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Revised Concept for the Estimation of Insulin Sensitivity From a Single Sample

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Insulin resistance is common in the general population and is related to glucose intolerance, dyslipidemia, and high blood pressure. Accurate and reproducible methods for measuring insulin sensitivity in vivo, such as the euglycemic clamp or the minimal model procedure, require trained personnel and are rather expensive [1]. There is undoubtedly a need for simpler tests, especially in the field of large epidemiological studies. The circulating level of insulin has been widely used as a surrogate for insulin sensitivity, since a high plasma insulin concentration is supposed to reflect a state of insulin resistance, when the insulin-glucose feedback is considered. Different indexes have been proposed from baseline values of plasma insulin and glucose. Actually, there is a paradox concerning this approach, since both the product of fasting insulin and fasting glucose and their ratio are found to be correlated with insulin sensitivity. Recently, Kahn et al. [2] supported the concept that a hyperbolic relationship existed between fasting insulin and insulin sensitivity. Such a relationship could be described by a formula on the model of insulin sensitivity (S_I) = a/insulin (I), where the coefficient a would be a constant. Therefore, the general ratio a/I could be proposed as a new index of insulin sensitivity.

First, we tried to determine a value for coefficient a. A sample of 70 subjects (22 normal subjects who had participated as control subjects in previous metabolic studies, and 48 overweight patients; age 11-73 years, BMI 17-43 kg/m^2, female/male ratio 1:1) was randomly selected from a file of patients who performed an intravenous glucose tolerance test for calculation of S_I by the minimal model, as previously described [3,4]. They represented the whole range of S_I values (0.01-25 10^{-4} min^{-1} [centered dot] [micro U/ml]$^{-1}$). All subjects were nondiabetic, control subjects had normal glucose tolerance, and 21 overweight patients were glucose intolerant, according to World Health Organization criteria. Plasma insulin was assayed by the Bi-Insulin immunoradiometric assay kit (ERIA-Diagnostics Pasteur, Marnes la Coquette, France), which shows excellent performance characteristics in terms of sensitivity

(0.2 micro U/ml) and reproducibility and does not cross-react with proinsulin. Plasma glucose was measured by the glucose oxidase method (Beckman, Palo Alto, CA).

The best-fit relationship was described by S_I (10^{-4} min ($^{-1}$) [centered dot] (micro U/ml)$^{-1}$ x I (micro U/ml) = 39.65 ($r = 0.880$, $P < 0.0001$), i.e., S_I x I = [approximately] 40.

Second, a separate sample of 49 subjects (14 normal subjects and 35 overweight patients; age 19-62 years, BMI 19-41.5 kg/m^2) was built on the same criteria to compare the accuracy of four indexes in the assessment of insulin sensitivity: the well-known HOMA-R (homeostatis model assessment, defined as the product of fasting insulin and fasting glucose divide by 22.5) [5], fasting insulin, the ratio of fasting insulin to fasting glucose (I/G), and the above-defined ratio 40/I. The statistical analysis was performed using the SigmaStat package (Jandel Scientific, Erkrath, Germany). The index 40/I gave a better prediction of minimal model-derived S_I ($r = 0.882$, $P < 0.0001$, Figure 1) than did HOMA-R ($r = 0.546$, $P < 0.01$), fasting insulin ($r = 0.589$, $P < 0.01$), and I/G ($r = 0.597$, $P < 0.01$). Fasting glucose was not correlated to S_I ($r = 0.09$, NS).

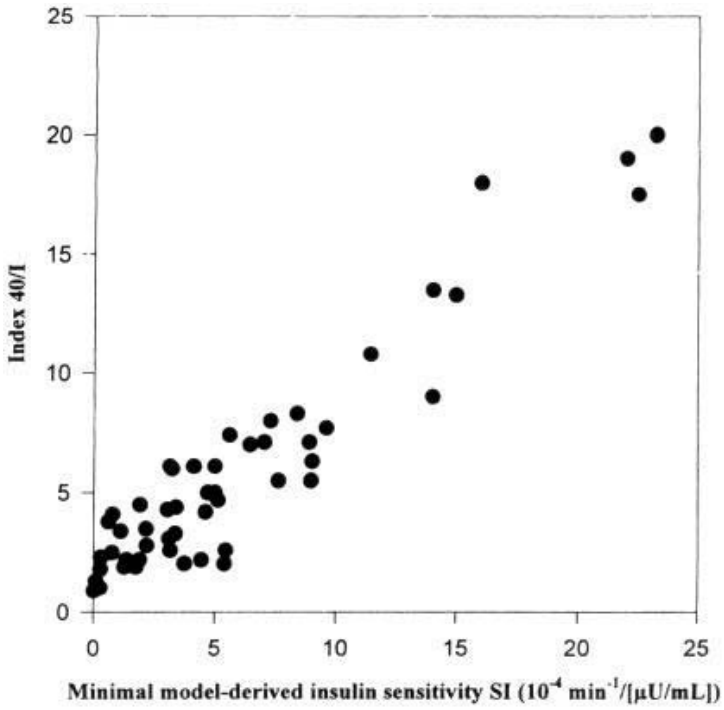

Figure 1. Correlation between S_I and the index 40/I. $n = 49$, $r = 0.882$, $P < 0.0001$.

In conclusion, the ratio 40/I, with methods and units used in this study, proved to be a more precise marker of insulin sensitivity than the fasting value of insulin recommended by epidemiologists. Nevertheless, further studies are needed to validate this measure in other populations.

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