Quantitative Insulin Sensitivity Check Index and the Reciprocal Index of Homeostasis Model Assessment in Normal Range Weight and Moderately Obese Type 2 Diabetic Patients

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OBJECTIVE — To investigate whether the quantitative insulin sensitivity check index (QUICKI) and the reciprocal index of homeostasis model assessment (1/HOMA-IR) derived from fasting plasma glucose and insulin level are excellent surrogate indices of insulin resistance in both normal range–weight and moderately obese type 2 diabetic and healthy subjects.

RESEARCH DESIGN AND METHODS — The association between QUICKI or 1/HOMA-IR and insulin resistance index assessed by euglycemic-hyperinsulinemic clamp (clamp-IR) was investigated in 121 type 2 diabetic and 29 healthy subjects recruited from among 120 (age 55 ± 11, 48 ± 15, and 52 ± 15 years [means ± SD], respectively). Type 2 diabetic subjects were divided into groups of 76 normal range–weight and 45 moderately obese subjects (BMI 21.4 ± 2.3 vs. 27.2 ± 2.2 kg/m^2, $P < 0.0001$).

RESULTS — QUICKI and 1/HOMA-IR were significantly lower in the moderately obese group than in the normal range–weight type 2 diabetic and healthy groups ($n = 120$) (QUICKI, 0.338 ± 0.030, 0.371 ± 0.037, and 0.389 ± 0.041, respectively, $P < 0.0001$; 1/HOMA-IR, 0.50 ± 0.33, 0.92 ± 0.55, and 1.24 ± 0.82, $P < 0.0001$). QUICKI was strongly correlated with clamp-IR in normal range–weight, moderately obese type 2 diabetic, and healthy subjects ($r = 0.641$, 0.570, and 0.502, respectively; all subjects, $r = 0.608$, $P < 0.01$) and 1/HOMA-IR exhibited correlations comparable to those of QUICKI with clamp-IR ($r = 0.637$, 0.530, and 0.461, respectively; all subjects, $r = 0.589$, $P < 0.001$). In multiple regression models including QUICKI or 1/HOMA-IR as an independent variable, the estimation formula accounted for 55% of the variability of clamp-IR for the group of all type 2 diabetic subjects ($R^2 = 0.547$ and 0.551, respectively, $P \leq 0.0001$).

CONCLUSIONS — QUICKI and 1/HOMA-IR were highly correlated with clamp-IR, with comparable coefficients in both normal range–weight and moderately obese type 2 diabetic patients and nondiabetic subjects. The latter can probably be applied clinically in view of its convenience.

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Abbreviations: FIRI, fasting immunoreactive insulin; FPG, fasting plasma glucose; HOMA, homeostasis model assessment; HOMA-IR, HOMA of insulin resistance; 1/HOMA-IR, reciprocal of HOMA-IR; OHA, oral hypoglycemic agent; QUICKI, quantitative insulin sensitivity check index; SSPI, steady-state plasma insulin.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Insulin resistance might play an important role in hyperglycemia in type 2 diabetes, which eventually induces the development of diabetic microangiopathy (1). To achieve excellent glycemic control to prevent these complications, several oral hypoglycemic agents (OHAs) that improve insulin resistance (such as thiazolidinediones and biguanides) have been developed and are available clinically (2,3). Furthermore, insulin resistance is proposed to play important roles in the pathogenesis of cardiovascular diseases (4), the most common cause of death in diabetic patients. Therefore, it is important clinically and epidemiologically to evaluate insulin resistance simply and accurately in individual diabetic patients.

The euglycemic-hyperinsulinemic clamp, the gold standard technique for estimation of insulin resistance, is accurate but complex and laborious enough that it is not practical for evaluation of a large number of type 2 diabetic patients or populations at risk for insulin resistance (5). Many investigators have studied simple surrogate indices of insulin resistance in comparison with the index assessed by euglycemic-hyperinsulinemic clamp (clamp-IR); for example, fasting plasma insulin (6), homeostasis model assessment (HOMA) of insulin resistance (HOMA-IR) (7), and the fasting glucose–to–insulin ratio (8). It has been established that HOMA-IR is a useful surrogate index of insulin resistance in diabetic and nondiabetic subjects and that its logarithmic transformation makes it more accurate (9–11). Recently, Katz and colleagues (12,13) proposed that the quantitative insulin sensitivity check index (QUICKI) derived from logarithmic-transformed fasting plasma glucose (FPG) and insulin levels is an excellent index of insulin resistance in comparison with clamp-IR in a study of mainly nondiabetic subjects. Another in-

vestigator subsequently reported the low validity of QUICKI in nonobese nondiabetic subjects (14), and there are recent controversial reports concerning the validation of QUICKI in evaluating changes in insulin resistance during exercise training (15,16). To date, no reports are available on the validity of QUICKI in type 2 diabetic patients with a wide range of obesity.

The aim of the present study was to investigate whether QUICKI is a simple surrogate index of insulin resistance in both moderately obese and normal range weight type 2 diabetic and nondiabetic subjects in comparison with clamp-IR. The second aim was to compare the validity of the reciprocal index of HOMA (1/HOMA-IR) with that of QUICKI to obtain an index that can be more easily determined in clinical practice.

RESEARCH DESIGN AND METHODS

We selected 121 type 2 diabetic subjects, 81 men and 40 women, participating in diabetes education programs from among patients attending our diabetes center at Osaka City University Hospital. The diagnosis of diabetes was based on a previous history of diabetes or on the American Diabetes Association criteria (17). The diabetic subjects treated with any insulin therapy were excluded because fasting plasma insulin level, an essential component for the calculation of the QUICKI or HOMA as described below, may be affected by insulin therapy. The means (±SD) of age and duration of diabetes of type 2 diabetic subjects were 52.4 ± 12.7 and 8.4 ± 7.2 years, respectively. The BMI of type 2 diabetic subjects ranged from 14.6 to 34.3 kg/m^2, with a mean of 23.6 ± 3.6. Our diabetic underweight and normal range–weight subjects were defined as the normal range–weight group (BMI <25.0 kg/m^2), and preobese and class 1 obese subjects as the moderately obese group (BMI ≥25.0), according to the criteria of the World Health Organization (18,19). Fifty-six diabetic subjects were treated with sulfonylureas, 5 with α-glucosidase inhibitors, 12 with a combination of sulfonylureas and α-glucosidase inhibitors, and 48 with medical nutritional therapy alone. Uremic subjects with serum creatinine levels >176.8 μmol/l and other active medical diseases were excluded.

Another 120 apparently healthy subjects, 80 men and 40 women, participating in the health check program were also included for data analysis of QUICKI and HOMA as a control group. The age and BMI of healthy subjects ranged from 17 to 75 with a mean of 52.0 ± 15.3 years, and from 17.3 to 35.2 with a mean of 22.8 ± 2.6 kg/m^2, respectively. Informed consent was obtained from all participants in the present study, and the study that included the clamp protocol was approved by the local ethics committee.

Study design

After admission, all subjects were under medical nutritional therapy (energy 25–30 kcal/kg ideal body wt), and a clamp-IR was performed within 1–2 weeks after admission as described below. Oral hypoglycemic agents were taken until the day before the clamp study. After a 12-h overnight fast, a fasting blood sample was taken for the determination of FPG and fasting immunoreactive insulin (FIRI).

Of the 120 healthy subjects, 29 who gave informed consent for further participation in the clamp study were enrolled in the same clamp protocol as the diabetic subjects.

Plasma glucose levels were measured by the glucose oxidase method, HbA_{1c} by high-pressure liquid chromatography (normal range 4.0–5.8%), and plasma insulin levels by immunoradiometric assay (Insulin Riabead II kit; Dainabot, Tokyo). Serum creatinine, serum total cholesterol, triglyceride, HDL cholesterol, and free fatty acid levels were measured by enzymatic methods adapted to an autoanalyzer (Hitachi 7450; Hitachi, Tokyo).

Methods

QUICKI, HOMA-IR, and 1/HOMA-IR

QUICKI was calculated from FPG and FIRI levels according to the report by Katz et al. (12) with the formula QUICKI = 1/(log [FIRI in mU/l] + log [FPG in mg/dl]). The HOMA-IR was calculated from FPG and FIRI according to the report by Matthews et al. (7) with the formula HOMA-IR = FIRI in mU/l × FPG in mg/dl/405. 1/HOMA-IR was also calculated. To evaluate the reproducibility of these surrogate indices, we calculated the day-to-day coefficients of variance (CVs) for QUICKI and 1/HOMA-IR as previously reported (7,9), which were 2.0 and 11.4%, respectively. The correlation coefficient between the first and second QUICKIs was 0.468 and for 1/HOMA-IRs was 0.985 (P <0.0001).

Euglycemic-hyperinsulinemic clamp

Euglycemic-hyperinsulinemic clamp (clamp) was performed according to the method of DeFronzo et al. (5) using an STG 22 artificial pancreas model (Nikkiso, Tokyo). After an overnight fast, venous blood sampling and measurement of blood pressure in the supine position were performed and the euglycemic-hyperinsulinemic clamp protocol was begun as previously described (9,20,21). In brief, insulin (Humulin; Eli Lilly, Indianapolis, IN) was infused in a continuous fashion at a rate of 1.25 mU·kg^{-1}·min^{-1} after the priming insulin infusion during the first 10 min of the clamp at the same doses as reported previously. Blood glucose levels were determined every 5 min during the 120-min clamp study, and euglycemia (5.0 mmol/l) was maintained by infusion of variable amounts of 20% glucose solution, which were determined by the built-in computer program according to the control algorithm. The mean CV of blood glucose in maintaining euglycemia was 1.29% and ranged from 0.4 to 2.9%. The total-body glucose disposal rate was evaluated as the mean of the glucose infusion rate during the last 30 min of the clamp. The mean (±SD) steady-state plasma insulin (SSPI) level was 647 ± 191 pmol/l in all diabetic subjects. The CVs for SSPI and glucose infusion rate were 8.4 ± 1.0% and 5.9 ± 0.4% (mean ± SE), respectively. The insulin sensitivity index (clamp-IR) derived from the clamp study was calculated by dividing the mean glucose infusion rate by SSPI level during the last 30 min of the clamp and multiplying by 100.

Statistical analysis

All values are means ± SD, unless otherwise indicated. Statistical analysis was performed by the StatView 5 system on a Windows computer. Student's t test or the χ^2 test was appropriately used for group comparisons. Linear simple or multiple regression analysis was performed for analysis of associations among clamp-IR and clinical covariates, including QUICKI, HOMA-IR, or 1/HOMA-IR. P values <0.05 were considered statistically significant.

RESULTS

Table 1 shows the clinical characteristics of all type 2 diabetic and

Table 1—*Clinical characteristics of the subjects*

	Type 2 diabetes			
	Normal range weight	Moderately obese	Healthy subjects	*P*
n	76	45	120	—
Sex (M/F)	52/24	29/16	80/40	0.903*
Age (years)	54.9 ± 10.8	48.2 ± 14.6†	52.0 ± 15.3	0.042
Duration of diabetes (years)	8.6 ± 6.9	8.1 ± 7.8	—	0.686
Blood pressure (mmHg)				
Systolic	126 ± 20	130 ± 22	125 ± 15	0.302
Diastolic	72 ± 10‡	75 ± 11	78 ± 11	0.002
BMI (kg/m^2)	21.4 ± 2.3‡	27.2 ± 2.2†‡	22.8 ± 2.6	<0.0001
FPG (mmol/l)	8.2 ± 2.4‡	7.5 ± 2.0‡	5.2 ± 0.4	<0.0001
HbA_{1c} (%)	9.0 ± 2.3‡	8.3 ± 1.9‡	5.0 ± 2.1	<0.0001
Fasting insulin (pmol/l)	26.4 ± 18.0	49.8 ± 25.2†‡	31.2 ± 26.4	<0.0001
Total cholesterol (mmol/l)	4.91 ± 1.13	4.91 ± 0.91	5.02 ± 0.88	0.704
Triglyceride (mmol/l)	1.28 ± 0.79	1.55 ± 0.96†	1.18 ± 0.72	0.035
HDL cholesterol (mmol/l)	1.16 ± 0.39‡	1.06 ± 0.26‡	1.53 ± 0.44	<0.0001
Free fatty acids (mEq/l)	0.52 ± 0.27	0.56 ± 0.21	0.39 ± 0.19	0.088
Serum creatinine (μ mol/l)	62.8 ± 16.8‡	67.1 ± 23.0‡	88.4 ± 23.0	<0.0001
GIR	5.72 ± 2.14‡	4.14 ± 1.53†‡	9.60 ± 4.48§	<0.0001
clamp-IR	6.33 ± 3.05‡	3.85 ± 1.62†‡	9.79 ± 5.35§	<0.0001
HOMA-IR	1.60 ± 1.19	2.83 ± 1.91†‡	1.22 ± 1.16	<0.0001
1/HOMA-IR	0.92 ± 0.55‡	0.50 ± 0.33†‡	1.24 ± 0.82	<0.0001
QUICKI	0.371 ± 0.037	0.338 ± 0.030‡	0.389 ± 0.041	<0.0001

Data are means ± SD. *P values determined by ANOVA among three groups or by χ^2 test; †$P < 0.05$ vs. normal range–weight type 2 diabetic group by Scheffe's F test; ‡$P < 0.05$ vs. healthy subjects; §data from 29 healthy subjects. GIR, mean of glucose infusion rate during steady state of euglcyemic-hyperinsulinemic clamp; clamp-IR, GIR corrected by plasma insulin levels during steady state of clamp.

healthy subjects. There were no significant differences in sex, systolic blood pressure, total cholesterol, or free fatty acid level among moderately obese, normal range weight type 2 diabetic and healthy groups. The means of FPG and HbA_{1c} in type 2 diabetic subjects were significantly higher than those in nondiabetic subjects. The means of BMI and FIRI were significantly higher in the moderately obese diabetic group than in the normal range–weight diabetic and healthy groups. The mean age of the moderately obese diabetic group was significantly lower than those of the normal range–weight diabetic and healthy groups.

QUICKI ranged from 0.274 to 0.424 in moderately obese subjects, from 0.285 to 0.469 in normal range weight subjects, and from 0.274 to 0.524 in healthy subjects. QUICKI and 1/HOMA-IR were significantly lower in the moderately obese diabetic group than in the healthy group. HOMA-IR was significantly higher in the moderately obese diabetic group than in the normal range weight diabetic and healthy groups.

Simple regression analysis demonstrated that QUICKI was highly correlated with clamp-IR in the normal range–weight, moderately obese, and healthy groups ($r = 0.641$, 0.570, and 0.502, respectively; all groups, $r = 0.608$, $P < 0.0001$) (Fig. 1*A* and *B*). Both HOMA-IR and FIRI were also significantly correlated with clamp-IR in all groups, but their correlation coefficients were lower than those for QUICKI (Table 2). 1/HOMA-IR exhibited a correlation coefficient comparable to that of QUICKI in the normal range–weight, moderately obese, and healthy groups ($r = 0.637$, 0.530, and 0.461, respectively; all groups, $r = 0.589$, $P < 0.05$) (Fig. 1*C* and *D*). As expected, BMI exhibited significant correlations with clamp-IR in all diabetic subjects and healthy subjects. To explore the estimated best fit for clamp-IR and avoid mutual interactions in diabetic subjects, we performed multiple regression analysis, in which clamp-IR was included as a dependent variable. Sex and BMI are entered in all models as common independent variables and HOMA-IR (model 2), 1/HOMA-IR (model 3), or QUICKI (model 4) as an additional independent variable in individual models. In all diabetic groups, QUICKI was a strong independent contributor in model 4, which explained 54.7% of clamp-IR variability. However, model 3, which included 1/HOMA-IR as an independent variable, had the highest coefficient determination among the models ($R^2 = 0.551$, $P < 0.001$). When determined separately for the moderately obese and normal range–weight diabetic groups, the R^2s of model 3 (0.299) and model 4 (0.337) in the moderately obese diabetic group were lower than those in the normal range–weight diabetic group, although in the moderately obese diabetic group QUICKI and 1/HOMA-IR made significant independent contributions to clamp-IR.

CONCLUSIONS — The present study demonstrated that QUICKI and 1/HOMA-IR were strongly correlated with insulin resistance index assessed by euglycemic-hyperinsulinemic clamp, the gold standard method, in both moderately obese and normal range-weight type 2 diabetic patients as well as healthy subjects. These results prove the validity of QUICKI and 1/HOMA-IR in type 2 diabetic patients with or without obesity.

Katz et al. (12) first proposed that QUICKI was strongly correlated with the insulin resistance index assessed by clamp-IR in 56 subjects, including 15 type 2 diabetic patients. Subsequently, a few investigators (13,14) have demonstrated good correlations of QUICKI with insulin sensitivity index by clamp-IR in lean and obese nondiabetic subjects and pregnant women. The correlation coefficient between QUICKI and clamp-IR in lean nondiabetic subjects is reported to be relatively low (13,14,22). Our nondiabetic subjects (mean BMI 22.8 kg/m^2) (Table 1), had comparable coefficients of correlation between QUICKI and clamp-IR with nondiabetic subjects in other reports. A relatively small number of type 2 diabetic patients were enrolled in these studies (13,14). Type 2 diabetic patients have pathological characteristics different from those of nondiabetic subjects, which may affect the association with QUICKI and the clamp-based index, that is, decreased insulin secretion capacity, fasting hyperglycemia, obesity, and modification of various OHAs may influence fasting insulin levels in clinical prac-

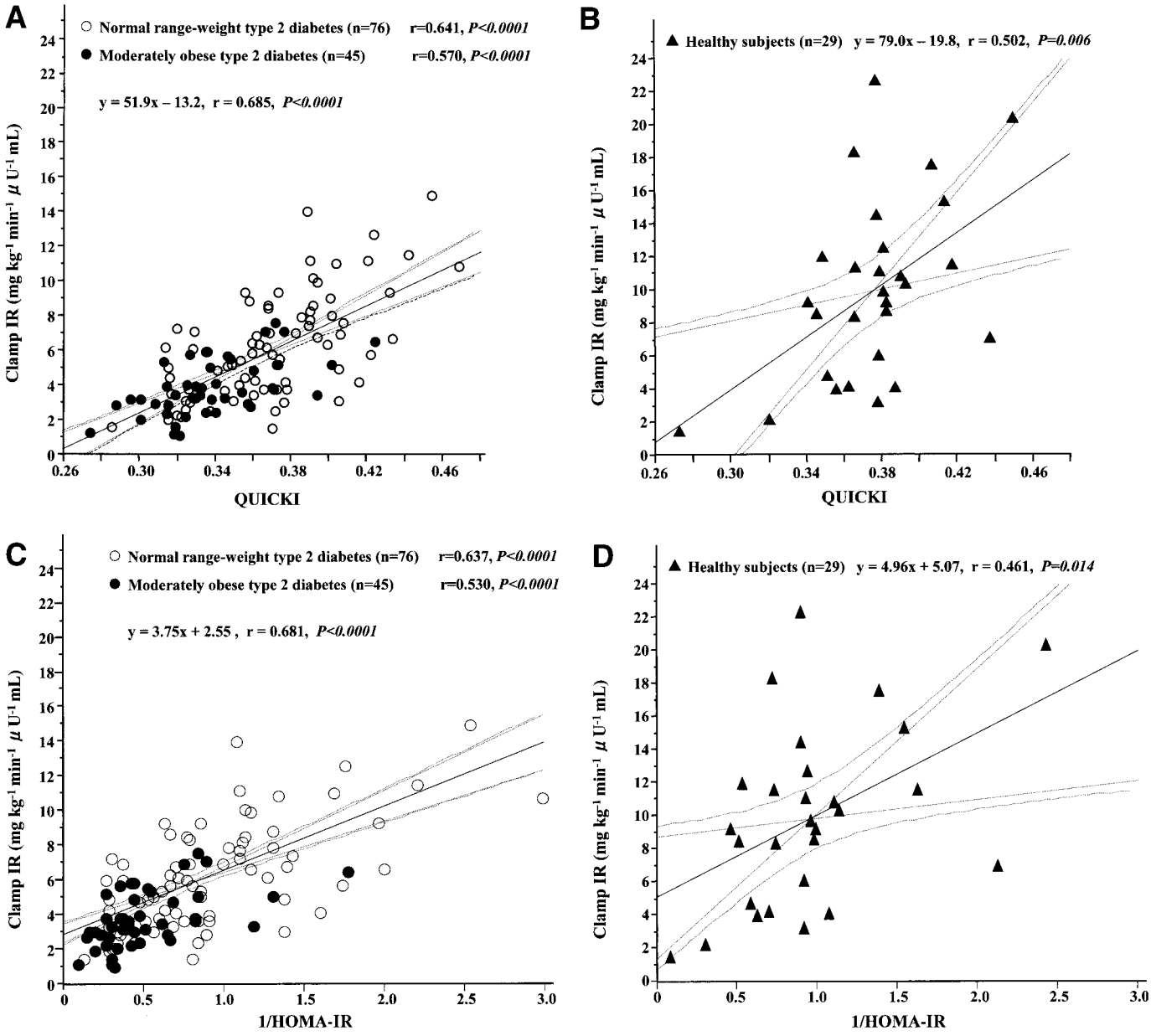

Figure 1—*Correlations between QUICKI or 1/HOMA-IR and clamp-IR in 76 normal range–weight and 45 moderately obese type 2 diabetic and 29 healthy subjects. QUICKI was strongly correlated with clamp-IR in both normal range–weight (○) and moderately obese (●) type 2 diabetic subjects* (r = *0.641 and 0.570, respectively; all diabetic subjects,* r = *0.685,* P < *0.0001)* (A)*, as well as in healthy subjects* (▲; r = *0.502,* P = *0.006)* (B)*. 1/HOMA-IR was also strongly correlated with clamp-IR in both normal range–weight* (○) *and moderately obese* (●) *type 2 diabetic subjects* (r = *0.637 and 0.530, respectively; all diabetic subjects,* r = *0.681,* P < *0.0001)* (C)*, as well as in healthy subjects* (r = *0.461,* P = *0.014)* (D)*. Note the differences in 90 percentiles of the slopes and intercepts of the linear regression lines for the group of all diabetic patients and the group of healthy subjects.*

tice. Thus, the validity of QUICKI in type 2 diabetic patients must be investigated considering these clinical factors. Katsuki et al. (16) demonstrated that QUICKI was highly correlated with clamp-IR in 60 Japanese type 2 diabetic patients both before and after exercise treatment. The present study included type 2 diabetic patients with a wide range of BMI and clearly demonstrated excellent correlations of QUICKI with clamp-IR in both normal range weight and moderately obese type 2 diabetic patients. Thus, our findings make another confirmation of close correlation between QUICKI and clamp-IR in a large number of type 2 diabetic patients reported by Katsuki et al. The comparable degree of obesity and the same ethnicity of our subjects to those in their report may largely contribute the same consequence concerning excellent correlations between these two indices. Our normal range–weight diabetic patients had lower BMI than those of western populations in previous reports. The correlation coefficient for normal range–weight type 2 diabetic patients was found to be comparable not only to that for nonobese but also to that for obese healthy subjects described in previous reports (13,14).

Table 2—*Correlation coefficients of surrogate insulin resistance indices or clinical factors possibly affecting insulin resistance with clamp-IR determined by simple linear regression analyses*

	Type 2 diabetes				
	Normal range weight	Moderately obese	All	Healthy subjects	All subjects
QUICKI	0.641*	0.570*	0.685*	0.502†	0.608*
HOMA-IR	0.527*	0.508*	0.540*	0.410‡	0.482*
1/HOMA-IR	0.637*	0.530*	0.681*	0.461‡	0.589*
Fasting insulin	0.528*	0.518*	0.579*	0.425‡	0.425*
BMI	0.455*	0.130	0.536*	0.403‡	0.481*
Triglyceride	0.178	0.117	0.146	0.557†	0.284*
Free fatty acids	0.164	0.150	0.174	0.482	0.209*

All values are correlation coefficients (*r* values) determined by simple linear regression analysis with level of significance: *$P < 0.001$; †$P < 0.01$; ‡$P < 0.05$.

Two reasons may be considered for the excellent correlation between QUICKI and clamp-IR, even in normal range–weight type 2 diabetic patients. First, clamp-IR in our normal range–weight type 2 diabetic patients was widely distributed from severe insulin resistance to a considerably sensitive state because of inclusion of subjects with various clinical profiles affecting insulin resistance in addition to obesity. Second, the number of our type 2 diabetic subjects was larger than those in previous studies. Taken together, our data provide conclusive evidence of the strong correlation between QUICKI and clamp-IR in both normal range–weight and moderately obese type 2 diabetic patients.

Another finding of our study was that the regression line between QUICKI and clamp-IR for type 2 diabetic patients differed from that for healthy subjects (slope, 51.9 vs. 79; intercept, −13.2 vs. −19.8, respectively). Although the reason for this remains unclear, it may be that the relationship between fasting glucose and insulin in diabetic patients is modified by decreased insulin secretion capacity, hyperglycemia, or other factors. This is important when we try to predict clamp-IR from QUICKI in the same study while including subjects across the range of glucose tolerance, from normal to diabetic.

The direct relationship between fasting insulin levels and clamp-IR is hyperbolic rather than linear (23). Two groups, Hermans et al. (11,24) and us (9), have proposed that the logarithmic transformation of fasting insulin or HOMA-IR made the relationship linear and stronger. QUICKI is also mathematically considered the logarithmic transformation of fasting insulin or HOMA-IR. Recently, Abbassi et al. (22) demonstrated that QUICKI did not exhibit superiority over log-transformed HOMA-IR. In the present study, we further explored the re-

Table 3—*Coefficient of determinations of the models including surrogate indices of insulin resistance as independent variables with clamp-IR determined by multiple regression analyses*

	Model 1		Model 2		Model 3		Model 4	
	β	*P*	β	*P*	β	*P*	β	*P*
Normal range weight								
Sex	0.300	0.003	0.250	0.006	0.196	0.024	0.200	0.020
BMI	−0.416	<0.001	−0.333	<0.001	−0.274	0.002	−0.271	0.002
HOMA IR	—	—	−0.420	<0.001	—	—	—	—
1/HOMA IR	—	—	—	—	0.504	<0.001	—	—
QUICKI	—	—	—	—	—	—	0.511	<0.001
R^2	0.296*		0.461*		0.515*		0.522*	
Moderately obese								
Sex	0.241	0.113	0.149	0.278	0.134	0.324	0.116	0.382
BMI	−0.135	0.367	−0.042	0.756	−0.024	0.860	−0.007	0.956
HOMA IR	—	—	−0.471	0.001	—	—	—	—
1/HOMA IR	—	—	—	—	0.497	<0.001	—	—
QUICKI	—	—	—	—	—	—	0.542	<0.001
R^2	0.075		0.280*		0.299*		0.337*	
All diabetic								
Sex	0.261	<0.001	0.213	0.003	0.163	0.012	0.164	0.012
BMI	−0.515	<0.001	−0.376	<0.001	−0.286	<0.001	−0.270	<0.001
HOMA IR	—	—	−0.352	<0.001	—	—	—	—
1/HOMA IR	—	—	—	—	0.512	<0.001	—	—
QUICKI	—	—	—	—	—	—	0.516	<0.001
R^2	0.355*		0.456*		0.551*		0.547*	

β is standard coefficient of each independent variable and R^2 the coefficient of determination of each model. Sex (male as 1, female as 0) and BMI are (1–4) entered as common independent variables in all models and HOMA-IR (model 2), 1/HOMA-IR (model 3), or QUICKI (model 4) as an additional independent variable in individual models. *$P < 0.001$.

lationship between 1/HOMA-IR and clamp-IR, because the logarithmic transformation, log HOMA-IR or QUICKI, is not easy to calculate without a pocket calculator in situations such as outpatient clinics. In both normal range–weight and moderately obese type 2 diabetic and healthy subjects, 1/HOMA-IR exhibited excellent correlations with clamp-IR comparable to those of QUICKI, which are better than those of HOMA-IR or fasting insulin (Table 2). In our multiple regression analyses, the coefficients of determination of the model, including 1/HOMA-IR, were also found to be almost the same as those of QUICKI, as discussed below. Thus, 1/HOMA-IR is more convenient than QUICKI in clinical practice.

Finally, we consider with what degree of reliability we could predict clamp-IR from HOMA-IR, 1/HOMA-IR, or QUICKI. For the group of all diabetic patients, the multiple regression model (model 4) for clamp-IR, including sex, BMI, and QUICKI as independent variables, explained 55% (R^2) of the variability in difference in clamp-IR, with a formula to estimate clamp-IR of clamp-IR = $-4.231 + 0.995 \times \text{sex} - 0.214 \times \text{BMI} + 39.076 \times \text{QUICKI}$. Here, 1 for men or 0 for women is applied to sex. Model 3, including 1/HOMA-IR in place of QUICKI, yielded the same coefficient of determination (R^2, 55%), with a formula of clamp-IR = $7.942 + 0.992 \times \text{sex} - 0.227 \times \text{BMI} + 2.816 \times (1/\text{HOMA-IR})$. These results mean that the reminder, 45% of variability of clamp-IR, cannot be accounted for by these models and that QUICKI or 1/HOMA-IR cannot completely predict clamp-IR.

There are limitations of our study. First, there is a possibility that the higher level of SSPI during the clamp than that in our study may make the correlations of QUICKI and 1/HOMA-IR with clamp-IR better because of more complete suppression of hepatic glucose production in severely insulin-resistant patients. Second, acute change from fasting hyperglycemia to euglycemia during the euglycemic clamp may affect insulin sensitivity. Third, we cannot deny the possibility of an ethnic difference in the validity of QUICKI and 1/HOMA-IR in our study.

In conclusion, QUICKI and 1/HOMA-IR may provide simple clinical indices of insulin resistance in both normal range–weight and moderately obese type 2 diabetic patients but must be interpreted with caution because of the wide degree of variability compared with clamp-IR. 1/HOMA-IR, which is more convenient for clinicians in various clinical settings, is not inferior to QUICKI in validity.

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