Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy

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ORIGINAL RESEARCH

Performance of body mass index and percentage of body fat in predicting cardiometabolic risk factors in Thai adults

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Background: Body mass index (BMI) and percentage of body fat (PBF) are used to measure obesity; however, their performance in identifying cardiometabolic risk in Southeast Asians is unclear. Generally, Asian women have higher PBF and lower BMI than do men and other ethnic populations. This study was conducted to address whether a discord exists between these measures in predicting obesity-related cardiometabolic risk in a Thai population and to test whether associations between the measures and risk factors for cardiovascular disease have a sex-specific inclination.

Methods: A total of 234 (76 men and 158 women) outpatients were recruited. BMI obesity cutoff points were ≥25.0 and ≥27.0 kg/m^2 and PBF cutoff points were ≥35.0% and ≥25.0% for women and men, respectively. Blood samples were analyzed for total cholesterol, triglycerides, low-density lipoprotein-cholesterol, high-density lipoprotein-cholesterol, lipoprotein subclasses, apolipoprotein A-I, apolipoprotein B, glucose, hemoglobin A1c, insulin, high-sensitive C-reactive protein (hsCRP), adiponectin, leptin, and 25-hydroxyvitamin D.

Results: Twenty-five percent of participants classified as normal-BMI had excessive fat, whereas 9% classified as normal-PBF had excessive BMI. Good relationships were found between BMI and PBF using sex stratification (R^2 >0.5). The prevalence of metabolic syndrome was markedly increased in overweight and/or excess body fat groups compared with lean group. Logistic regression analyses showed that BMI was the best predictor of hypertension. BMI was an independent predictor of insulin resistance, hyperglycemia, hypertriglyceridemia, and hyperleptinemia in women, whereas PBF was for men. However, PBF proved to be a good indicator for atherogenic lipoprotein particles in both sexes. Notably, neither index predicted increased hsCRP or 25-hydroxyvitamin D insufficiency.

Conclusion: Considerable sex-specific variations were observed between BMI and PBF in their associations with and predictability of numerous cardiometabolic biomarkers. No single measure provides a comprehensive risk predication as shown herein with the Thai population, and therefore both should be applied in screening activities.

Keywords: obesity, body mass index, percentage of body fat, Southeast Asian population, cardiometabolic risk biomarkers, obesity-related metabolic disorders

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Introduction

The prevalence of obesity is increasing globally, and obesity is thus becoming a major public health concern.[1,2] The global obesity prevalence is predicted to reach 18% in men and over 21% in women by 2025.[2] Obesity results from a lack of balance between calorie intake and energy expenditure, which increases adipose tissue and activates endocrine entities.[3] Adipose tissue secretes adipokines, which influence many metabolic

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functions (including appetite, satiety, energy expenditure, activity, insulin sensitivity and secretion, glucose and lipid metabolism, fat distribution, neuroendocrine regulation, and immune system function). Consequently, obesity plays a major role in causing cardiometabolic complications including hypertension, type II diabetes mellitus, dyslipidemia, and certain cancers.[4]

Although visceral fat mass and, in particular, liver fat content have been shown to be valuable in predicting cardiometabolic risk, conducting such measurements is limited by costs, availability of instruments, and the requirement of highly trained technicians.[5] By contrast, the body mass index (BMI) is easy to use because it is calculated using body weight in kilograms divided by the square of an individual's height in meters (kg/m^2). As such, it is the most commonly used measure of weight status in epidemiology, clinical care, and clinical nutrition. BMI represents weight adjusted for height and aims to represent fat mass, fat-free mass, and body fluid. Scientific evidence indicates that a high BMI is associated with being overweight and obese, and is a predictor for all-cause mortality.[6,7] However, BMI does not address fat distribution or discriminate between lean mass and fat mass, and these need to be defined using different methods because they represent body adiposity.[8] In this respect, the percentage of body fat (PBF) is an effective measure of adiposity because it has been shown to be associated with metabolic dysregulation, regardless of body weight.[9] Large-scale studies have shown that BMI correlates highly with PBF and such correlation is stable with height.[10,11] For example, a study conducted on a US adult population demonstrated a high relationship between BMI and PBF, enabling the prediction of PBF based on BMI classification.[11] In global clinical practice, both BMI and PBF are widely accepted as accurate measures of obesity.[12]

On the basis of general trends in the relationship between BMI and morbidity and mortality rates, the World Health Organization uses BMI cutoff points for classifying overweight and obesity in the global adult population that are greater than, or equal to, 25 and 30 kg/m^2, respectively.[13] These cutoff points have been applied in research and clinical practice, regardless of age, sex, or race/ethnicity.[14] However, considering a population-specific BMI cutoff in Asian populations is necessary because Asians have different contributions of bone mass, muscle mass, and fluid to body weight than European populations, resulting in a reduced association between BMI, PBF, and health risk.[15] In addition, Asian populations have higher or lower PBF at a specific BMI than white or European populations, and this is dependent on cultural subgroups, social and economic conditions, and nutritional factors.[15,16] For example, a recent study conducted with Asian–Americans showed that BMI did not accurately reflect underlying adiposity and thus showed poor sensitivity in detecting PBF, especially in women.[17] Women have a higher PBF than men at all ages and in all ethnic groups. A relatively high PBF may put Asian–American women at risk of future obesity-related diseases. In Thai populations, Pongchaiyakul et al determined the optimal cutoff values of BMI for defining obesity in men and women.[18] However, the PBF cutoff points do not agree with those of BMI with respect to given sex-specific obesity cutoff points. For example, the optimum BMI obesity cutoff point for women (≥25.0 kg/m^2) is actually lower than that for men (≥27.0 kg/m^2), whereas the corresponding PBF cutoff point is higher for women (≥35%) than for men (≥25%). Therefore, BMI and PBF values are not directly comparable.

Obesity causes chronic inflammatory diseases and mainly contributes to the development of insulin resistance, several components of metabolic syndrome (MetS), and systematic low-grade inflammation. As mentioned, BMI and PBF results associated with obesity-related risk factors are controversial with respect to differing racial/ethnicity populations, and less is known about the performance of these obesity measures in Southeast Asian countries, most of which are classified as "developing countries".[14,19] Therefore, the aim of this study was to compare the performance of BMI and PBF in identifying major risk factors and new emerging risk factors for cardiovascular disease (CVD) in an adult Thai population. We also conducted the study to test whether associations between the measures and cardiometabolic risk factors have a sex-specific inclination. Information obtained in this study could be applied across Southeast Asian populations with similar ethnic and cultural subgroups, degrees of urbanization, and social and economic determinants of health and nutrition statuses.

Materials and methods

Study participants

This cross-sectional study enrolled a total of 234 outpatients who were aged at least 20 years and were receiving wellness check-ups in the general clinic at Ramathibodi Hospital, a hospital associated with the Faculty of Medicine of Mahidol University in Bangkok, Thailand. Patient exclusion criteria included a prior history of CVD or taking lipid-lowering drugs, or having had cancer, end-stage chronic kidney disease, or another serious medical condition. Data were obtained using a questionnaire and physical examination. All participants provided written informed consent, and the study

protocol was reviewed and approved by the Committee on Human Rights Related to Research Involving Human Subjects, Faculty of Medicine, Ramathibodi Hospital, Mahidol University (MURA2017/348). All methods were carried out in accordance with the Declaration of Helsinki.

Body composition analysis was conducted using a multifrequency bioelectrical impedance analyzer (Biospace™ InBody 720 body composition analyzer; GE Healthcare, Chicago, IL, USA). Criteria for defining obesity in the adult Thai population were a BMI level of ≥25.0 kg/m^2 for women and ≥27.0 kg/m^2 for men, and a PBF level of ≥35% for women and ≥25% for men.[18] Participants with BMI measurements below or above mentioned cutoff points were defined as being of a normal weight or overweight, respectively. Participants with PBF measurements below or above mentioned cutoff points were defined as lean or fat, respectively. MetS was defined using National Cholesterol Education Program-Third Adult Treatment Panel (NCEP ATP III) criteria modified for Asian populations.[20]

Biochemical measurements

Blood samples were collected during a fasting state. All samples were analyzed for total cholesterol, triglycerides, low density lipoprotein-cholesterol (LDL-C), high density lipoprotein-cholesterol (HDL-C), glucose, apolipoprotein (apo) A-I (apoA-I), apoB, lipoprotein subclass, high-sensitive C-reactive protein (hsCRP), insulin, adiponectin, leptin, 25-hydroxyvitamin D, and hemoglobin A1c (HbA1c). Lipid profiles and glucose were measured using enzymatic methods (Siemens Medical Solution Diagnostics, Tarrytown, NY, USA). ApoA-I, apoB, and hsCRP were measured using a Siemens BN ProSpec, and adiponectin and leptin levels were quantified using the ELISA system (Mediagnost Gesellschaft für Forschung und Herstellung von Diagnostika GmbH, Kusterdigen, Germany). HbA1c was determined using the Cobas Integra immunoturbidimetric method (Roche Diagnostics Ltd., Rotkreuz, Switzerland), and insulin and 25-hydroxyvitamin D levels were determined using the Immulite H2975 (Siemens Medical Solution Diagnostics) and LIAISON® Analyzer (DiaSorin, Stillwater, MN, USA), respectively. Insulin resistance was estimated using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), the index for which was calculated according to the following formula: HOMA-IR = fasting insulin (μIU/mL) × fasting glucose (mmol/L)/22.5.

Lipoprotein subclass was analyzed using polyacrylamide tube gel electrophoresis (Lipoprint™; Quantimetrix, Redondo Beach, CA, USA), which electrophoretically separates plasma lipoproteins into the following bands: very low density (VLDL); intermediate low density (IDL): midband-C (MIDC), midband-B (MIDB) and midband-A (MIDA); large-buoyant LDL (LDL1 and LDL2); small-dense LDL (LDL3–LDL7); and HDL. Relative areas for each lipoprotein band were determined by densitometry and multiplied by total cholesterol concentration to yield the amount of cholesterol for each band. Mean LDL particle sizes were computed. The atherogenic lipoprotein pattern was defined by a small-dense LDL of >0.16 mmol/L or a mean LDL particle size of <26.5 nm.

Statistical analyses

Data are expressed as mean values (standard error of mean), and categorical variables are presented as numbers and percentages. Data were compared using the χ^2 test, Student's *t*-test, Mann–Whitney *U* test, or ANOVA, as appropriate. The correlation between BMI and PBF was analyzed using Pearson's correlation test. All participants were stratified into four groups based on BMI and PBF cutoff points: normal weight and lean (Group A), BMI <25.0 kg/m^2 for women and <27.0 kg/m^2 for men, and PBF <35% for women and <25% for men; overweight and lean (Group B), BMI ≥25.0 kg/m^2 for women and ≥27.0 kg/m^2 for men, and PBF <35% for women and <25% for men; normal weight and fat (Group C), BMI <25.0 kg/m^2 for women and <27.0 kg/m^2 for men, and PBF ≥35% for women and ≥25% for men; and overweight and fat (Group D), BMI ≥25.0 kg/m^2 for women and ≥27.0 kg/m^2 for men, and PBF ≥35% for women and ≥25% for men. To conduct a risk analysis among patient groups, the odds ratios (ORs) and 95% confidence intervals (CIs) of cardiometabolic risk factors (classified as dichotomous variables) in Groups B, C, and D were compared with those in Group A (used as a reference) and analyzed using the multinomial logistic regression model adjusted for sex, age group (divided into four groups: <40, 40–<50, 50–<60, ≥60 years), and smoking status. A backward, stepwise multivariable logistic regression model adjusted for age, height, and smoking status was used to determine the association of each cardiometabolic risk (set as a dependent variable) with BMI and PBF (set as independent variables). Sex stratification was used in the analysis. Outcomes were considered statistically significant when *P*-values were <0.05, and all analyses were performed using SPSS version 18 (SPSS Inc., Chicago, IL, USA).

Results

Characteristics and biomarkers of study population

Table 1 presents a summary of the demographic characteristics and biochemical test results for all participants (76 men

Table 1 Characteristics of participants defined as nonobese and obese using obesity measures

Variables	Body mass index			Percentage of body fat		
	Normal weight (N = 169)	Overweight (N = 65)	*P*-value	Lean (N = 139)	Fat (N = 95)	*P*-value
Male, n (%)	56 (33.1)	20 (30.8)	0.758	46 (33.1)	30 (31.6)	0.808
Age, years	51.4 (1.1)	52.7 (1.4)	0.509	49.4 (1.2)	55.3 (1.1)	0.001
Body mass, kg	56.8 (0.6)	71.6 (1.4)	<0.001	56.9 (0.8)	66.8 (1.2)	<0.001
Height (cm)	160.4 (0.6)	158.7 (1.0)	0.145	160.9 (0.7)	158.5 (0.8)	0.026
Waist circumference, cm	80.5 (0.8)	93.6 (1.1)	<0.001	79.7 (1.0)	90.7 (0.9)	<0.001
Body mass index, kg/m^2	22.00 (0.16)	28.32 (0.38)	<0.001	21.88 (0.21)	26.50 (0.37)	<0.001
Lean body mass, kg	22.31 (0.41)	24.77 (0.80)	0.002	23.19 (0.50)	22.70 (0.58)	0.517
Body fat mass, kg	15.80 (0.35)	26.34 (0.79)	<0.001	14.49 (0.33)	24.87 (0.59)	<0.001
Body fat mass, %	27.95 (0.59)	37.11 (0.95)	<0.001	25.72 (0.56)	37.43 (0.65)	<0.001
Waist-hip fat ratio	0.890 (0.004)	0.945 (0.007)	<0.001	0.879 (0.004)	0.945 (0.005)	<0.001
Visceral fat area, cm^2	86.6 (2.0)	123.8 (3.5)	<0.001	79.7 (2.0)	122.0 (2.5)	<0.001
Biochemical measures						
Insulin, μIU/mL	3.98 (0.32)	6.85 (0.68)	<0.001	3.64 (0.33)	6.45 (0.55)	<0.001
HOMA-IR	0.972 (0.083)	1.935 (0.264)	<0.001	0.895 (0.100)	1.743 (0.188)	<0.001
Glucose, mmol/L	5.34 (0.08)	5.84 (0.20)	0.004	5.27 (0.08)	5.80 (0.15)	0.001
HbA1c, mmol/mol	42.4 (0.7)	45.2 (1.1)	0.038	41.7 (0.8)	45.3 (0.9)	0.003
Triglycerides, mmol/L	1.20 (0.04)	1.66 (0.10)	<0.001	1.15 (0.05)	1.58 (0.08)	<0.001
Total cholesterol, mmol/L	5.67 (0.08)	5.65 (0.13)	0.865	5.66 (0.08)	5.68 (0.11)	0.875
HDL-C, mmol/L	1.47 (0.03)	1.29 (0.04)	<0.001	1.49 (0.03)	1.32 (0.03)	<0.001
LDL-C, mmol/L	3.44 (0.06)	3.51 (0.10)	0.593	3.42 (0.07)	3.53 (0.09)	0.344
Lipoprotein subclass, mmo/L						
VLDL	0.88 (0.02)	0.98 (0.03)	0.005	0.87 (0.02)	0.95 (0.03)	0.014
MIDC	0.47 (0.01)	0.48 (0.02)	0.853	0.46 (0.01)	0.49 (0.02)	0.137
MIDB	0.40 (0.01)	0.40 (0.02)	0.797	0.40 (0.01)	0.41 (0.01)	0.677
MIDA	0.55 (0.02)	0.51 (0.03)	0.261	0.55 (0.02)	0.52 (0.02)	0.339
LDL1	1.08 (0.02)	1.01 (0.05)	0.133	1.10 (0.03)	1.00 (0.04)	0.039
LDL2	0.69 (0.02)	0.72 (0.03)	0.441	0.68 (0.02)	0.73 (0.03)	0.187
Small-dense LDL	0.23 (0.02)	0.36 (0.05)	0.009	0.20 (0.02)	0.36 (0.04)	<0.001
Mean LDL particle size, nm	26.80 (0.04)	26.58 (0.08)	0.005	26.84 (0.04)	26.59 (0.06)	<0.001
Non-HDL-C, mmol/L	4.19 (0.08)	4.34 (0.12)	0.308	4.16 (0.08)	4.34 (0.11)	0.173
ApoA-I, mg/dL	160.2 (1.9)	152.3 (3.2)	0.034	161.6 (2.1)	152.7 (2.6)	0.009
ApoB, mg/dL	97.8 (1.7)	103.8 (2.7)	0.058	96.4 (1.7)	104.0 (2.4)	0.009
hsCRP, mg/L	1.811 (0.352)	3.670 (0.837)	0.016	1.315 (0.177)	3.809 (0.795)	<0.001
25-hydroxyvitamin D, nmol/L	53.0 (1.5)	49.6 (2.0)	0.208	53.0 (1.8)	50.6 (1.5)	0.310
Leptin, ng/mL	8.04 (0.45)	16.66 (1.36)	<0.001	7.19 (0.47)	15.26 (1.00)	<0.001
Adiponectin, mg/mL	23.00 (1.29)	17.06 (1.30)	0.009	23.45 (1.48)	18.21 (1.16)	0.012

Notes: Data except for number (%) are the mean (standard error of mean). All biochemical markers are expressed in Système International units; conversions to conventional units are as follows: fasting glucose (mg/dL), multiply by 18.02; HbA1c (%), use the formula: [0.0915 HbA1c (mmol/mol) + 2.15]; triglycerides (mg/dL), multiply by 88.5; cholesterol (mg/dL), multiply by 38.6; 25-hydroxyvitamin D (ng/mL), multiply by 0.40.

Abbreviations: ApoA-I, apolipoprotein A-I; ApoB, apolipoprotein B; HbA1c, hemoglobin A1c; HDL, high density lipoprotein; HDL-C, high density lipoprotein-cholesterol; HOMA-IR, Homeostasis Model Assessment of Insulin Resistance; hsCRP, high sensitive C-reactive protein; LDL, low density lipoprotein; LDL-C, low density lipoprotein–cholesterol; MID, intermediate density lipoprotein midband; VLDL, very low density lipoprotein.

and 158 women) who had a mean age of 51.8 years (min–max: 21–79 years) and were classified as obese or nonobese using BMI or PBF cutoff points. More participants exceeded the PBF cutoff for fat (40.6%) than for BMI-based overweight (27.8%). Participants classified as either overweight or fat had a significantly higher body fat mass, waist–hip fat ratio, and visceral fat area than those classified as normal weight or lean. A wide range of PBF (7.3%–50.7%) was observed among normal-weight participants. Similarly, a wide range of BMI (16.9–29.5 kg/m^2) was observed among lean participants. The results obtained for metabolic biomarkers were similar for the normal-weight and overweight groups and the lean and fat groups, with the exception of LDL1 and apoB, which showed significant differences between the lean and fat groups. The following were noted in participants who were considered overweight or fat compared with the normal-weight or lean group: higher levels of glucose homeostasis markers (insulin, HOMA-IR, fasting glucose, and HbA1c),

triglycerides, VLDL, small-dense LDL, apoB, leptin, and hsCRP, but lower levels of HDL-C, ApoA-I, and adiponectin concentrations and mean LDL particle sizes. However, the results revealed no significant differences in mean concentrations of total cholesterol, LDL-C, IDL-C (MIDC to MIDA), non-HDL-C, and 25-hydroxyvitamin D between the normal-weight and overweight or lean and fat groups.

Correlation between BMI and PBF

The correlation between BMI and PBF for all participants is shown in Figure 1A. Linear regression statistics revealed a moderate relationship between BMI (x) and PBF (y): $y = 1.25\times + 0.82$, $R^2 = 0.287$. A superior relationship was found with respect to sex stratification, where linear regression statistics were $y = 1.51\times - 13.20$, $R^2 = 0.556$ for men (Figure 1B) and $y = 1.44\times + 0.05$, $R^2 = 0.522$ for women (Figure 1C).

Characteristics and biomarkers of groups based on different obesity measures

Participants were categorized into four groups based on whether they exceeded BMI or PBF cutoff points. The proportions of men did not differ among all groups (Table 2). Of participants classified as normal weight, 25% had higher than cutoff values for PBF, whereas 9% of those classified as lean had a BMI that was higher than the cutoff value. For body composition, significant differences were observed between parameter values for all four groups, particularly with respect to the waist-to-hip fat ratios and visceral fat areas, which were clearly elevated in the participants with normal weight and fat and overweight and fat. A marked difference was found between the groups with respect to risk for individual components of MetS. Abdominal obesity, hypertension, hypertriglyceridemia, and hyperglycemia were more highly prevalent in the subjects with overweight and fat, but those with overweight and lean had the highest prevalence of low HDL-C. The results indicated a marked increase in the prevalence of MetS (more than 50%) in the groups of overweight and/or fat compared with normal weight and lean group.

Statistically significant differences were observed among the groups for most of the monitored variables, including glucose homeostatic biomarkers (insulin, HOMA-IR, glucose, and HbA1c), lipid biomarkers (VLDL, small-dense LDL, LDL particle size, triglycerides, HDL-C, and apoA-I), hsCRP, leptin, and adiponectin, as shown in Table 3. However, no significant differences in the levels of apoB and 25-hydroxyvitamin D were observed between the groups.

To compare the risk of cardiometabolic risk factors in the groups of overweight and/or fat with that of normal weight and lean, a multinomial logistic regression model was applied (Figure 2). The ORs (95% CIs) for hypertension (Figure 2A) were significant in Group B, overweight and lean (7.28 [1.86–28.56]), and Group D, overweight and fat, (5.61 [2.51–12.54]) but they were not significant in Group C, normal weight and fat (2.05 [0.88–4.80]). Insulin resistance (Figure 2B) was statistically significant in normal weight and fat and overweight and fat groups: ORs (95% CIs) were 2.43 (1.01–5.84) and 6.39 (2.97–13.77), respectively. However, impaired fasting glucose was only statistically significant in overweight and fat group (3.36 [1.59–7.11]) (Figure 2C). By contrast, there were no significant differences in the increased risk of HbA1c (Figure 2D) between all groups. For the lipid metabolic profile, the participants with overweight and/or fat showed a significantly high risk of hypertriglyceridemia (Figure 2E), with the corresponding ORs (95% CI) being 5.33 (1.40–20.29), 2.80 (1.19–6.60), and 4.49 (2.03–9.92), respectively. Similarly, these participants showed a significant risk of low HDL-C (Figure 2F); however, large ORs were observed in overweight and lean group (6.71 [1.81–24.86]) and overweight and fat group (4.23 [1.90–9.44]). For the atherogenic lipoprotein pattern, the participants with overweight showed statistically significant ORs for increasing small-dense LDL (Figure 2G) and decreasing mean LDL particle size (Figure 2H).

Association between BMI and PBF and cardiometabolic risk factors stratified by sex

A backward, stepwise removal process was applied to remove cardiometabolic risk factors exhibiting no significant ($P > 0.05$) association with BMI or PBF, and the remaining variables adjusted for age, height, and smoking status for analysis are shown in Table 4. BMI was associated with hypertension for both sexes. HOMA-IR and fasting glucose were associated with PBF for men, but were associated with BMI for women. HbA1c, hsCRP, and 25-hydroxyvitamin D were not associated with any measure for either sex. Differences were observed with respect to an association between the measures and lipid metabolic biomarkers. Similar to fasting glucose and HOMA-IR, triglycerides were associated with PBF for men but with BMI for women. HDL-C was related to BMI for both sexes, but atherogenic lipoprotein patterns (including small-dense LDL and mean LDL particle size) were related to PBF for both sexes. For adipokines,

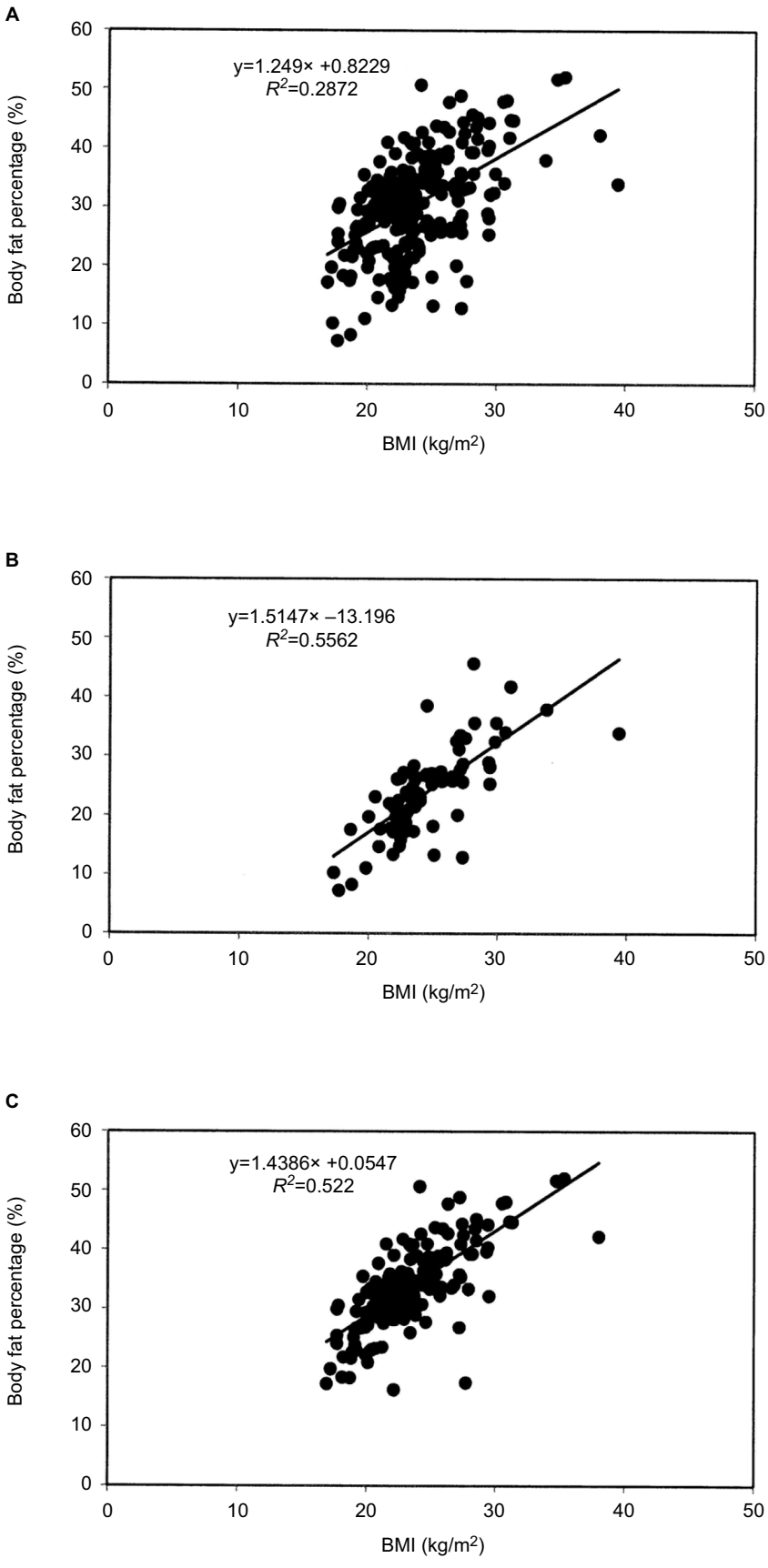

Figure 1 Correlation plots of body mass index (BMI) versus percentage of body fat (PBF) in (**A**) all participants; (**B**) men; and (**C**) women.

Table 2 Characteristics of participants by group, as classified by BMI and PBF

Variables[a]	Categories of obesity indices[b]				*P*-value
	Group A (N = 126)	Group B (N = 13)	Group C (N = 43)	Group D (N = 52)	
Male, n (%)	42 (33.3)	4 (30.8)	14 (32.6)	16 (30.8)	0.995
Age, years	49.4 (1.3)	49.3 (3.2)	57.3 (1.5)	53.6 (1.6)	0.005
Smoke, n (%)	16 (12.8)	3 (23.1)	7 (16.7)	7 (13.5)	0.736
Height, cm	160.7 (0.7)	163.1 (2.2)	159.6 (1.2)	157.6 (1.1)	0.058
Body mass index, kg/m^2	21.34 (0.17)	27.21 (0.36)	23.96 (0.19)	28.60 (0.45)	<0.001
Bioelectrical impedance analysis					
Lean body mass, kg	22.55 (0.48)	29.47 (1.87)	21.61 (0.79)	23.59 (0.82)	<0.001
Body fat mass, kg	13.93 (0.31)	19.88 (1.17)	21.14 (0.41)	27.96 (0.80)	<0.001
Body fat mass, %	25.49 (0.58)	27.92 (2.01)	35.04 (0.93)	39.40 (0.82)	<0.001
Waist-hip fat ratio	0.876 (0.004)	0.902 (0.018)	0.932 (0.005)	0.955 (0.007)	<0.001
Visceral fat area, cm^2	77.86 (2.02)	97.00 (5.80)	111.71 (2.60)	130.99 (3.60)	<0.001
Abdominal obesity, n (%)[c]	35 (27.8)	12 (92.3)	33 (75.0)	50 (98.0)	<0.001
Hypertension, n (%)[d]	22 (17.5)	6 (46.2)	15 (34.9)	27 (51.9)	<0.001
Triglycerides ≥1.70 mmol/L, n (%)	18 (14.3)	5 (38.5)	16 (37.2)	22 (42.3)	<0.001
HDL-C <1.04 mmol/L (men) or <1.30 mmol/L (women), n (%)	17 (13.5)	6 (46.2)	14 (32.6)	20 (38.5)	<0.001
Hyperglycemia, n (%)[e]	29 (23.0)	5 (38.5)	16 (37.2)	27 (51.9)	0.002
Metabolic syndrome, n (%)[f]	18 (14.3)	7 (53.8)	22 (51.2)	34 (65.4)	<0.001

Notes: [a]Data except for number (%) are the mean (standard error of mean). [b]Individual group is defined as follows: Group A (normal-weight and lean), BMI <25.0 kg/m^2 for women and <27.0 kg/m^2 for men and PBF <35% for women and <25% for men; Group B (overweight and lean), BMI ≥25.0 kg/m^2 for women and ≥27.0 kg/m^2 for men and PBF <35% for women and <25% for men; Group C (normal-weight and fat), BMI <25.0 kg/m^2 for female and <27.0 kg/m^2 for men and PBF ≥35% for women and ≥25% for men; and Group D (overweight and fat), BMI ≥25.0 kg/m^2 for women and ≥27.0 kg/m^2 for men and PBF ≥35% for women and ≥25% for men. [c]Defined as waist circumference ≥90 cm for men or ≥80 cm for women. [d]Defined as systolic ≥130 and/or diastolic ≥85 mmHg or treatment with antihypertensive drug. [e]Defined as fasting glucose ≥5.55 mmol/L or previous diagnosis of diabetes. [f]Metabolic syndrome is defined using the NCEP ATP III criteria modified for Asian population.[20]

Abbreviations: BMI, body mass index; PBF, percentage of body fat; HDL-C, high density lipoprotein-cholesterol; NCEP ATP III, National Cholesterol Education Program-Third Adult Treatment Panel.

Table 3 Comparison of metabolic biomarkers between groups defined using different obesity measures

Variables[a]	Categories of obesity indices[b]				*P*-value
	Group A N = 126	Group B N = 13	Group C N = 43	Group D N = 52	
Insulin, μIU/mL	3.52 (0.33)	4.75 (1.54)	5.33 (0.79)	7.37 (0.75)	<0.001
HOMA-IR	0.850 (0.087)	1.330 (0.578)	1.328 (0.195)	2.087 (0.297)	<0.001
Glucose, mmol/L	5.24 (0.08)	5.46 (0.27)	5.63 (0.18)	5.94 (0.23)	0.004
HbA1c, mmol/mol	41.5 (0.8)	43.7 (2.3)	45.0 (1.3)	45.6 (1.3)	0.023
VLDL, mmol/L	0.87 (0.02)	0.98 (0.08)	0.92 (0.04)	0.97 (0.04)	0.020
Small-dense LDL, mmol/L	0.20 (0.02)	0.28 (0.07)	0.34 (0.062)	0.38 (0.06)	0.003
Mean LDL particle size, nm	26.86 (0.04)	26.68 (0.13)	26.62 (0.09)	26.55 (0.09)	0.002
Triglycerides, mmol/L	1.11 (0.05)	1.58 (0.20)	1.45 (0.10)	1.68 (0.14)	<0.001
HDL-C, mmol/L	1.51 (0.03)	1.27 (0.10)	1.34 (0.05)	1.30 (0.04)	<0.001
ApoA-I, mg/dL	163.0 (2.3)	148.0 (7.4)	151.9 (3.8)	153.4 (3.5)	0.011
ApoB, mg/dL	96.1 (1.9)	99.5 (3.9)	102.8 (3.7)	104.9 (3.2)	0.064
hsCRP, mg/L	1.232 (0.185)	2.118 (0.565)	3.507 (1.249)	4.058 (1.032)	0.004
25-hydroxyvitamin D, nmol/L	53.8 (1.9)	45.7 (4.1)	50.5 (1.9)	50.6 (2.2)	0.339
Leptin, ng/mL	6.70 (0.44)	11.72 (2.23)	12.02 (1.02)	18.02 (1.58)	<0.001
Adiponectin, μg/mL	24.07 (1.59)	17.75 (3.73)	19.79 (1.98)	16.87 (1.33)	0.026

Notes: [a]Data are given as mean (standard error of mean). [b]Individual group is defined as in Table 2.

Abbreviations: ApoA-I, apolipoprotein A-I; ApoB, apolipoprotein B; hsCRP, high sensitive C-reactive protein; HbA1c, hemoglobin A1c; HOMA-IR, Homeostasis Model Assessment of Insulin Resistance; HDL-C, high density lipoprotein-cholesterol; hsCRP, high sensitive C-reactive protein; LDL, low density lipoprotein; VLDL, very low density lipoprotein.

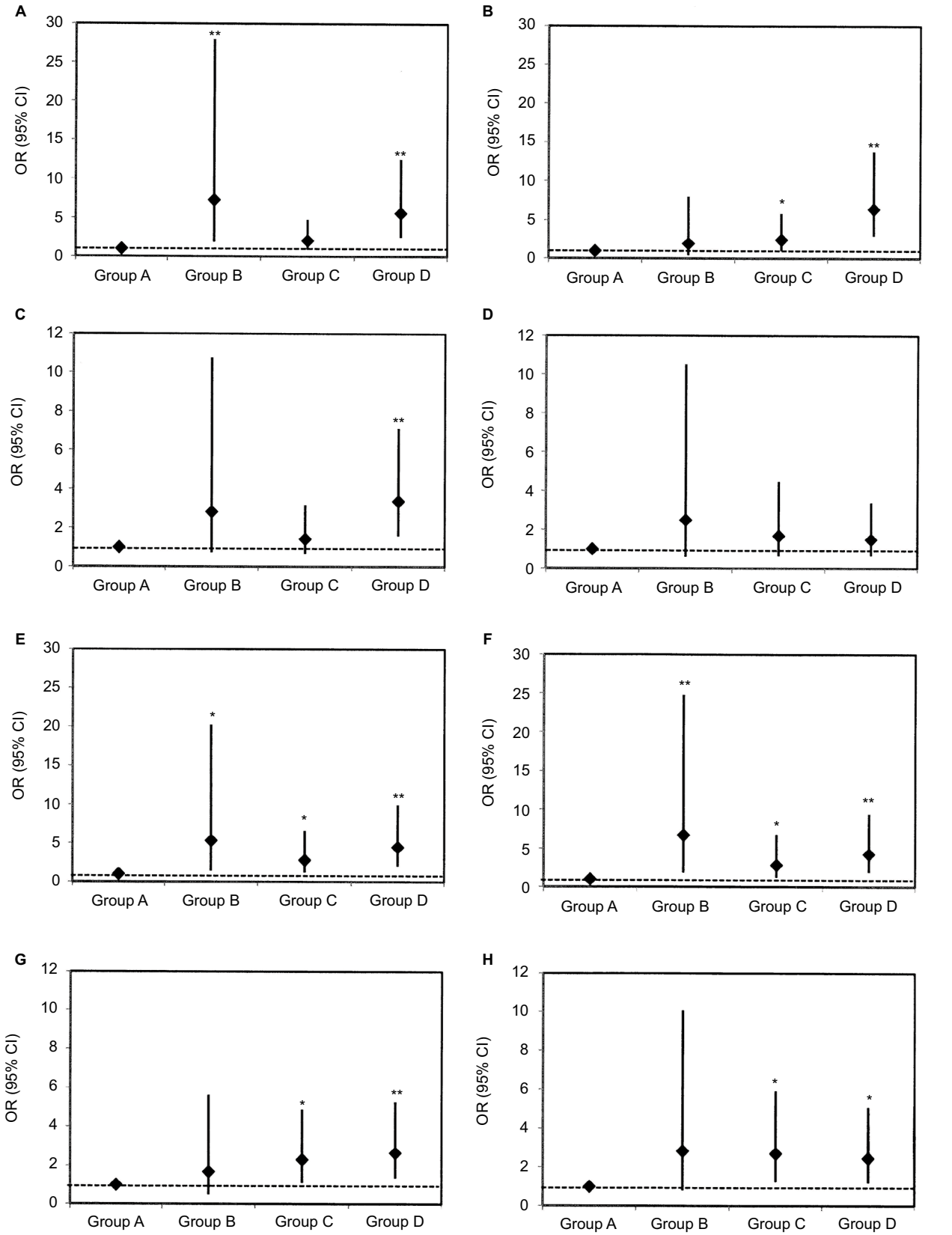

Figure 2 Multinomial logistic regression analysis for (**A**) hypertension, (**B**) insulin resistance, (**C**) impaired fasting glucose, (**D**) increased HbA1c, (**E**) hypertriglyceridemia, (**F**) hypo HDL cholesterolemia, (**G**) atherogenic lipoproteins, and (**H**) atherogenic lipoprotein pattern for the following groups compared with the reference normal-weight and lean group (Group A): overweight and lean (Group B), BMI ≥25.0 kg/m^2 for women and ≥27.0 kg/m^2 for men, and PBF <35% for women and <25% for men; normal weight and fat (Group C), body mass index (BMI) <25.0 kg/m^2 for women and <27.0 kg/m^2 for men, and percentage of body fat (PBF) ≥35% for women and ≥25% for men; and overweight and fat (Group D), BMI ≥25.0 kg/m^2 for women and ≥27.0 kg/m^2 for men, and PBF ≥35% for women and ≥25% for men.
Note: *P < 0.05; **P < 0.01.

Table 4 Logistic regression analysis of obesity measures associated with CVD risk factors

Dependent variables	Independent variables	Men		Women	
		OR (95% CI)[a]	*P*-value	OR (95% CI)[a]	*P*-value
Blood pressure[b]	BMI	7.65 (2.23–26.32)	0.001	3.56 (1.53–8.27)	0.003
	PBF	–	–	–	–
HOMA-IR[c]	BMI	–	–	3.23 (1.45–7.00)	0.003
	PBF	9.37 (2.90–30.29)	<0.001	–	–
Fasting glucose[d]	BMI	–	–	2.40 (1.07–5.38)	0.033
	PBF	4.25 (1.54–11.78)	0.005	–	–
HbA1c[e]	BMI	–	–	–	–
	PBF	–	–	–	–
Triglycerides[f]	BMI	–	–	2.74 (1.19–6.32)	0.018
	PBF	5.38 (1.93–15.00)	<0.001	–	–
HDL-C[g]	BMI	6.69 (1.61–27.8)	0.009	2.91 (1.35–6.26)	0.006
	PBF	–	–	–	–
Small-dense LDL[h]	BMI	–	–	–	–
	PBF	3.27 (1.20–8.87)	0.020	2.31 (1.20–4.47)	0.013
LDL particle size[i]	BMI	–	–	–	–
	PBF	3.48 (1.27–9.58)	0.016	2.16 (1.06–4.39)	0.033
hsCRP[j]	BMI	–	–	–	–
	PBF	–	–	–	–
25-hydroxyvitamin D[k]	BMI	–	–	–	–
	PBF	–	–	–	–
Leptin[l]	BMI	–	–	27.5 (3.37–224.6)	0.002
	PBF	15.09 (1.50–152.1)	0.021	–	–
Adiponectin[m]	BMI	–	–	2.51 (1.21–5.23)	0.014
	PBF	–	–	–	–

Notes: [a]Data are from logistic regression analyses adjusted for age, height, and smoking; Dashes mean variable removed from the equation by backward stepwise selection. [b]Defined as systolic ≥130 and/or diastolic ≥85 mmHg or treatment with antihypertensive drug. [c]Defined as HOMA-IR ≥3.0. [d]Defined as glucose ≥5.55 mmol/L or previous diagnosis of diabetes. [e]Defined as HbA1c ≥38.8 mmol/mol. [f]Defined as triglycerides ≥1.70 mmol/L. [g]Defined as HDL-C <1.04 mmol/L (men) or <1.30 mmol/L (women). [h]Defined as small-dense LDL >0.16 mmol/L. [i]Defined as mean LDL particle size <26.5 nm. [j]Defined as hsCRP >3.0 mg/L. [k]Defined as 25-hydroxyvitamin D <50 nmol/L. [l]Defined as leptin over upper limit: >12.0 ng/mL (men) or >24.2 ng/mL (women). [m]Defined as adiponectin lower upper limit: <13.9 µg/mL (men) or <19.4 µg/mL (women).
Abbreviations: BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; HbA1c, hemoglobin A1c; HOMA-IR, Homeostasis Model Assessment of Insulin Resistance; HDL-C, high density lipoprotein-cholesterol; hsCRP, high sensitive C-reactive protein; LDL, low density lipoprotein; OR, odds ratio; PBF, percentage of body fat.

leptin was associated with PBF for men and BMI for women, whereas adiponectin had no association in any way for men, but agreed with BMI for women.

Discussion

BMI and PBF are two different clinical measures of obesity. However, whether the two measures are equally applicable in certain populations is unclear. For example, Asian populations tend to have a higher PBF and related complications compared with other ethnic populations with the same BMI.[16] Moreover, many results have indicated sex-related differences in regulation of adipose tissue; women have a greater amount of PBF than men with an equivalent BMI.[17,21] The question is whether the use of only one measure or the other is sufficient. Our results reveal that neither measure used alone is sufficient.

For the Thai population, our results show a good relationship between BMI and PBF when sex stratification was accounted for. According to our data, the proportions of men were similar in all groups when using either BMI or PBF for classification (Tables 1 and 2). This implies that sex-specific cutoff points regarding BMI and PBF are appropriate for defining excess body weight and body fat for the adult Thai population. According to such criteria, 27.8% of the participants were identified to be obese using the sex-specific BMI cutoff, but 40.6% were determined to be fat using the PBF cutoff. Our results are similar to those of the recently published study of Gába and Přidalová, who demonstrated that although 21% of Caucasian women studied had a BMI of ≥30 kg/m^2, 40% had a high excess fat mass.[22] Notably, among our normal-weight participants, 25% were found to have PBF that was higher than the cutoff value. Indeed, in Group C and D, there was a marked increase in the waist-to-hip fat ratio and the visceral fat area compared with Group A and B. Such results indicate the poor diagnostic performance of BMI in measuring increased body fat (adiposity) in this population.

In the present study, we observed that BMI and PBF differed considerably in their predictive abilities for numerous

cardiometabolic risk markers (Figure 2). Furthermore, we observed large differences in the abilities of the BMI and PBF measures to identify specific risk factors, as shown by the ORs (Table 4). A good discriminator for individual participants being at risk of hypertension was being overweight (with or without fat). Moreover, BMI, and not PBF, was strongly associated with hypertension, independent of age, height, or sex. A study of Chinese adults by Hou et al found that BMI adequately reflected body volume and mass, and this was associated with blood viscosity and blood volume and was closely related to blood pressure.[23] However, in our Thai population, the magnitude of the association between BMI and hypertension was much higher in men (an OR that was twice as large in men than in women).

According to results of glucose and lipid metabolic profiles, individual participants who were overweight and fat clearly demonstrated a high risk of all metabolic regulations, except for increased HbA1c. Additionally, our data indicate that participants with a contradictory BMI and PBF (normal weight and fat or overweight and lean) may be misidentified as being at risk of glucose and lipid metabolic dysregulations. Furthermore, participants identified as being of a normal weight but fat also demonstrated a risk of insulin resistance. This result supports the report by Romero-Corral et al that individuals with a high body fat content but a normal weight were more predisposed to type II diabetes mellitus than those who were overweight but had a normal fat mass.[24] Notably, however, our results indicate that participants who were either normal weight and fat or overweight and/or fat did not appear to be at risk of increasing levels of HbA1c. This finding is in agreement with that of Mainous et al, who reported that BMI and waist circumference showed no association with HbA1c.[25] HbA1c reflects an increase in average glucose levels. However, participants in Group D were overweight and fat (Table 3), but they showed no marked glucose increase compared with Group A (107.1 *vs* 94.5 mg/dL, only a 14% increase), which may not be sufficient to significantly increase hemoglobin glycosylation. Insulin resistance differed between the participants with overweight and fat and normal weight and lean (2.087 vs 0.850, a 145% increase). An increase in insulin secretion (7.37 vs 3.52 μIU/mL, a 108% increase) may have restrained the glucose concentration. Another population-based study showed that the agreement between HbA1c and oral glucose tolerance test criteria in classifying participants' glycemia decreased with an increase in the participants' BMI, particularly when screening for prediabetes (HbA1c ranged from 5.7% to 6.4%).[26]

We noted a large sex-specific variation between BMI and PBF with respect to their association with the serum metabolite profile. Multiple studies have shown that individuals with a large body fat content are predisposed not only to type II diabetes mellitus but also to CVD.[4–7] We observed that HOMA-IR, fasting glucose, and triglycerides were similarly associated with PBF in men but not in women. By contrast, BMI was shown to be a good predictor of these risk factors in women. Women tend to have more body fat than men. Furthermore, because of distinct differences in fatty acid mobilization and oxidation and storage, women tend to store more fat in the gluteal–femoral region, whereas men store more fat in the visceral depot.[27] Therefore, the use of BMI as an indicator of CVD and type II diabetes mellitus for women is preferable over the use of PBF in evaluating changes in body adiposity over time, because changes in body weight are more likely to represent an increase in the volume of adipose tissue.

The lipid metabolic profiles showed differences between BMI and PBF in their ability to predict each of the lipid risk factors. Although numerous studies have reported a direct correlation between increasing adiposity and dyslipidemia, our results reveal no significant differences in total cholesterol, LDL-C, IDL-C, or non-HDL-C between the normal-weight and overweight or lean and fat groups.[28,29] However, notably, PBF in both sexes was a predictor for only increased small-dense LDL particle size and decreased LDL particle size, which play an important role in the development of atherosclerosis. These data are consistent with the data of Rainwater et al, who showed that changes in metabolic conditions (such as obesity) predominantly affect LDL particle size more than LDL absolute levels.[30] Notably, many studies have demonstrated that small-dense LDL particles were strongly associated with raised triglycerides and decreased HDL-C concentrations, whereas we found differences between the obesity measures in their ability to predict these lipids abnormalities.[31,32] BMI was strongly associated with low HDL-C in both sexes, whereas PBF was strongly associated with small-dense LDL particles. In addition, we observed a trend where participants who were overweight exhibited a greater probability of having low HDL-C compared with those who were considered fat (Figure 2F). According to Pietrobelli et al, the composition of HDL may be altered through muscle lipoprotein lipase-mediated transfer of cholesterol esters from HDL to triglycerides-rich lipoprotein remnants, which leads to increased HDL catabolism.[33] Furthermore, a recent cohort

study in women with a high prevalence of MetS showed that trunk fat-free soft tissue mass may have detrimental effects on HDL levels.[34] Data from the current study also demonstrate that participants classified as being obese according to BMI but having normal fat mass according to PBF tended to have a high muscle mass, and they showed the lowest HDL-C and apoA-I levels (Table 3). Therefore, not only adipose tissue but also nonadipose components, particularly muscle mass, may play an important role in HDL metabolism.

Notably, the predictive abilities of both BMI and PBF were quite similar with respect to HOMA-IR and to glucose and triglyceride concentrations; BMI was a better predictor for women and PBF for men. Remarkably, these patterns were also observed for leptin levels. This indicates that muscle and adipose tissues influence the regulation of several important physiological functions and that there is a close link between adipokine and glucose and lipid metabolisms.

Hypertension, insulin resistance, hyperglycemia, dyslipidemia, increase inflammatory markers, and 25-hydroxyvitamin D deficiency have been studied with respect to an associated CVD risk.[35,36] However, our results reveal no association between BMI or PBF and hsCRP or 25-hydroxyvitamin D. Although low 25-hydroxyvitamin D levels have been extensively reported in obesity, we notably found that 25-hydroxyvitamin D levels were similar between normal and obese participants, independent of the obesity measure used.[37] Inconsistencies in the reporting of associations between serum 25-hydroxyvitamin D and obesity may be due to the high levels of vitamin D inadequacy in the Thai population, which were up to 44.3% and 91.9%, as defined by 25-hydroxyvitamin D levels less than 50 and 75 nmol/L, respectively.[38]

Our study has some limitations. First, only a few participants were defined as having an excess BMI with a normal PBF, which may limit our conclusions. Therefore, further studies involving larger and different Southeast Asian populations are required to confirm the findings presented herein. Second, age, sex, height, and smoking status are known to be risk factors associated with developing CVD risk factors; although these factors were accounted for and adjusted in our analysis, other factors were not accounted for, despite being known to be risk factors in developing CVD (such as dietary intake, level of education, physical activity, and family history). Third, we measured PBF in this study by using bioelectrical impedance analysis, which tends to underestimate body fat in subjects.[39] However, this method of analysis is used in large-scale epidemiological investigations because it is least expensive and is the most simple and reproducible method used to conduct PBF evaluations and other body composition assessments.[40]

Conclusion

This study was conducted on a Thai population, and the results reveal that Thai women have a higher PBF than men. In particular, the two measures of obesity (BMI and PBF) exhibited considerable sex-specific variations in terms of their associations with cardiometabolic risk profiles. With respect to glucose homeostasis and to triglyceride and leptin concentrations, BMI was a better predictor for women and PBF for men. In addition, we clearly demonstrated that participants with a contradictory BMI and PBF could be misidentified as being at risk of glucose and lipid metabolic dysregulations. The differences between the two measures in terms of their prediction of cardiometabolic risk indicate that using exclusively one or the other measure provides an inferior risk prediction than using both measures, as shown herein with the Thai population. Therefore, because both BMI and PBF are easy and inexpensive to use, both should be applied in screening activities.

Availability of data and material

The datasets used and/or analyzed during the current study will not be shared. For access to this data, please contact Pornpen Srisawasdi, PhD, the supervisor of the study, at pornpen.sri@mahidol.ac.th or srisawasdiP@yahoo.com

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Author contributions

All the authors participated in the interpretation and the review of the manuscript. PS, SV, and MR designed the study. PS, SV, NK, and KK conducted the data retrieval and analyzed the data. PS, SV, and MHK wrote the manuscript. PS, SV, MR, and MHK gave constructive suggestions during

the preparation of the manuscript. All the authors read and approved the final manuscript. All the authors also participated in revision of the manuscript.

Disclosure

The authors report no conflicts of interest in this work.

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