

SUPPLEMENTARY DATA

Following the analytical approach suggested by Nagasaka et al[1], the calculation of the OGTT-derived surrogate of GE is based on the calculation of three parameters:

1. Post load plasma glucose without insulin / without GE [PGwoI/GE]

$$\text{Post load plasma glucose}_{(mg/dl)} = \text{FPG}_{(mg/dl)} + [0.75 * 75000] / [0.19 * \text{body weight}_{(kg)} * 10]$$

0.75 is the absorption rate of the oral glucose load, 75000 is the glucose load in mg and $0.19 * \text{weight} * 10$ represents the glucose space in dl[2, 3].

The glucose space may be modified by lean body mass which can be assessed better with BMI yet the high correlation of weight and BMI in this cohort ($r=0.88$, $p<0.001$) suggests that body weight is a reliable measure for this calculation

2. Post load plasma glucose without insulin/ with GE [PGwoI/wGE]

This is calculated based on the relation of the oral disposition index (oDI) and the 2-hr plasma glucose on the OGTT. The oDI is the product of whole body insulin sensitivity (calculated using the Matsuda index) and the acute insulin response (the insulinogenic index). In contrast to Nagasaka et al who used 3 time points to calculate the Matsuda index, we used 7 points of the OGTT. We have previously shown that in this study population, a hyperbolic relation indeed exists between these two parameters[4]. The equations for the linear regressions the oDI and 2-hr plasma glucose in this cohort are as follows:

$$\text{NGT: 2-hr Glucose} = 133.01 - 24.22 * \text{Log}(oDI)$$

$$\text{IGT/IFG: 2-hr Glucose} = 160.05 - 19.14 * \text{Log}(oDI)$$

$$\text{T2DM: 2-hr Glucose} = 241.17 - 34.19 * \text{Log}(oDI)$$

In order to calculate 2-hr plasma glucose without insulin/with GE, the oDI should be theoretically zero yet upon log transformation – this value is indefinite. We used the minus 3 standard deviations of log (oDI), which in this dataset was equal to -1.15, for these equations (3 subjects with T2DM had a value below this threshold). The corresponding plasma glucose values achieved using these calculations were 160.85, 184.79 and 280.76 mg/dl for NGT, IGT/IFG and T2DM respectively.

3. Expected 2-hr plasma glucose [2hrPG_{exp}]

This is calculated by inserting the individual $\log_{10}(oDI)$ values into the equations described in section 2 above. This allows calculation of the ratio of actual 2-hr glucose/expected 2-hr glucose. This ratio within each glucose tolerance category is greater if GE is lower and vice versa.

4. Calculation of glucose effectiveness

$$\text{GE (mg/dl per min)} = \{ \text{PGwoI/GE} - [\text{PGwoI/wGE}] * (2\text{hrPG}/2\text{hrPG}_{\text{exp}}) \} / 120$$

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1. Nagasaka, S., et al., *Index of glucose effectiveness derived from oral glucose tolerance test*. Acta Diabetol, 2012. **49 Suppl 1**: p. S195-204.
2. Cederholm, J. and L. Wibell, *Evaluation of insulin release and relative peripheral resistance with use of the oral glucose tolerance test: a study in subjects with normoglycaemia, glucose intolerance and non-insulin-dependent diabetes mellitus*. Scand J Clin Lab Invest, 1985. **45(8)**: p. 741-51.
3. Soonthornpun, S., et al., *Novel insulin sensitivity index derived from oral glucose tolerance test*. J Clin Endocrinol Metab, 2003. **88(3)**: p. 1019-23.
4. Weiss, R., et al., *Ethnic differences in beta cell adaptation to insulin resistance in obese children and adolescents*. Diabetologia, 2006. **49(3)**: p. 571-9.