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Computational Methods Are Significant Determinants of the Associations and Definitions of Insulin Resistance Using the Homeostasis Model Assessment in Women of Reproductive Age

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BACKGROUND: Insulin resistance (IR) plays an important role in the pathogenesis of polycystic ovary syndrome (PCOS), but identification of insulin-resistant individuals is difficult. The homeostasis model assessment (HOMA), a surrogate marker of IR, is available in 2 computational models: HOMA1-IR (formula) and HOMA2-IR (computer program), which differ in incorporated physiological assumptions. This study evaluates the associations of the 2 models as markers of IR, the metabolic syndrome (MS), and PCOS.

METHODS: Anthropometric, hormonal, and biochemical parameters were measured in 92 PCOS women and 110 controls. HOMA1 and HOMA2 were used to assess IR. Regression analyses were used to find the associations of the 2 models with different variables, MS, and PCOS.

RESULTS: The cutoff levels for definition of IR were HOMA1-IR $\geq$2.9 and HOMA2-IR $\geq$1.7. Mean HOMA1-IR (2.79) and HOMA2-IR (1.42) differed substantially. The difference (HOMA1-IR − HOMA2-IR) was significantly correlated with insulin, fasting plasma glucose, triglycerides, HDL cholesterol, waist circumference, leptin, and adiponectin (all $P < 0.05$). HOMA1-IR and HOMA2-IR were significantly associated with MS (odds ratio 5.7 and 4.2, respectively) and PCOS (odds ratio 3.7 and 3.5, respectively).

CONCLUSIONS: HOMA computational methods significantly affect the associations and cutoff values used for definition of IR. The correlations of the difference in the computational methods corroborate differences in captured physiological mechanisms. As precise identification of IR in PCOS patients is of practical importance, practitioners and researchers should be aware of these differences in the HOMA computational methods.

Insulin resistance (IR),[4] a state of reduced sensitivity or responsiveness to the metabolic actions of insulin, is well known to have great impact on health morbidities. It is linked to obesity *(1)* and possibly contributes to hyperandrogenism *(2, 3)*. IR is widely accepted to play a central role in the pathogenesis of polycystic ovary syndrome (PCOS) and its metabolic components *(4, 5)*, the metabolic syndrome (MS) *(5, 6)*, and type 2 diabetes mellitus *(7)* and hence may increase the risk of coronary artery disease *(5, 8)*. The exact underlying mechanism for IR in PCOS is unclear, but several hypotheses have been suggested *(9)*.

Despite the importance of IR in the clinical setting, defining IR in individual patients is complicated. Literature review shows that a variety of methods of varying complexity are used to estimate IR, and each of these methods has its own advantages and disadvantages *(10)*. The choice of method depends on the size and type of study being conducted, and no single method is appropriate under all circumstances. The hyperinsulinemic-euglycemic clamp method is the gold standard for measuring insulin sensitivity *(10, 11)*, but it is impractical for routine use, expensive, time-consuming, and labor-intensive *(12)* compared with homeostatic measurements *(10, 13)*. Currently, the homeostasis model assessment (HOMA) model, which correlates well with gold standard clamp techniques, is widely used in clinical and epidemiological research because of its simplicity. The original HOMA1 model was first described in 1985 by Matthews et al. *(14)* and has been used in many longitudinal and epi-

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[4] Nonstandard abbreviations: IR, insulin resistance; PCOS, polycystic ovary syndrome; HOMA, homeostasis model assessment; %B, β-cell function; FPG, fasting plasma glucose; %S, insulin sensitivity; WC, waist circumference; TG, triglycerides; OR, odds ratio.

demiological studies to derive β-cell function (%B) and IR values from fasting plasma insulin (FPI) (mIU/L) and fasting plasma glucose (FPG) (mmol/L) with the formulae: HOMA1-IR = (FPI × FPG)/22.5 and HOMA1%B = (20 × FPI)/(FPG − 3.5) *(12)*. The use of this equation was followed by the development of "the correctly solved computer model," HOMA2 (the computer program), which can also be used to calculate steady-state %B, insulin sensitivity (%S), and HOMA of insulin resistance (HOMA-IR) from fasting glucose (mmol/L) and insulin (mIU/L) or C-peptide concentrations *(15, 16)*. The 2 models differ in captured physiological mechanisms of the glucose-insulin feedback system in the fasting state. For example, HOMA2-IR corrects for peripheral and hepatic glucose resistance and also includes correction for renal glucose loss, making it suitable for use in hyperglycemic individuals *(12, 15)*.

Reported cutoff values for the definition of IR from different studies across populations have been highly variable *(10, 17–19)* because of several factors *(20)*. The high variability has resulted in widely different estimates of IR in study groups such as patients with PCOS. Despite the widespread use of the HOMA computational methods, the differences in the physiological mechanisms captured in each model have been largely ignored, and there are no previous studies that have compared the 2 methods in terms of their associations and definition of IR. Therefore, the aim of this study was to determine the effect of HOMA computational method on the associations and identification of IR in MS phenotypes and PCOS.

Materials and Methods

The study was approved by both ethics committees of the Faculty of Medicine of Kuwait University and the Ministry of Health. Signed informed consent was obtained from each individual before enrolling in the study. We recruited a total of 92 women with PCOS and 110 apparently healthy control women with regular menstrual cycles (age range 18–48 years) from hospital outpatient clinics and from volunteers (medical students and staff) in the Faculty of Medicine. All the participants were Kuwaiti and were asked to report after fasting for 12–14 h on the second to fourth day of their menstrual cycle. None of the study participants were receiving any treatment that may have interfered with our results.

Each participant was clinically evaluated; weight, height, and waist circumference (WC) were measured; and body mass index (kg/m^2) was calculated. Blood pressure was recorded, and fasting venous blood samples were obtained for biochemical and hormonal analysis.

LABORATORY METHODS

Insulin assay. Quantitative measurement of fasting insulin was performed on the Immulite 1000 automated immunoassay analyzer (Siemens Medical Solutions Diagnostics) by using a solid-phase, 2-site chemiluminescent immunometric assay. The within-run and total CVs for insulin at a mean concentration of 7.39 mIU/L were 6.4% and 8%, respectively.

Routine biochemistry tests. All routine biochemistry tests were performed immediately after sample collection. FPG, total cholesterol, triglycerides (TG), and HDL cholesterol were analyzed on the Beckman DXC 800 automated analyzer (Beckman). The LDL cholesterol was calculated with the Friedewald formula *(21)*. The formula is valid as long as TG concentrations are ≤4.5 mmol/L.

Other hormone assays. Total testosterone, sex hormone–binding globulin, dehydroepiandrosterone sulfate (DHEA-S), and andostenedione were measured by using chemiluminescent immunometric methods on the Immulite 1000 automated immunoassay analyzer (Siemens Medical Solutions Diagnostics). Quantitative determinations of luteinizing hormone, follicle-stimulating hormone, estradiol, and prolactin were performed on the Beckman DXI 800 automated analyzer. 17 hydroxyprogesterone was determined by radioimmunoassay (Immunotech).

Adiponectin and leptin assays. ELISA kits were used to determine adiponectin (Linco Research) and leptin (BioVendor) concentrations.

CATEGORIES AND DEFINITIONS

The HOMA1-IR formula and HOMA2-IR online calculator downloaded from http://www.dtu.ox.ac.uk were used to calculate IR. IR was defined as the upper quartile of HOMA-IR as recommended *(22)*. The presence of PCOS was defined according to the Rotterdam 2003 criteria *(23)*. Hyperandrogenism was defined when the study participant had the clinical manifestation of hyperandrogenism and/or when the biochemical androgen levels were above the laboratory's upper reference interval limits. MS was defined according to the International Diabetes Federation criteria *(24)* by using European cutoff values for WC (≥80 cm for women). Participants were classified as MS positive if they met these criteria or as MS negative if they did not.

STATISTICAL METHODS

All data were tested for normality. Nonparametric tests were used because several variables of interest (HOMA-IR, insulin, FPG, TG, HDL cholesterol, adiponectin, and leptin) significantly diverged from nor-

mal distribution, even after they were log transformed. The data were expressed as mean (SD) unless otherwise specified. Mann–Whitney *U*-tests were used for comparison between 2 groups, and categorical variables were compared by using the χ^2 test. Spearman correlation coefficients were used to describe the association between HOMA-IR and other continuous variables of interest. Linear regression analysis was used to determine the associations of metabolic variables with the difference of HOMA computational models (HOMA1-IR − HOMA2-IR). Binary logistic regression analyses were used to ascertain the associations of HOMA-IR in general and IR ≥1.7 and IR ≥2.9 groups with the risk of MS, PCOS, and hyperandrogenism with and without adjustment for the confounding effect of WC. The Bland–Altman analysis was used to show the degree of agreement between the 2 computational models.

All the statistical methods were performed with SPSS Windows version 17.0 software (SPSS), and a *P* value <0.05 was considered statistically significant for all analyses.

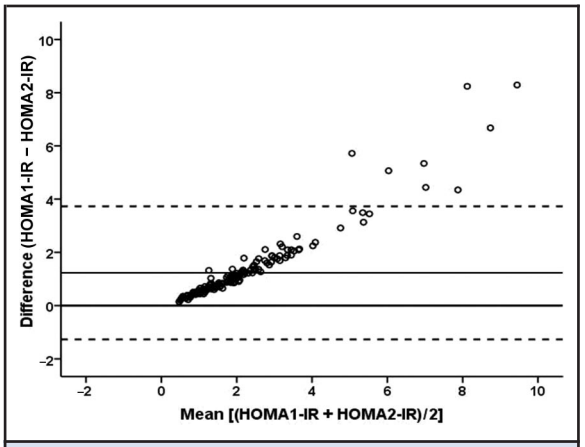

Fig. 1. Bland–Altman analysis showing limits of agreement between HOMA1-IR and HOMA2-IR.

The upper solid line represents the mean difference. The dashed lines represent limits of agreement: mean (2 SD). The lower solid line represents 0 bias.

Results

In this study, a total of 202 women were recruited, and 92 of them were classified as having PCOS (Rotterdam criteria). Because estimation of HOMA-IR using the online HOMA2-IR calculator is limited to the concentration ranges of 3–25 mmol/L for glucose and 2.9–57.6 mIU/L for insulin, the total number of results differed for HOMA1-IR (n = 202) and HOMA2-IR (n = 183). A total of 33.7% (31 of 92) of PCOS patients and 23.6% (26 of 110) of non-PCOS controls had MS. Hyperandrogenism was present in 96.7% (89 of 92) of PCOS patients and 36.4% (40 of 110) of the non-PCOS control women.

Our results revealed a noticeable difference in the estimated HOMA1-IR (mean 2.79) and HOMA2-IR (mean 1.42). This finding is further supported by the Bland–Altman analysis (Fig. 1), which shows the discrepancy in the IR results obtained from both HOMA models. In general, HOMA1-IR results were higher than results of the online calculator HOMA2-IR, and the differences between results of the 2 methods become greater at higher insulin concentrations (Fig. 2).

Because IR develops as a continuous trait, there is no precise definition of an absolute cutoff value for IR. Therefore, when viewed as a continuum of varying degrees of IR, the individuals in the highest quartile could be taken as being the most insulin resistant. The 75th percentile cutoff values were HOMA1-IR = 2.9 and HOMA2-IR = 1.7. According to these cutoff values, 25.2% (51 of 202) and 26.2% (48 of 183) of women were classified as insulin resistant by using HOMA1-IR and HOMA2-IR, respectively. Using HOMA1-IR, IR was present in 50.9% (29 of 57) of all women with MS and 37.0% (34 of 92) of patients with PCOS. This contrasts with using HOMA2-IR, which showed IR in 45.6% (26 of 57) of all women with MS and 34.8% (32 of 92) of PCOS patients. Table 1 summarizes the main anthropometric, biochemical, and metabolic characteristics of the study population according to IR subgroups.

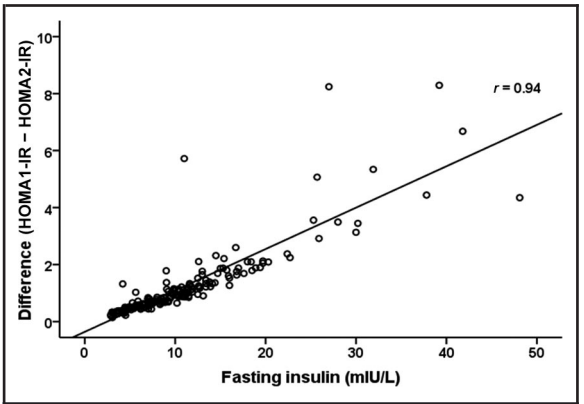

Fig. 2. Scatter diagram showing the correlation between the difference of HOMA computational methods (HOMA1-IR − HOMA2-IR) with insulin concentration (mIU/L).

Line represents the best fit line through the data points.

Table 1. Anthropometric, biochemical, and metabolic characteristics of the study population according to HOMA-IR subgroups.[a]

	HOMA1[b]		HOMA2[c]	
	IR <2.9	IR ≥2.9	IR <1.7	IR ≥1.7
n	151	51	135	48
Age, years	32.1 (6.7)	33.6 (6.3)	32.6 (6.4)	33.5 (6.3)
WC, cm	87.5 (13.1)	106.6 (14.0)****[d]	89.3 (13.0)	106.0 (14.1)****
BMI, kg/m^2	28.5 (6.0)	36.0 (7.1)****	29.3 (5.9)	36.0 (7.3)****
Systolic blood pressure, mmHg	110.3 (11.8)	116.2 (13.5)**	111.0 (12.0)	115.7 (13.6)
Diastolic blood pressure, mmHg	72.2 (7.4)	75.5 (9.0)*	72.7 (7.2)	75.0 (9.0)
FPG, mmol/L	5.0 (0.6)	6.1 (2.0)****	5.1 (0.7)	5.9 (1.8)****
Insulin, mIU/L	7.0 (3.1)	22.6 (15.6)****	7.6 (2.7)	20.2 (8.4)****
Total cholesterol, mmol/L	4.9 (0.9)	5.0 (1.0)	4.9 (0.9)	5.0 (1.0)
TG, mmol/L	0.9 (0.5)	1.4 (1.1)****	0.9 (0.5)	1.4 (1.2)****
HDL cholesterol, mmol/L	1.2 (0.3)	1.0 (0.4)****	1.2 (0.3)	1.0 (0.4)***
LDL cholesterol, mmol/L	3.3 (0.8)	3.4 (0.9)	3.4 (0.8)	3.4 (0.9)
Adiponectin, mg/L	11.0 (4.8)	6.8 (3.6)****	10.3 (4.1)	6.8 (3.7)****
Leptin, μg/L	31.5 (18.0)	49.4 (22.7)****	33.9 (17.3)	50.1 (22.4)****

[a] Data are means (SD).
[b] Comparisons between individuals with HOMA1-IR <2.9 and HOMA1-IR ≥2.9 IU/L.
[c] Comparisons between individuals with HOMA2-IR <1.7 and HOMA2-IR ≥1.7 IU/L.
[d] *P* values of Mann–Whitney *U*-tests: $P > 0.05$, no asterisk; *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$; ****$P < 0.0001$.

CORRELATIONS OF HOMA COMPUTATIONAL METHODS

Table 2 shows that, in both PCOS and non-PCOS (control) women, HOMA1-IR and HOMA2-IR showed comparable significant positive correlations with anthropometric measurements (WC, body mass index, and fat%) and some biochemical and metabolic variables (FPG, TG, insulin, and leptin) and significant negative correlations with adiponectin. In addition, in PCOS patients only, both HOMA-IR methods showed significant negative correlations with HDL cholesterol, luteinizing hormone, follicle-stimulating hormone, and sex hormone–binding globulin. However, HOMA1-IR (but not HOMA2-IR) showed significant correlations with HDL cholesterol, luteinizing hormone, and sex hormone–binding globulin in the control group. In general, the correlation coefficients (r) were found to be higher in patients with PCOS and with the HOMA1-IR method (Table 2).

Interestingly, the difference in the computation methods (HOMA1-IR − HOMA2-IR) was significantly ($P < 0.05$) positively correlated with insulin ($r = 0.94$), FPG ($r = 0.58$), TG ($r = 0.37$), WC ($r = 0.48$), and leptin ($r = 0.37$) and negatively correlated with HDL cholesterol ($r = -0.35$) and adiponectin ($r = -0.52$), suggesting differences in the pathophysiological mechanisms that are captured or not captured in each model. Table 3 shows the unadjusted, linear regression analysis, which indicated that metabolic variables were significant predictors of the difference between the computational methods.

ASSESSMENT OF RISK ASSOCIATIONS OF IR COMPUTATIONAL METHODS WITH PCOS, MS, AND HYPERANDROGENISM

Results of logistic regression analyses revealed that both HOMA1-IR and HOMA2-IR were significantly associated with PCOS, MS, and hyperandrogenism, and these associations were maintained after correction for WC (Table 4).

In further binary logistic models, we assessed the risk associations of the insulin-resistant groups (HOMA1-IR ≥2.9, HOMA2-IR ≥1.7) with PCOS, MS, and hyperandrogenism. Interestingly, our data showed higher associated risk of HOMA1-IR ≥2.9 or HOMA2-IR ≥1.7 with MS (odds ratios [OR] of 5.7 and 4.2, respectively; $P < 0.0001$), with PCOS (OR 3.7, $P = 0.007$, and OR 3.5, $P = 0.004$), and with hyperandrogenism (OR 2.8, $P = 0.029$, and OR 2.6, $P = 0.042$), respectively. After inclusion of WC as a confounding factor, all the significant associations of HOMA1-IR ≥2.9 or HOMA2-IR ≥1.7 were maintained except for the hyperandrogenic group, which suggests that the association of IR with hyperandrogenism is obesity dependent.

Table 2. Spearman correlations of HOMA computational methods with some variables[a] in the study groups.

	Controls				PCOS			
	HOMA1-IR		HOMA2-IR		HOMA1-IR		HOMA2-IR	
	r[b]	*P*	*r*	*P*	*r*	*P*	*r*	*P*
WC, cm	0.49	<0.0001	0.37	<0.0001	0.64	<0.0001	0.59	<0.0001
Body mass index, kg/m^2	0.44	<0.0001	0.34	0.001	0.62	<0.0001	0.54	<0.0001
Fat%	0.38	<0.0001	0.27	0.007	0.56	<0.0001	0.46	<0.0001
Fasting glucose, mmol/L	0.47	<0.0001	0.25	0.013	0.65	<0.0001	0.51	<0.0001
TG, mmol/L	0.41	<0.0001	0.35	0.001	0.35	0.001	0.31	0.004
HDL cholesterol, mmol/L	−0.32	0.001	−0.18	0.074	−0.42	<0.0001	−0.39	<0.0001
Insulin, mIU/L	0.97	<0.0001	0.99	<0.0001	0.98	<0.0001	0.99	<0.0001
Luteinizing hormone, IU/L	−0.21	0.030	−0.14	0.184	−0.21	0.041	−0.24	0.032
Follicle-stimulating hormone, IU/L	−0.13	0.188	−0.14	0.179	−0.27	0.009	−0.29	0.007
DHEA-S,[c] μmol/L	−0.04	0.677	0.02	0.873	−0.25	0.019	−0.19	0.087
Sex hormone–binding globulin, nmol/L	−0.30	0.002	−0.18	0.073	−0.36	<0.0001	−0.23	0.032
Free androgen index	0.16	0.094	0.17	0.109	0.21	0.041	0.17	0.132
Adiponectin, mg/L	−0.52	<0.0001	−0.41	<0.0001	−0.57	<0.0001	−0.49	<0.0001
Leptin, μg/L	0.52	<0.0001	0.45	<0.0001	0.41	<0.0001	0.28	0.011

[a] Variables not shown did not have significant correlations in both PCOS patients and controls.
[b] Correlation coefficient.
[c] Dehydroepiandrosterone sulfate.

Discussion

Although IR is a well-established phenomenon associated with different morbidities, the precise definition of IR and identification of insulin-resistant individuals are difficult. In this study, we assessed the use of 2 computational HOMA methods for identification of the insulin-resistant group and the associations of IR with metabolic characteristics in women of reproductive age. Our results showed that, even in this mono-ethnic population, the difference in mean HOMA-IR obtained by the 2 computational methods are substantial enough to affect the identification of insulin-resistant individuals and, therefore, may affect clinical decision-making. The differences explain, in part, the wide variability of the cutoff values reported in different studies. We have also shown that the 2 methods had comparable significant correlations with different metabolic variables, but these correlations were generally higher in PCOS patients and with the HOMA1-IR compared with HOMA2-IR (Table 2).

Table 3. Unadjusted linear regression analysis of metabolic variables with difference in HOMA computational methods (HOMA1-IR − HOMA2-IR).

	P	β[a]	95% CI
WC, cm	<0.0001	0.42	0.02–0.04
Fasting glucose, mmol/L	<0.0001	0.62	0.51–0.75
Insulin, mIU/L	<0.0001	0.86	0.09–0.11
TG, mmol/L	<0.0001	0.32	0.31–0.78
HDL cholesterol, mmol/L	0.006	−0.20	−1.32 to −0.22
Adiponectin, mg/L	<0.0001	−0.42	−0.14 to −0.07
Leptin, μg/L	<0.0001	0.29	0.01–0.23

[a] Standardized coefficient.

Several factors could account for the differences observed in the computational methods. Our results (Fig. 2) revealed a greater difference in the 2 computational methods (HOMA1-IR − HOMA2-IR) at higher insulin levels, suggesting that the differences of the 2 computational methods could be due to the properties of each HOMA model. The fact that several metabolic variables are significant predictors of the difference between the 2 computational methods (Table 3) is an indication that different physiological mechanisms are differentially captured in the 2 models. Another important factor is the insulin assay used in the current study. The HOMA2-IR calculator, the correctly solved computer model, has been recalibrated in line with current insulin assays *(12, 15)*, because it allows the incorporation of estimates of proinsulin secretion and thus al-

Table 4. Binary logistic regression analyses showing risk associations of insulin resistance (HOMA1-IR and HOMA2-IR) with PCOS, MS, and hyperandrogenism.

	PCOS			Metabolic syndrome			Hyperandrogenism		
	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*
HOMA1-IR	1.49	1.11–1.98	0.007	1.61	1.31–1.98	<0.0001	1.36	1.05–1.76	0.018
HOMA1-IR adjusted for WC	1.49	1.08–2.06	0.016	1.37	1.12–1.69	0.003	1.39	1.03–1.86	0.029
HOMA1-IR ≥2.9	3.71	1.42–9.69	0.007	5.70	2.86–11.36	<0.0001	2.80	1.10–7.04	0.029
HOMA1-IR ≥2.9 adjusted for WC	3.33	1.12–9.87	0.030	2.71	1.22–6.03	0.015	2.66	0.94–7.53	0.065
HOMA2-IR	2.61	1.35–4.86	0.004	2.07	1.42–3.02	<0.0001	2.11	1.19–3.76	0.011
HOMA2-IR adjusted for WC	2.60	1.30–5.18	0.007	1.55	1.04–2.32	0.031	2.15	1.15–4.02	0.016
HOMA2-IR ≥1.7	3.49	1.32–9.23	0.012	4.24	2.10–8.55	<0.0001	2.64	1.04–6.73	0.042
HOMA2-IR ≥1.7 adjusted for WC	3.33	1.12–9.90	0.031	2.23	1.05–5.13	0.038	2.50	0.89–7.04	0.082

lows a wider range of insulin assays. On the other hand, the HOMA1-IR formula is based on a model calibrated to an insulin assay used in the 1970s that underestimates %S and overestimates %B when compared with newer assays *(12)*. Unlike hemoglobin A_{1c} assays that were aligned to assays used in major clinical trials before standardization *(25)*, current insulin assays have not been aligned to the assays used for HOMA computation models in the absence of an international reference method. Although the insulin assay used in the current study performed well in an evaluation of 11 insulin assays, Manley et al. *(26)* pointed out that the interassay variation could be as high as a factor of 2. The interassay variability could further account for the wide ranges of HOMA-IR reported in the literature.

Our study shows that IR is significantly associated with hyperandrogenism (Table 4). However, the association of IR with hyperandrogenism yielded inconsistent and variable results in previous studies on PCOS *(2, 27, 28)* and non-PCOS women *(29, 30)*. The inconsistent results could be explained partly by the racial differences as reported in a study *(29)* but, as we have shown, may be due to the computational method used for estimation of IR. Although the previous reports on the effect of ethnicity, age, and obesity on IR cannot be ignored *(29, 31, 32)*, our results show that, even in 1 population, there could be variability in estimates of IR due to differences in the cutoff point derived from the 2 computational methods. The significance of the effect of computational method on the associations of IR are best illustrated in Table 2, which shows that if 2 studies were conducted to evaluate the association between HOMA and free androgen index in patients with PCOS, the 2 studies would come to different conclusions if one used HOMA1 and the other used HOMA2. Nevertheless, IR is known to play a pivotal role in the pathogenesis of PCOS. In fact, although results are variable, various studies have put estimates of IR and hyperinsulinemia at approximately 40% to 70% of women with PCOS *(10, 33)*. In our study, IR was significantly associated with PCOS, as shown in Table 4, and this association was maintained after correction for WC. Therefore, identification of IR is of practical clinical importance for the treatment of PCOS patients. However, several factors could affect practical identification of insulin-resistant individuals. Differences in HOMA computational methods, which affect the cutoff values used to identify insulin-resistant individuals as well as the effect of ethnicity *(10)*, may obscure the clinical decision for treatment.

The main limitation of the present study is the cross-sectional design. As has been done frequently in other studies, the use of single measurements of glucose and insulin for estimation of HOMA is also a limitation. The pulsatile pattern of insulin secretion and the relatively high within-person CVs for HOMA-%S and HOMA-%B *(12)* make the use of a single sample less than ideal. Ideally, insulin should be estimated from 3 samples collected at 5-min intervals *(12)*. Other issues such as the lack of traceability of different commercial methods with differences in assay specificity and sensitivity, the lack of a standardized international insulin assay reference method, and preanalytical and analytical factors that may affect the reproducibility of the results *(20)* should be taken into consideration when comparing our estimates of HOMA with other studies.

In conclusion, our results show that computational methods significantly affect the identification of insulin-resistant individuals, the observed associations of HOMA with certain variables, and the detection of associated PCOS, MS, and hyperandrogenism in women of reproductive age. Because precise identification of IR in PCOS patients is of practical importance,

practitioners and researchers should be aware of these differences in the HOMA computational methods. We suggest that each population be studied by use of a uniform HOMA computational method and that comparison of HOMA results between studies be done with caution.

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