correlated with 1-h PG and glucose spike, even in subjects with any glucose tolerance, unlike log ISIc.

**DISCUSSION**

We demonstrated the inverse relationship between IGI and some indexes of insulin sensitivity and found that it was expressed as a power function, but not necessarily a hyperbolic function, in Japanese NGT subjects. As shown in Fig. 1, the plotted points were placed at lower left in the non-NGT subjects. This finding indicated that β-cells could not compensate for decreased insulin sensitivity for maintaining normal glucose level. The BI that we proposed in the present study expressed this phenomenon, and the index indeed decreased in individuals without NGT. Those characteristics of BI resembled those of DI (8, 22). Recently, it was shown that FPG and 2-h PG rose more steeply when DI was decreased in the range of low DI than in the range of high DI (23). Our result (Fig. 4) was concordant with that finding. Thus we thought that the BI was a useful tool that could be derived from OGTT data for estimation of β-cell function. Although IGI is also a useful index for insulin secretion capacity, the use of BI is more reasonable for the estimation of β-cell function because this index implies the feedback system of insulin sensitivity to β-cells. In addition, BI was better correlated with PG than IGI. However, to be exact, BI must be compared with standard DI in the same subjects.

The relationships between IGI and some insulin sensitivity indexes were not hyperbolic in the present study, differing from that between AIR and SI as previously shown in a Caucasian population (9). One of the reasons for the discrepan-

![Fig. 3. Correlation of log ISIc, log IGI, and log BI with fasting plasma glucose (FPG), 1-h PG, 2-h PG, and glucose spike in all subjects. The Pearson’s correlation coefficient (r) is shown for each relationship. All correlations were statistically significant.](image)

**Table 3. Correlation analysis of the association between plasma glucose level or glucose spike and β-cell function or insulin sensitivity**

<table>
<thead>
<tr>
<th></th>
<th>Partial Correlation Coefficient</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>NGT subjects</td>
</tr>
<tr>
<td>log BI</td>
<td>log ISIc</td>
</tr>
<tr>
<td>FPG</td>
<td>−0.225*</td>
</tr>
<tr>
<td>1-h PG</td>
<td>−0.735</td>
</tr>
<tr>
<td>2-h PG</td>
<td>−0.257*</td>
</tr>
<tr>
<td>spike</td>
<td>−0.664</td>
</tr>
</tbody>
</table>

Two kinds of analyses were performed according to subjects. One included only NGT subjects, and the other included subjects without NGT. P values of all partial correlation coefficients are statistically significant (*P < 0.01; P < 0.001 for all other values).
ancy may be the difference in ethnicity. Because it is known that the insulin secretion capacity of Japanese populations is smaller than that of Caucasians (6), the relationship between insulin secretion and insulin sensitivity is likely different among ethnicities. Even if there is a hyperbolic relationship between AIR and SI in the Japanese population, the difference in the indexes used in this study may account for the nonhyperbolic relationship. Unless employed insulin sensitivity indexes are proportional to minimal model-derived SI, they may no longer have a hyperbolic relationship even with AIR (4, 13).

Insulin sensitivity indexes used in the present study are probably correlated with SI, but they may not be correlated proportionally. Accordingly, when the relationship between insulin secretion and insulin sensitivity is considered with any index, it should be evaluated in the appropriate control population. The relationship may be generalized into the power function $y = k \times x^{-\alpha}$ ($x$, insulin sensitivity; $y$, insulin secretion) (13) rather than hyperbolic, although it is unknown whether this is the best regression equation. We determined $\alpha$ when IGI and separate insulin sensitivity indexes were used in Japanese NGT subjects in the present study. However, the $R^2$ value was low in the present study. Further study is necessary to confirm the reproducibility of this relationship in other populations.

Only when $\alpha$ is not different from 1, can $x \times y$ be used as a DI-like index for the estimation of $\beta$-cell function. Although the simple product of insulin secretion index and insulin sensitivity index obtained from different variables has often been used for the estimation of $\beta$-cell function without the correct confirmation about the validity, our results suggested that such a product has no mathematical basis. The relationship between IGI and OGIS was investigated, the 95% CI of $-\alpha$ included $-1$, suggesting that the use of IGI $\times$ OGIS was acceptable. We think that the use of BI ($x^{\alpha} \times y$) is proper for the correct estimation of $\beta$-cell function, as previously pointed out (13). However, $x \times y$ might be available for easy and relative comparison of $\beta$-cell function, because there is only a difference in $\alpha$, 1 or not. In our subjects, $x \times y$ (HOMA-IR and IGI $\times$ ISIc) had a similar trend in results compared with those using BI (data not shown).

Among the insulin sensitivity indexes employed in the present study, the relationships of 1/HOMA-IR and ISIc with IGI better fitted to power functions. Although all the indexes and SI were demonstrated to correlate with the euglycemic insulin sensitivity indexes are proportional to minimal model-derived SI, they may no longer have a hyperbolic relationship even with AIR (4, 13). Insulin sensitivity indexes used in the present study are probably correlated with SI, but they may not be correlated proportionally. Accordingly, when the relationship between insulin secretion and insulin sensitivity is considered with any index, it should be evaluated in the appropriate control population. The relationship may be generalized into the power function $y = k \times x^{-\alpha}$ ($x$, insulin sensitivity; $y$, insulin secretion) (13) rather than hyperbolic, although it is unknown whether this is the best regression equation. We determined $\alpha$ when IGI and separate insulin sensitivity indexes were used in Japanese NGT subjects in the present study. However, the $R^2$ value was low in the present study. Further study is necessary to confirm the reproducibility of this relationship in other populations.

When the relationship between insulin secretion and sensitivity is assessed, both indexes must be as independent as possible. The independency of IGI and OGTT-derived insulin sensitivity indexes may not necessarily be as strong as that of AIR and SI. For instance, all the calculations of HOMA-IR, ISIc, OGIS index, and IGI include fasting insulin level. Because OGIS is a model-based index and IGI is an empirical index, the combination of these two indexes may be more independent in the points of methods by which the indexes were obtained. However, we do not think that only a weak independency causes the relationships between IGI and ISIc, because their relationship with the power function is not self-evident mathematically.

On the basis of the validity of BI, we indicated two findings. First, BI was better correlated with FPG and 2-h PG than insulin sensitivity in non-NGT subjects, whereas the associations of both BI and insulin sensitivity with FPG and 2-h PG were of a similar extent in NGT subjects. Our result suggested that there is a difference in the main determinant of FPG and 2-h PG levels according to the stages of glucose tolerance and that the status of glucose tolerance was associated with impaired $\beta$-cell function rather than decreased insulin sensitivity. Second, log BI had good linear correlations with 1-h PG and glucose spike at every stage of glucose tolerance. To the best of our knowledge, the relationship between 1-h PG and $\beta$-cell function has not been documented. Our findings suggested that 1-h PG is a good index of deteriorated $\beta$-cell function.

The correlation per se between BI and each PG level or glucose spike may have a risk of autocorrelation, because the calculation of BI included each PG value. However, we accentuate the difference in degree of correlation, that is, correlation coefficient, between NGT and non-NGT subjects. This suggests the importance of $\beta$-cell dysfunction in developing glucose intolerance. Furthermore, we think it is noteworthy that there were differences in the degree of the correlation with BI among PG values during OGTT.

In conclusion, the relationship between insulin secretion and insulin sensitivity was not always hyperbolic. BI is a useful method for the estimation of $\beta$-cell function with a mathematical basis. Using the BI, we demonstrated that the association of $\beta$-cell function with FPG and 2-h PG is closer than insulin sensitivity as glucose intolerance develops. In addition, $\beta$-cell function is more strongly correlated with 1-h PG and glucose spike than insulin sensitivity throughout the stages of glucose tolerance. Further studies in other populations are necessary to establish the validity of the use of BI.

REFERENCES


