Table 1. Estimated Insulin Sensitivity, Metabolic Clearance Rates, and β-Cell Function Indexes in BLSA Subjects With Fasting Euglycemia

Time Points	Insulin Sensitivity Index (μmol · kg^{-1} · min^{-1} · pmol/L)			Metabolic Clearance Rate (mL · kg^{-1} · min^{-1})		
	Normal	Impaired	Diabetic	Normal	Impaired	Diabetic
2-hour plasma glucose						
0, 120 or 0, 60, 120	0.10 ± 0.003	0.08 ± 0.004 (<.001)	0.06 ± 0.006 (<.001)	8.85 ± 0.23	6.81 ± 0.31 (<.001)	5.44 ± 0.49 (<.001)
0, 30	0.09 ± 0.003	0.09 ± 0.003	0.09 ± 0.004	8.06 ± 0.25	7.78 ± 0.23	7.64 ± 0.32
0, 30, 60	0.01 ± 0.004	0.08 ± 0.003 (<.05)	0.08 ± 0.005 (<.05)	8.37 ± 0.27	7.29 ± 0.25 (<.05)	6.74 ± 0.35 (<.05)
0, 120* or 0, 60, 120*	0.20 ± 0.001	0.19 ± 0.005 (<.01)	0.19 ± 0.008 (<.05)	16.3 ± 0.12	14.5 ± 0.29 (.001)	13.4 ± 0.46 (<.001; <.05)
0, 30*	0.20 ± 0.002	0.2 ± 0.002	0.2 ± 0.002	17.2 ± 0.15	17.1 ± 0.11	17.3 ± 0.15
0, 30, 60*	0.20 ± 0.002	0.19 ± 0.002 (<.01)	0.18 ± 0.003 (<.05)	16.9 ± 0.15	16.2 ± 0.15 (<.01)	15.8 ± 0.21 (<.01)
	Estimated β-Cell Function					
	First Phase (pmol/L)			Second Phase (pmol/L)		
2-hour plasma glucose						
0, 120	1,020 ± 58	807 ± 83	300 ± 119 (<.001; <.01)	264 ± 12	209 ± 25	76 ± 37 (<.01; <.001)
0, 60, 120	998 ± 71	759 ± 87	360 ± 98 (<.001)	266 ± 17	215 ± 21	124 ± 24 (<.01)
0, 30, or 0, 30, 60	878 ± 55	707 ± 83	420 ± 82 (<.01)	238 ± 13	207 ± 19	146 ± 19 (<.05)
0, 120*	282 ± 49	44 ± 79 (<.05)	−486 ± 113 (<.001;<.001)	122 ± 10	62 ± 24 (<.05)	−75 ± 36 (<.001; <.001)
0, 60, 120*	438 ± 62	184 ± 79 (<.05)	−207 ± 89 (<.001; <.05)	161 ± 15	108 ± 20	18 ± 21 (<.001)
0, 30* or 0, 30, 60*	880 ± 55	709 ± 83	422 ± 82 (<.01)	238 ± 13	207 ± 19	146 ± 19 (<.05)

NOTE. *P* values are shown in parentheses; the first number denotes statistically significant difference compared to subjects with normal glucose tolerance and the second number denotes statistically significant difference compared to subjects with impaired 2-hour plasma glucose levels.
*Inclusion of demographic parameters (age and BMI) in model.

$0.800 \times \mathrm{Ins}_0 - 42.79 \times \mathrm{Gluc}_{120} + 0.321 \times \mathrm{Ins}_{120} + 5.338 \times \mathrm{BMI}$) should be utilized with just the 2 end points of the OGTT (fasting and 2-hour glucose and insulin plasma levels) in lieu of frequently unavailable and cumbersome clamp studies. Its simplicity and superiority over other OGTT-derived indices of insulin sensitivity, especially the HOMA, in early detection of subtle differences in ISI, MCR, and most importantly β-cell function, renders this equation an ingenious and practical epidemiological tool in the hands of the clinical diabetes researcher.

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Commentary

To the Editor:

In 2000,[1] we reported equations based on plasma insulin and glucose values obtained during standard oral glucose tolerance tests (OGTT) in individuals with normal or impaired glucose tolerance produced estimates of β-cell function and insulin sensitivity which were reasonably well correlated ($r \sim 0.78$) with those obtained from hyperglycemic and euglycemic-hyperinsulinemic clamps performed in the same individuals. These results suggested that measurements of plasma glucose and insulin levels during OGTTs might be useful surrogates for clamp experiments.

Clamp procedures are considered the "gold standard" for assessing β-cell function and insulin sensitivity because they permit responses to identical stimuli to be measured, eg, the plasma insulin response at a specific plasma glucose level and the glucose infusion rate at a specific plasma insulin-glucose level.[2,3] However, since these clamp procedures are time-consuming, labor-intensive, and require trained personnel, they are not particularly well suited for large epidemiologic studies or routine clinical practice. Consequently, many investigators have sought simpler approaches using either fasting plasma glucose − insulin levels or those obtained at various times during the OGTT as a surrogate for these clamps.[4-7]

A year after our original publication, we reported equations using various combinations of different sampling times for insulin and glucose during the OGTT to assess β-cell function and insulin sensitivity in response to inquiries from investigators who had data from sampling times other than those previously reported[8]: these equations produced estimates of β-cell function and insulin sensitivity that were still reasonably well correlated with clamp estimates (eg, correlation coefficients ranging from 0.62 to 0.78).

Theodorakis et al have applied some of these equations to data obtained as part of the Baltimore Longitudinal Study on Aging which not only included individuals with normal or impaired glucose tolerance as in our original report but also those individuals with type 2 diabetes. Their results indicate that use of plasma glucose and insulin values from as few as 2 sampling points (eg, 0 and 120 minutes) could detect significant differences in β-cell function (both first- and second-phase insulin release) and insulin sensitivity (metabolic clearance rate) not only between individuals with normal glucose tolerance and those with either impaired glucose tolerance and type 2 diabetes, but also,

more importantly, between those with impaired glucose tolerance and type 2 diabetes.

The results of Theodorakis et al are also important in that they also confirm prior observations based on clamp experiments[9] that both β-cell function and insulin sensitivity are reduced in individuals with impaired glucose tolerance and that both deteriorate further in individuals with type 2 diabetes. The significance of this concordance in results from clamp OGTT data is that it suggests that simple use of plasma glucose and insulin values obtained from OGTTs may have the sensitivity to detect modest changes in insulin sensitivity and beta cell function previously thought to be possible only with clamp studies.

Thus the data of Theodorakis et al suggest that OGTT data may provide useful information for the epidemiologist and clinician regarding alterations in β-cell function and insulin sensitivity, who do not have the resources to perform clamp studies.

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