

## LETTER TO EDITOR

# CONCERNING THE VALIDITY OF THE "FIRI" INSULIN RESISTANCE INDEX

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Since Duncan *et al.* [1] recently proposed a new fasting insulin resistance index (FIRI, fasting glucose  $\times$  fasting insulin/25), conflicting reports have successively described it as a poor or a fair estimation of insulin sensitivity [2, 3]. We read with great interest the contribution of Bastard *et al.* about FIRI [4] and totally agree with their final conclusions. FIRI seems to be a reasonable surrogate measurement of insulin sensitivity, as assessed by the euglycaemic clamp technique and the minimal model procedure. It would be useful for large clinical or epidemiological studies. Nevertheless, it was rather surprising that the negative relationship between  $\log_{10}$ FIRI and insulin-mediated glucose disposal was less significant when insulin was assayed by the Bi-Insulin IRMA kit (ERIA-Diagnostics Pasteur, France). We have had technical and clinical experience with this assay, which shows excellent performance characteristics in terms of sensitivity, reproducibility and accuracy, and does not cross-react with proinsulin.

Since radioimmunoassay is still the reference method for peptide hormones, we compared Bi-insulin IRMA with a competitive radioimmunoassay (Insik-5, Sorin Biomedica, Italy). FIRI and the minimal model-derived parameters of glucose assimilation were measured in 49 individuals (normal subjects, who participated as controls in metabolic studies, and overweight patients; mean age 35 years, range 19-62; body mass index 32, range 19-41.5 kg/m<sup>2</sup>). Minimal model analysis of the frequently sampled intravenous glucose tolerance test provided an estimation of insulin sensitivity (SI) and glucose effectiveness (S<sub>G</sub>). The basal insulin component of S<sub>G</sub> (BIE) was calculated as the product of basal insulin and SI. The contribution of the non-insulin-dependent component (S<sub>G</sub> at zero insulin,

GEZI) was the difference between total S<sub>G</sub> and BIE [5]. This analysis also allowed estimation of insulin- and non-insulin-mediated glucose uptake (IMGU and NIMGU, respectively) [6].

Ln FIRI was negatively correlated with SI ( $r = -0.79$ ,  $p < 0.0001$ ; see the figure), BIE ( $r = -0.64$ ,  $p < 0.0001$ ) and IMGU ( $r = -0.41$ ,  $p = 0.004$ ), but not with GEZI and NIMGU. The relationship between Ln FIRI and SI was less significant when insulin was assayed with the Insik-5 kit ( $r = -0.61$ ,  $p = 0.001$ ), which is less sensitive than Bi-Insulin IRMA (detection limit 4  $\mu$ U/ml vs 0.2  $\mu$ U/ml) and has significant cross-reaction with proinsulin. It is noteworthy that there was a strong negative relationship between Ln FIRI and SI when plasma

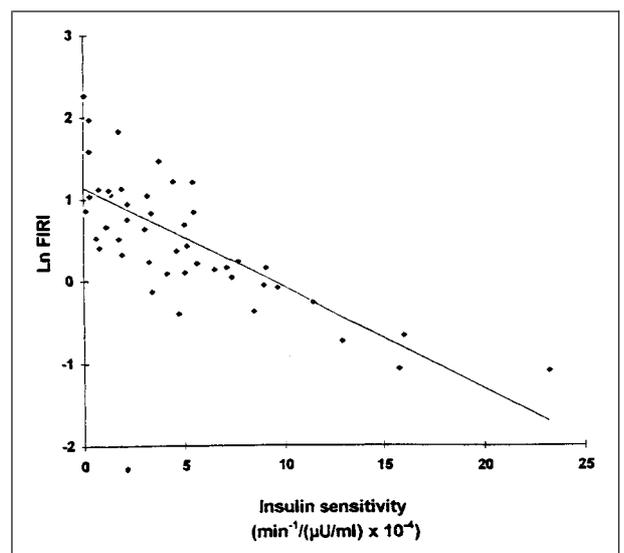


FIG. 1. Correlation between fasting insulin resistance index (FIRI) and insulin sensitivity (SI) in 49 individuals ( $r = 0.79$ ,  $p < 0.0001$ ). Insulin was measured by an immunoradiometric assay (Bi-insulin IRMA, ERIA-Diagnostics Pasteur, France).

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insulin was measured with the Bi-Insulin IRMA kit. The reason for the discrepancy between this result and that of Bastard *et al.* is not very apparent. We believe that it is not a question of direct or indirect techniques for the estimation of insulin action. Most of the differences between studies on this topic are due to cross-reactivity of conventional assays with proinsulin and its split/des-amino products, which cannot provide an explanation in this case. Within-run or run-to-run reproducibility might account for the observed variation.

In conclusion, it should be noted that the choice of an insulin assay is a major determinant of the validity of FIRI, and that analytical variation needs to be carefully controlled.

Yours sincerely.

## REFERENCES

- 1 Duncan MH, Singh BM, Wise PH, Carter G, Alagband-Zadeh J. A simple measure of insulin resistance. *Lancet*, 1995, 346, 120-21.
- 2 Del Prato S, Pozzilli P. FIRI: fasting or false insulin resistance index ? *Lancet*, 1996, 347, 132.
- 3 Cleland SJ, Petrie JR, Morris AD, Ueda S, Dorrian CA, Connell JMC. FIRI: a fair insulin resistance index ? *Lancet*, 1996, 347, 770.
- 4 Bastard JP, Grimaldi A, Jardel C, Porquet D, Bruckert E, Hainque B. A simple index of insulin resistance. *Diabetes Metab*, 1997, 23, 87-88.
- 5 Brun JF, Guinrand-Hugret R, Boegner C, Bouix O, Orsetti A. Influence of short-term submaximal exercise on parameters of glucose assimilation analyzed with the minimal model. *Metabolism*, 1995, 44, 833-40.
- 6 Welch S, Gebhart SSP, Bergman RN, Phillips LS. Minimal model analysis of intravenous glucose tolerance test-derived insulin sensitivity in diabetic subjects. *J Clin Endocrinol Metab*, 1990, 71, 1508-18.