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Insulin resistance is associated with C-reactive protein independent of abdominal obesity in nondiabetic Taiwanese

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Abstract

Insulin resistance, which plays a fundamental role in the pathogenesis of metabolic syndrome and type 2 diabetes mellitus, is associated with serum levels of inflammatory markers and abdominal obesity. Whether insulin resistance is caused by inflammation or is an epiphenomenon of obesity remains unresolved. We therefore conducted a cross-sectional study to investigate whether the association between insulin resistance and C-reactive protein (CRP) levels is independent of abdominal obesity in a nondiabetic Taiwanese population. The study included 574 Taiwanese participants (300 men and 274 women) who were nondiabetic persons with CRP levels not exceeding 10 mg/L and who did not have a history of cardiovascular disease or were taking medication for dyslipidemia. All participants were of Han-Chinese origin. The degree of insulin resistance was determined using the homeostasis model assessment of insulin resistance (HOMA-IR). The CRP levels were categorized into quartiles from the lowest to the highest concentrations (Q1-Q4). Blood pressure, fasting glucose level, triglycerides level, waist circumference, and HOMA-IR were all found to be significantly higher in Q3 and Q4 than in Q1 and Q2. Stratified analysis by sex and abdominal obesity showed that HOMA-IR was significantly associated with CRP levels in both sexes in either obese or nonobese populations. Multiple linear regression analysis adjusting for age, smoking, components of metabolic syndrome, and waist circumference showed that the association between HOMA-IR and CRP levels remained significant in both men and women ($P = .029$ for men and $P < .001$ for women). These findings confirm that insulin resistance is strongly associated with CRP levels independent of abdominal obesity in nondiabetic Taiwanese. Factors other than abdominal obesity, such as polymorphisms in the CRP gene, may influence the association of insulin resistance with CRP levels in different ethnic populations.

1. Introduction

Current evidence supports a central role for low-grade inflammation in the development of atherosclerotic coronary heart disease (CHD). C-reactive protein (CRP), a marker of systemic inflammation, is an easily measured inflammatory marker that has been proven to be a strong predictor of cardiac events in patients with [1] and without [2] preexisting cardiovascular disease. C-reactive protein activity is stimulated by other cytokines, especially interleukin-6 (IL-6), which mainly originates from abdominal adipose tissue [3]. Several studies have shown a strong association between CRP and abdominal obesity [4,5].

Insulin resistance is fundamental to the pathogenesis of metabolic syndrome and type 2 diabetes mellitus [6]. Like CRP, insulin resistance is an independent risk factor for cardiovascular events in the normal population and in patients with preexisting cardiovascular disease [7,8]. During the last few years, insulin resistance has been

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shown to be strongly associated with CRP [9-16] and body fat, particularly visceral fat [17-19]. However, the relationships among obesity, CRP, and insulin resistance are complex. Several studies have shown that the association of CRP with insulin resistance is independent of obesity [9-12]. Other studies, however, demonstrated that the association between CRP and insulin resistance is obesity dependent in healthy men and women [13-16]. In these studies, the association of CRP and insulin resistance was no longer evident after adjusting for various parameters related to obesity. This raises the hypothesis that adipose tissue might be the common antecedent of both CRP and insulin resistance.

C-reactive protein concentrations are quite different among ethnic groups. Chinese and Japanese populations have relatively lower CRP concentrations than Hispanic and white populations, which can only partially be explained by their lower body mass index (BMI) [20-22]. Thus, the relationships among CRP, insulin resistance, and abdominal obesity may be different among different ethnic groups. The aim of the present study was to investigate whether insulin resistance is associated with CRP in a Taiwanese population, independent of abdominal obesity.

2. Subjects and methods

2.1. Subjects

After informed consent was obtained, the study subjects were recruited during routine health examinations. Only subjects without a known history of major systemic disease or cardiovascular disease were enrolled. Exclusion criteria included age younger than 18 years, cancer, current renal or liver disease, and a history of myocardial infarction, stroke, or transient ischemic attack. Furthermore, subjects with *diabetes mellitus* (defined as blood glucose levels before a meal of $\geq$7.0 mmol/L or the regular use of medications for diabetes mellitus), lipid-lowering drug treatment, and CRP levels greater than 10 mg/L were also excluded. There were 574 subjects (300 men with a mean age of 45.0 ± 9.8 years; 274 women with a mean age of 46.5 ± 9.7 years) that were enrolled in this analysis. All participants reported their ethnicity as Han-Chinese origin. The Ethics Committee of the Chang-Gung Memorial Hospital approved the study.

2.2. Medical records

Clinical history, including hypertension, diabetes, habitual smoking, and drug therapy, was recorded for all participants. *Current smoker* was defined as smoking at least 1 cigarette per day at the time of survey. The blood pressure (BP) was measured with a random-zero sphygmomanometer by trained physicians or nurses. After a 5-minute period of rest in the supine position, 2 BP measurements were made at 5-minute intervals with the subjects in the seated position. The mean of the 2 values was used as a measure of BP. Hypertension was defined as a systolic BP of at least 140 mm Hg and/or a diastolic BP of at least 90 mm Hg, or regular antihypertensive medication use.

2.3. Anthropometric measurements

Anthropometrics were obtained with the participant in light clothing with no footwear and after 12 hours of fasting. Body weight was measured to the nearest kilogram using a digital scale, and height was measured to the nearest centimeter in the standing position using a wall stadiometer. Body mass index was computed as the ratio of weight to the square of height (in kilograms per square meter). Waist circumference (WC) was measured to the nearest centimeter at the midpoint between the lower limit of the rib cage and the iliac crest. For Asians, the cutoff value of WC was 90 cm for men and 80 cm for women [23]. *Abdominal obesity* was thus defined as male subjects with WC of at least 90 cm and female subjects with WC of at least 80 cm. The metabolic syndrome was diagnosed according to the National Cholesterol Education Program Adult Treatment Panel III as modified for WC criteria.

2.4. Laboratory examination

A total of 15 mL of venous blood was collected in the morning after an overnight (8-12 hours) fast. Venous blood samples were drawn from an antecubital vein with a 21-gauge needle. Serum, EDTA, sodium fluoride, and sodium citrate plasma were obtained by centrifuging the blood at 3000*g* for 15 minutes at 4°C. Immediately after centrifugation, the serum/plasma samples were frozen and stored at −80°C before analysis. All measurements were performed in a central laboratory. Insulin resistance was estimated by the homeostasis model assessment of insulin resistance (HOMA-IR) using the following formula: fasting serum insulin (in microunits per milliliter) × fasting plasma glucose (in millimoles per liter)/22.5. Highly-sensitive CRP was measured using high-sensitivity enzyme-linked immunosorbent assay for CRP, developed in-house and performed in sandwich format [24]. The interassay and intraassay coefficients of variation were less than 5% for the measurements.

2.5. Statistic analysis

The clinical characteristics of the participants are expressed as means ± SD and percentages except when the distribution was strongly skewed; in that case, the median and interquartile ranges are given. The χ^2 test or χ^2 test for trend was used to determine the significance of differences between sexes in the distribution of categorical data. The clinical characteristics of the continuous variables were compared between sexes by independent *t* tests. The subjects were then divided into quartiles of CRP. Continuous and dichotomous variables were compared by analysis of variance and χ^2 test among these quartiles, respectively. Post hoc analysis after analysis of variance was conducted

Table 1
Baseline characteristics of study subjects according to sex

	Total (n = 574)	Men (n = 300)	Women (n = 274)	*P* value
Age (y)	45.8 ± 9.8	45 ± 9.8	46.5 ± 9.7	.07
Smoking (%)	25.3%	43.7%	5.1%	<.001
Systolic BP (mm Hg)	114.8 ± 17.5	115.8 ± 16.2	113.7 ± 18.8	.15
Diastolic BP (mm Hg)	76.0 ± 10.6	78.1 ± 10.3	73.8 ± 10.4	<.001
Total cholesterol (mmol/L)	5.16 ± 0.93	5.22 ± 0.94	5.09 ± 0.93	.11
Triglycerides (mmol/L)[a]	1.31 (0.86-1.86)	1.53 (1.04-2.33)	1.03 (0.75-1.52)	<.001
HDL-C (mmol/L)[a]	1.40 (1.17-1.68)	1.24 (1.09-1.42)	1.59 (1.32-1.84)	<.001
BMI (kg/m^2)	24.3 ± 3.4	25.0 ± 3.1	23.5 ± 3.6	<.001
WC (cm)	85.0 ± 9.5	88.0 ± 7.6	81.8 ± 10.3	<.001
Fasting glucose (mmol/L)	5.32 ± 1.18	5.48 ± 1.44	5.14 ± 0.76	<.001
Fasting insulin (μU/mL)[a]	7.97 (6.15-10.87)	8.44 (6.50-11.5)	7.57 (5.87-10.34)	.005
Metabolic syndrome (%)	17.2%(99)	19.3%	15.0%	.185
Obese (%)	38.9%	47%	29.9%	<.001
CRP (mg/L)[a]	0.61 (0.25-1.21)	0.65 (0.29-1.23)	0.54 (0.24-1.18)	.15
HOMA-IR[a]	1.86 (1.40-2.61)	2.05 (1.54-2.70)	1.71 (1.28-2.38)	<.001

[a] Data with skewed distribution are presented as median (interquartile range) and logarithmically transformed before statistical testing to meet the assumption of normal distribution.

by the Bonferroni method. Multivariable analysis was performed using linear regression model with the stepwise method to determine the relationships between CRP and HOMA-IR as well as the various components of metabolic syndrome, including triglyceride, high-density lipoprotein cholesterol (HDL-C), and BP. C-reactive protein, HOMA-IR, triglycerides, and HDL-C were logarithmically transformed before statistical analysis to produce a normal distribution. A P value < .05 using a 2-sided test was considered statistically significant. The multivariable analyses was then adjusted for age and smoking. To explore the relationship between CRP, HOMA-IR, and the components of metabolic syndrome independent of abdominal obesity, the models were also adjusted for WC as a continuous variable. All statistical analyses were conducted with the SPSS statistical package for Windows version 12.0 (SPSS, Chicago, IL).

3. Results

3.1. Clinical and biochemical characteristics of subjects stratified by sex

A summary of demographic features, clinical and lipid profiles, anthropometric measurements, CRP levels, and HOMA-IR stratified by sex is provided in Table 1. No

Table 2
Characteristics of participants according to the quartiles of CRP

	Q1, n = 145	Q2, n = 142	Q3, n = 143	Q4, n = 144
CRP level	0.08-0.25	0.26-0.60	0.61-1.20	1.21-9.79
Age (y)	44.45 ± 9.37	45.74 ± 10.22	46.72 ± 9.75	46.20 ± 9.66
Male (n) (%)	71 (50.0%)	72 (50.7%)	80 (55.9%)	77 (53.5%)
Smoker (n) (%)*	26 (17.9%)	33 (23.2%)	35 (24.5%)	51 (35.4%)
Central obese (n) (%)*	37 (25.5%)	51 (35.9%)	61 (42.7%)	90 (62.5%)
Systolic BP (mm Hg)	111.03 ± 16.54	113.31 ± 17.15	115.75 ± 17.15	119.12 ± 18.98‡,§
Diastolic BP (mm Hg)	74.12 ± 10.53	75.85 ± 9.52	75.25 ± 10.65	78.88 ± 11.05‡
Fasting glucose (mmol/L)	5.14 ± 0.23	5.24 ± 0.61	5.29 ± 1.33	5.61 ± 1.63†,§
Cholesterol (mmol/L)	5.08 ± 0.96	5.12 ± 0.92	5.14 ± 0.63	5.28 ± 0.97
Triglyceride (mmol/L)[a]	1.00 (0.73-1.42)	1.32 (0.89-1.74)	1.31 (0.87-2.05)†	1.59 (1.17-2.47)‡,§
HDL-C (mmol/L)[a]	1.53 (1.30-1.76)	1.40 (1.17-1.74)	1.37 (1.14-1.71)†	1.27 (1.06-1.48)‡,§
LDL-C (mmol/L)	2.97 ± 0.91	2.97 ± 0.80	3.00 ± 0.78	3.11 ± 0.91
BMI (kg/m^2)	22.79 ± 2.99	23.80 ± 3.11	24.47 ± 3.09‡	26.11 ± 3.64‡,‖
WC (cm)	81.03 ± 8.32	83.20 ± 8.80	85.41 ± 8.28‡	90.35 ± 9.97‡,‖
HOMA-IR[a]	1.56 (1.18-2.01)	1.70 (1.35-2.37)	1.97 (1.50-2.60)‡,§	2.46 (1.75-3.54)‡,‖

LDL-C indicates low-density lipoprotein cholesterol.

[a] Data with skewed distribution are presented as median (interquartile range) and logarithmically transformed before statistical testing to meet the assumption of normal distribution.

* P < .01 for χ^2 test.

† P < .05 vs Q1 by Bonferroni method.

‡ P < .001 vs Q1 by Bonferroni method.

§ P < .05 vs Q2 by Bonferroni method.

‖ P < .001 vs Q2 by Bonferroni method.

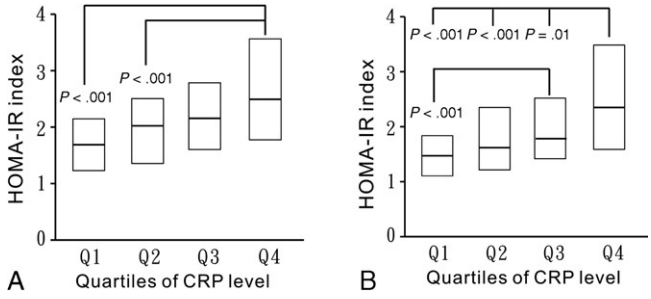

Fig. 1. Comparison of the HOMA-IR indexes among 300 Taiwanese men (A) and 274 Taiwanese women (B) between the quartiles of CRP level (Q1-Q4). Box plots demonstrate median and the 25th and 75th percentile value of HOMA-IR indexes.

statistically significant differences in age, systolic BP, cholesterol levels, frequency of metabolic syndrome, and levels of CRP were observed between sexes. Furthermore, the analysis showed that many variables were statistically significantly different between men and women. There was a higher percentage of current smokers ($P < .001$) and obesity ($P < .001$) in men than in women. Diastolic BP ($P < .001$), BMI ($P < .001$), WC ($P < .001$), triglycerides ($P < .001$), fasting insulin ($P = .005$), and HOMA-IR ($P < .001$) were also significantly higher in men than in women. In contrast, HDL-C levels ($P < .001$) were significantly lower in men than in women.

3.2. Relationships between CRP and conventional CHD risk factors

Differences in the conventional CHD risk factors according to the quartiles of CRP (Q1-Q4) are shown in Table 2. Current smoker and subjects with obesity differed significantly among the CRP quartiles as shown by the χ^2 test. Systolic BP, diastolic BP, and fasting glucose were higher in Q4 than in Q1 and Q2. Triglycerides, BMI, WC, and HOMA-IR index were significantly higher in Q3 and Q4 than in Q1 and Q2, whereas HDL-C was significantly lower in Q3 and Q4 than in Q1 and Q2.

Fig. 1 displays the distribution of HOMA-IR index after subjects were classified according to the quartiles of CRP. Post hoc analysis demonstrated statistically significant differences in the HOMA-IR index among the higher and lower CRP quartiles in both men and women (for men: Q1 vs Q4, $P < .001$; Q1 vs Q3, $P = .087$; Q2 vs Q4, $P < .001$; for women: Q1 vs Q4, $P < .001$; Q1 vs Q3, $P < .001$; Q2 vs Q4, $P < .001$).

Table 4
Multiple linear regression analysis of the relationship between CRP, factors of metabolic syndrome, and HOMA-IR, according to sex

	*P*1		*P*2	
	β coefficient	*P* value	β coefficient	*P* value
Men				
Triglycerides	0.269	.017	0.255	.025
HDL-C	−0.407	.156	−0.386	.179
Systolic BP	0.003	.163	0.003	.198
Diastolic BP	−0.001	.717	−0.001	.678
HOMA-IR	0.356	.005	0.298	.029
Women				
Triglycerides	0.111	.484	0.065	.676
HDL-C	−0.466	.133	−0.272	.376
Systolic BP	0.000	.917	0.001	.445
Diastolic BP	0.006	.163	−0.001	.215
HOMA-IR	0.900	<.001	0.722	<.001

P1: adjusted for age and smoking. P2: adjusted for age, smoking, and WC (as a continuous variable). Calculation of CRP, triglycerides, HDL-C, and HOMA-IR were based on log-transformed values.

3.3. CRP in relation to HOMA-IR and abdominal obesity

To explore the relationship between CRP and HOMA-IR independent of obesity, subjects were stratified according to sex and abdominal obesity; and the association between CRP and HOMA-IR was tested by linear regression analysis with log CRP as the dependent variable (Table 3). The HOMA-IR showed a significant association with CRP in obese men and both obese and nonobese women (for obese men: β coefficient, 0.770; $P < .001$; for nonobese women: β coefficient, 0.679; $P = .001$; for obese women: β coefficient, 1.129; $P < .001$). In addition, there was a trend for an association of HOMA-IR with CRP in nonobese men (β coefficient, 0.309; $P = .061$).

To evaluate the strength of the association between CRP and HOMA-IR as well as each of the components of metabolic syndrome, a multiple linear regression was performed (Table 4). After adjusting for age and smoking, only HOMA-IR in men and women, and triglycerides in men demonstrated a significant association with CRP. There was no significant association of CRP with HDL-C, systolic BP, or diastolic BP. These variables were then adjusted with

Table 3
Multiple linear regression analysis of the relationship between CRP and HOMA-IR, according to abdominal obesity and sex

Abdominal obesity	Men			Women		
	β coefficient	95% CI	*P* value	β coefficient	95% CI	*P* value
No	0.309	−0.015~0.633	.061	0.697	0.303~1.091	.001
Yes	0.770	0.367~1.173	<.001	1.129	0.729~1.530	<.001

Abdominal obesity is defined as subjects with WC ≥90 cm for men and WC ≥80 cm for women. All analyses are adjusted for age and smoking. Calculations of CRP and HOMA-IR are based on log-transformed values with log CRP as the dependent variable. CI indicates confidence interval.

WC in addition to age and smoking. The strength of the association of HOMA-IR with CRP after adjusting for WC was only mildly attenuated, but the association remained statistically significant in men and women. The result after controlling for BMI was virtually identical to the result after controlling for WC (data not shown).

4. Discussion

In this cross-sectional study of the correlation between insulin resistance and CRP concentration in nondiabetic Taiwanese population, we found a strong association between HOMA-IR and CRP concentration in both men and women in the stratified analysis by obesity. However, subjects with higher concentrations of CRP also had higher BP, increased anthropometric and lipid measurements, and a higher frequency of current smoking. These results indicate that CRP concentration was also influenced by many other clinical characteristics and factors of metabolic syndrome, which are also known to affect the level of HOMA-IR. To more precisely define the relationship between HOMA-IR and CRP concentration, we further examined this relationship after adjusting for these metabolic factors in addition to age and smoking. The association between HOMA-IR and CRP concentration remained statistically significant after adjusting for these covariates. Finally, WC was added into the multiple linear regression models. A positive association of HOMA-IR with CRP concentration was still evident after adjusting for WC, indicating that this association was independent of abdominal obesity in both men and women in the Taiwanese population.

Previous studies that examined the relationships among insulin resistance, CRP, and obesity were inconsistent. Several studies demonstrated that insulin resistance, as expressed by HOMA-IR, was significantly correlated with CRP concentrations in nondiabetic general populations. However, this correlation was abolished after adjusting for the parameters of obesity [13-15]. Similar observations were also made in a population that was at high risk for the development of type 2 diabetes mellitus [16]. In contrast, McLaughlin et al [10] reported that not all obese individuals had high CRP concentrations. Instead, CRP concentrations in insulin-sensitive, obese individuals were uniformly low' and elevated CRP concentrations were confined to those obese individuals who were also insulin resistant. The authors concluded that the relationship between CRP concentrations and insulin resistance was independent of obesity. In the Insulin Resistance Atherosclerosis Study, Festa et al [9] showed that CRP was strongly associated with insulin sensitivity, as assessed by a frequently sampled intravenous glucose tolerance test; and this association was independent of BMI. An additional study also demonstrated a strong association of fasting insulin with CRP concentration even after adjusting for BMI [12]. These studies, however, were limited to the European and North American populations. There is little information in the literature on the association between insulin resistance and CRP concentration in Asian populations. Our study investigated the relationship between HOMA-IR and CRP concentration in the nondiabetic Taiwanese general population and found that insulin resistance was strongly associated with CRP concentration, and this association was independent of abdominal obesity. This result was consistent with another Japanese study that demonstrated that the strength of the association between HOMA-IR and CRP was reduced, but the association remained statistically significant after adjusting for BMI [11].

There are several possible explanations for these contradictory findings, which are not necessarily exclusive. First, obesity, especially abdominal adiposity, might be a common antecedent of both CRP and insulin resistance; and the association of CRP with insulin resistance may thus be due to the association of obesity with both insulin resistance and the acute-phase inflammatory response. Hotamisligil et al [25] first introduced the concept of inflammation in relation to obesity and insulin resistance. The study demonstrated that adipocytes in a rodent model constitutively expressed tumor necrosis factor–α (TNF-α), a proinflammatory cytokine, and that neutralization of TNF-α by soluble TNF-α receptor decreased insulin resistance. Subsequent studies showed that adipose tissue in humans also expresses TNF-α and IL-6 constitutively [3,26]. Further work demonstrated that TNF-α and IL-6 could inhibit insulin receptor signal transduction [27,28], suggesting that inflammation plays a direct role in insulin resistance. The levels of CRP are predominantly modulated by the hepatic effects of IL-6 [29]. The release of inflammatory mediators by adipose tissue may account for the association between CRP levels and insulin resistance and also explain the reduction or elimination of this association after adjusting for obesity.

Second, insulin exerts an anti-inflammatory effect at the cellular and molecular level both in vitro and in vivo. Insulin has been shown to suppress several proinflammatory transcription factors, such as intracellular nuclear factor–κB, early growth response–1, and activating protein-1, as well as to suppress plasma concentrations of intracellular adhesion molecule–1 and monocyte chemotactic protein–1 [30,31]. Insulin also reduces the generation of reactive oxygen species by mononuclear cells and suppresses NADPH oxidase expression [31]. An interruption of insulin signal transduction because of insulin resistance would thus prevent the anti-inflammatory effect of insulin from being exerted. These evidences link the association of insulin resistance and CRP levels independent of obesity.

Finally, ethnic differences and genetic variations may play important roles in the status of CRP. Recent studies confirm that CRP concentrations vary significantly among ethnic groups [15,20-22], with the lowest concentration of CRP in Chinese [20-22] and Japanese populations [21]. Chinese and Japanese populations have a lower BMI than other races [20-22]. However, because adjusting for BMI

substantially reduces but does not eliminate the ethnic differences in CRP distribution [20,21], visceral adiposity may only partially explain the differences in CRP concentrations among ethnic groups. There is further evidence that polymorphisms in the CRP gene are associated with circulating CRP concentrations, with frequency differences observed in different ethnic groups [32,33]. It is possible that, in Chinese and Japanese populations, CRP concentration is influenced more by genetic variation and less by visceral adiposity due a reduced BMI. This may account for the observation that the association of CRP concentration with insulin resistance depends on obesity in some European and North American populations [13-15], but the association is independent of abdominal obesity in Chinese and Japanese populations.

Our study has several strengths. The subjects we included were all of Han-Chinese origin, a population in which the relationships among CRP, insulin resistance, and abdominal obesity have not been evaluated before. Besides, we used a uniform protocol, including standardized clinical assessments, anthropometric measurements, and biochemical measurements in a centralized core laboratory. However, a number of possible limitations of our study merit mention. First, because of the study's cross-sectional nature, our results do not establish causality. Second, subjects taking BP-lowering agents were not excluded from our study, which might have influenced the association of CRP levels with BP and might have also affected the association of CRP with insulin resistance in the multivariable analysis. However, the number of these subjects was relatively small (12.7% in men and 9.9% in women). Furthermore, an association between CRP and HOMA-IR was still found that was independent of abdominal adiposity in both men and women after excluding subjects who were taking BP-lowering agents (data not shown). Third, we used WC as a surrogate for abdominal obesity instead of more scientific measurements such as dual-energy x-ray absorptiometry or abdominal computed tomography scan; and this might limit the accurate measurement of abdominal obesity. However, WC is the simplest method that is widely used for measurement of abdominal obesity. Recent work in a large Chinese population also demonstrated the good correlation of WC and BMI with trunk obesity, as measured by dual-energy x-ray absorptiometry [34]. These evidences support us to use the WC to represent abdominal obesity in the Chinese population. Nevertheless, abdominal obesity, defined by WC, may only partially reflect the composition of visceral adipose tissue, which is more important for the development of cardiovascular risk factors and metabolic syndrome. Our results demonstrate that the association of insulin resistance with CRP is independent of abdominal obesity, but whether this association is independent of visceral adipose tissue needs further investigation. Finally, we used the HOMA-IR to assess insulin resistance instead of the euglycemic-hyperinsulinemic clamp method, which is thought to be the best way to measure insulin resistance. Nevertheless, the use of euglycemic-hyperinsulinemic clamp method in clinical practice is limited because of its invasiveness and high cost. The HOMA-IR is the simplest index of insulin resistance, particularly in epidemiologic studies. Moreover, the HOMA-IR has been shown to be strongly correlated with the euglycemic-hyperinsulinemic clamp method in various clinical trials. Thus, the HOMA-IR can be considered to be a reliable marker of insulin resistance.

In conclusion, we have shown that elevated CRP concentrations, even when they are within the clinically normal range, are strongly associated with HOMA-IR in both men and women in the nondiabetic Taiwanese population. These results indicate that subclinical inflammation plays an important role in insulin resistance. The association between CRP and insulin resistance was independent of WC, suggesting that abdominal obesity can only partly explain the link between subclinical inflammation and insulin resistance. Other factors, such as a genetic predisposition toward elevated CRP concentrations in the Taiwanese population, may account for these results.

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