Characterization of Cardiometabolic Risks in Different Combination of Anthropometric Parameters and Percentage Body Fat

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The prevalence of obesity was increasing and became a growing problem worldwide. Obesity increased the risk of developing metabolic abnormalities and was associated with adverse health outcomes. Our aim was to examine the associations among different combinations of obesity phenotypes (high body mass index > 27 kg/m² (O), high waist circumference (male > 90 cm, female > 80 cm) (W), fatty liver (F) and percentage body fat in top 40% (P)) and cardiometabolic diseases (type 2 diabetes mellitus (DM), hypertension (HTN), metabolic syndrome (MetS)). A total of 48426 eligible subjects were categorized based on the different definitions. After adjusting for all covariables, participants with O + F + P combination were more likely associated with the presence of DM. Participants with O + W combination were more associated with the presence of HTN than others. Participants with O + W + F + P had higher risk for the presence of MetS than others. The study addressed the associations between different obesity phenotypes and DM and HTN in the adult population. Better understanding the pathophysiological mechanisms underlined individual vulnerability and progression of cardiometabolic insults.

The epidemiology of obesity was prevalent and increasing dramatically worldwide in the past three decades¹. Recently, the trend of obesity was reported to be accelerating in some developed countries². It had become a growing public health issue not only in kinds of comorbidities but also in quality of life in Taiwan³. Obesity was proposed to be related to several adverse health outcomes such as metabolic syndrome (MetS), diabetes mellitus (DM), hypertension (HTN) and increased morbidity and mortality⁴. Numerous studies had proposed the associations between different obesity indices with metabolic disorders. As a traditional and commonly used indicator, body mass index (BMI) was reported to be associated with MetS and the risks of DM⁵. Abdominal obesity, caused by visceral fat accumulation, was significantly associated with insulin resistance⁶. Waist circumference (WC) was considered as a better index to predict MetS than others⁷.

Body fat distribution was reported to have a significant association with the development of impaired glucose metabolism and MetS⁸,⁹. In a previous study, high percentage body fat (PBF) was associated with a high cardiometabolic risks in Korean population¹⁰. Besides, PBF had association with all-cause and cardiovascular mortality, high fat mass had higher mortality risk than BMI¹¹,¹². Therefore, it may be crucial to determine the clinical usefulness of measuring PBF to evaluate the obesity-associated metabolic dysfunction. The aim of our study was to determine whether the different obesity phenotypes were closely related to glucose intolerance and HTN.

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There were 1507, 3082, 3997, and 247 participants in O, W, F, and P phenotype, respectively. O had higher inflammatory biomarkers than control group, suggesting that high PBF might be an important indicator for MetS. Obese subjects with higher PBF have higher insulin resistance and pro-inflammatory cytokines development of prediabetes and DM. However, our findings revealed that general obesity was considered a common risk factor for DM and cardiometabolic diseases. Rodriguez demonstrated that adiposity was a common risk factor for DM and cardiometabolic diseases. After fully adjusting for pertinent covariables, F was significantly associated with the presence of DM with odds ratios (ORs) of 2.85 (95% confidence interval (CI): 1.93–4.21). Other combinations of obesity phenotypes also had significant association with the presence of DM (P < 0.05). O + F + P had risk for the presence of DM with ORs of 8.07 (95% CI: 3.23–20.16). W was associated with the presence of HTN with ORs of 1.44 (95% CI: 1.07–1.93). O + W, O + F + W + F + P, O + W + F + P, O + W + F + P + F, O + W + F + P + F, O + W + F + P also had significant relationship with the presence of HTN. O + W had significantly higher risk of the presence of HTN with ORs of 5.43 (95% CI: 3.43–8.60) than others. W and F were associated with the presence of MetS with ORs of 8.57 (95% CI: 6.18–11.88) and 2.93 (95% CI: 2.22–3.86). O + W, O + F, W + F, W + P, P + F, O + W + F, O + W + P, O + F + P, W + F + P, and O + W + F + P were significantly associated with the presence of MetS (P < 0.05). O + W + F + P had higher risk for the presence of MetS than other combinations with odd ratios (ORs) of 38.26 (95% CI: 29.07–50.36).

### Discussion

In our study, the primary finding was that different obesity phenotypes were significantly associated with the presence of DM and HTN. The presence of DM was more likely associated with F phenotype than others. Those with W phenotype had closer relationship with HTN. Furthermore, subjects with different combinations of obesity phenotypes had higher risks of cardiometabolic diseases than those with single obesity phenotype. The combination of obesity phenotypes seems to have increased risk of obese individuals on the process for developing adverse health outcomes.

The clinical usefulness of PBF on MetS risks was addressed based on a nationally representative sample. High PBF was significantly associated with the presence of MetS (P < 0.05). Other combinations of obesity phenotypes also had significant association with the presence of MetS (P < 0.05). O + W + F + P had higher risk for the presence of MetS than other combinations with odd ratios (ORs) of 38.26 (95% CI: 29.07–50.36).

### Table 1. Characteristics of study sample in different obesity phenotypes.

| Variables | BMI > 27 (O) (N = 1507) | High WC (W) (N = 3082) | Fatty liver (F) (N = 3997) | High PBF (P) (N = 247) |
|-----------|-------------------------|-------------------------|--------------------------|-------------------------|
| Continuous Variables, mean (SD) | | | | |
| Age (years) | 43.7 (14.5) | 44.9 (13.4) | 48.7 (12.3) | 50.6 (13.4) |
| Body Mass Index (kg/m²) | 30.1 (3.1) | 28.1 (4.0) | 25.8 (3.7) | 27.9 (3.7) |
| Percentage body fat (%) | 33.7 (6.7) | 32.9 (6.5) | 29.9 (7.0) | 36.3 (5.0) |
| Waist circumference (cm) | 93.5 (9.2) | 92.4 (8.3) | 87.6 (9.9) | 92.4 (10.2) |
| Total cholesterol (mmol/L) | 4.9 (0.9) | 4.9 (0.9) | 4.9 (0.9) | 5.1 (0.9) |
| Triglycerides (mmol/L) | 2.93 (95% CI: 2.22–3.86) | 2.93 (95% CI: 2.22–3.86) | 2.93 (95% CI: 2.22–3.86) | 2.93 (95% CI: 2.22–3.86) |

### Results

#### Demographic characteristics of the study sample.

All demographic information of study participants was shown in Table 1. The mean age of these obesity phenotypes was 43.7 ± 14.5, 44.9 ± 13.4, 48.7 ± 12.3, and 50.6 ± 13.4 years, respectively. All participants were divided into four obesity phenotypes: BMI > 27 kg/m² (O), high waist circumference (male > 90 cm, female > 80 cm) (W), fatty liver (F), percentage body fat in top 40% (P). There were 1507, 3082, 3997, and 247 participants in O, W, F, and P phenotype, respectively.

#### Association between obesity phenotypes and the presence of DM, HTN and MetS.

After fully adjusting for pertinent covariables, F was significantly associated with the presence of DM with odds ratios (ORs) of 2.85 (95% confidence interval (CI): 1.93–4.21). Other combinations of obesity phenotypes including O + W, W + F, W + P, F + O, W + O + F + P, W + F + P, and O + W + F + P also had significant association with the presence of DM (P < 0.05). O + F + P had risk for the presence of DM with ORs of 8.07 (95% CI: 3.23–20.16). W was associated with the presence of HTN with ORs of 1.44 (95% CI: 1.07–1.93). O + W, O + F + W + F + P, O + W + F + P, O + W + F + P + F, O + W + F + P + F, O + W + F + P also had significant relationship with the presence of HTN. O + W had significantly higher risk of the presence of HTN with ORs of 5.43 (95% CI: 3.43–8.60) than others. W and F were associated with the presence of MetS with ORs of 8.57 (95% CI: 6.18–11.88) and 2.93 (95% CI: 2.22–3.86). O + W, O + F, W + F, W + P, F + O, W + F, O + W + F, O + W + P, O + F + P, W + F + P, and O + W + F + P were significantly associated with the presence of MetS (P < 0.05). O + W + F + P had higher risk for the presence of MetS than other combinations with odd ratios (ORs) of 38.26 (95% CI: 29.07–50.36).
as a better phenotype for predicting the risks of DM for both gender groups. In a cross-sectional study of 4828 participants concerning the prediabetes and DM development, PBF may be more imperative than BMI and WC22. Shea et al. indicated that participants in the highest tertile of PBF had high risks of developing cardiometabolic disease compared to those with low PBF23. Excess body fat was associated with numerous comorbidities including HTN, insulin resistance, dyslipidemia and systemic inflammation. In patients with and without DM, the leptin-to-adiponectin ratio was a useful indicator to assess insulin resistance and atherosclerotic risks24,25.

Table 2. Association between various combinations of obesity phenotypes and the presence of DM. *Adjusted covariates: Model 1 = age. Model 2 = Model 1 + proteinuria, serum total cholesterol, uric acid, creatinine, AST, albumin, hsCRP. Model 3 = Model 2 + history of smoking, drinking.

| Variable | Model 1 OR (95% CI) | P Value | Model 2 OR (95% CI) | P Value | Model 3 OR (95% CI) | P Value |
|----------|---------------------|---------|---------------------|---------|---------------------|---------|
| O (BMI > 27 kg/m²) | 2.25 (1.01–5.05) | 0.048 | 2.22 (0.98–5.04) | 0.057 | 2.17 (0.96–4.93) | 0.064 |
| W (high waist circumference) | 1.34 (1.01–1.78) | 0.040 | 1.44 (1.07–1.93) | 0.015 | 1.44 (1.07–1.93) | 0.016 |
| F (fatty liver) | 1.66 (1.39–1.99) | <0.001 | 1.15 (0.95–1.39) | 0.144 | 1.16 (0.96–1.40) | 0.134 |
| P (percentage body fat in top 40%) | 2.30 (1.49–3.53) | <0.001 | 1.55 (0.99–2.43) | 0.056 | 1.54 (0.98–2.42) | 0.060 |
| O + W | 6.28 (4.05–9.74) | <0.001 | 5.35 (3.38–8.46) | <0.001 | 5.43 (3.43–8.60) | <0.001 |
| O + F | 3.73 (2.08–6.69) | <0.001 | 2.48 (1.36–4.51) | 0.003 | 2.47 (1.35–4.50) | 0.003 |
| O + P | 4.23 (1.00–17.78) | 0.049 | 1.85 (0.41–8.42) | 0.425 | 1.88 (0.41–8.58) | 0.414 |
| W + F | 2.85 (2.32–3.51) | <0.001 | 2.25 (1.81–2.80) | <0.001 | 2.27 (1.83–2.83) | <0.001 |
| W + P | 2.15 (1.39–3.22) | <0.001 | 1.75 (1.11–2.76) | 0.017 | 1.75 (1.11–2.76) | 0.017 |
| F + P | 2.59 (1.85–3.62) | <0.001 | 1.53 (1.08–2.18) | 0.018 | 1.52 (1.07–2.16) | 0.021 |
| O + W + F | 3.20 (2.46–4.16) | <0.001 | 2.29 (1.74–3.01) | <0.001 | 2.33 (1.77–3.07) | <0.001 |
| O + W + P | 3.31 (2.12–5.16) | <0.001 | 2.40 (1.49–3.84) | <0.001 | 2.44 (1.52–3.91) | <0.001 |
| O + F + P | 2.91 (1.47–5.78) | 0.002 | 1.60 (0.79–3.24) | 0.189 | 1.64 (0.81–3.33) | 0.167 |
| W + F + P | 3.43 (2.68–4.39) | <0.001 | 2.47 (1.89–3.22) | <0.001 | 2.49 (1.91–3.25) | <0.001 |
| O + W + F + P | 4.81 (3.98–5.80) | <0.001 | 3.36 (2.74–4.12) | <0.001 | 3.39 (2.77–4.16) | <0.001 |

Table 3. Association between various combinations of obesity phenotypes and the presence of HTN. *Adjusted covariates: Model 1 = age. Model 2 = Model 1 + proteinuria, serum total cholesterol, uric acid, creatinine, AST, albumin, hsCRP. Model 3 = Model 2 + history of smoking, drinking.
of nitric oxide from oxidative stress might contribute to endothelial dysfunction in the pathophysiology of obesity. Hypoxia related adipose tissue inflammation secretes many reactive oxygen species and cytokines, leading to deterioration of nitric oxide signaling pathways in the endothelial cells. Elevated endothelin-1 activity also played an important role in obesity-associated endothelial dysfunction.

There were several potential limitations among our study. First, it was a cross-sectional design that casual inference was not assessible between obesity phenotypes and adverse outcomes. A longitudinal survey was suggested to be examined in further studies. Second, the study sample was obtained from health examinations in a single medical center. Limited ethnicity diversity in the participants might not reflect the association of obesity phenotypes and cardiometabolic diseases in racial difference. Third, the measurement for PBF in the health check-up was used by BIA, but not DEXA, a standard measurement for body composition with higher accuracy. Last, the diagnosis of fatty liver was determined by abdominal sonography, bias of image interpretation caused by physicians might occur. Despite the limitations mentioned above, our study had some advantages. A relatively large population-based sample included 20665 subjects was analyzed compared to others examined in small population-based samples.

Methods
Study design. The retrospective cross-sectional was performed from health examinations in Tri-Service General Hospital from 2010 to 2016. There were 69226 participants received comprehensive examinations enrolling in the health check-up during the period. According to the step-by-step orders of flow chart shown in Fig. 1, subjects with missing data such as biochemistry data, body composition exams, abdominal sonography was excluded. 48426 eligible participants were divided into non-obesity and various obesity phenotypes as following: O was defined as a BMI ≥ 27 kg/m² according to the criteria of the Department of Health in Taiwan; W was defined as subjects with high WC (male: > 90 cm; female: > 80 cm); F was defined as subjects with fatty liver diagnosed by abdominal sonography. P was categorized into subjects along with PBF in top 40% of the entire obesity population.

The protocol was approved by the Tri-Service General Hospital Institutional Review Board based on the Declaration of Helsinki. Written informed consent was obtained from participants prior to the study. During the entire study process, characteristics of participants correlated with individual identification were eliminated and remained anonymously.

Measurement of body composition. PBF was the indicator used in the study and was measured by BIA (InBody720, Biospace, Inc., Cerritos, CA, USA), an effective and validated method that was widely used for assessing body composition.

Definition of MetS. MetS was diagnosed when having ≥3 of the following features: (1) large waist circumference (WC); a waistline that measures at least 80 centimeters for women and 90 centimeters for men; (2) high

| Variable | Model 1 OR (95% CI) | P Value | Model 2 OR (95% CI) | P Value | Model 3 OR (95% CI) | P Value |
|-----------------|----------------------|---------|----------------------|---------|----------------------|---------|
| O (BMI > 27 kg/m²) | 2.69 (0.80–8.99) | 0.108 | 2.48 (0.74–8.39) | 0.143 | 2.53 (0.75–8.59) | 0.135 |
| W (high waist circumference) | 7.64 (5.57–10.48) | <0.001 | 8.62 (6.22–11.95) | <0.001 | 8.57 (6.18–11.88) | <0.001 |
| F (fatty liver) | 4.06 (3.11–5.32) | <0.001 | 2.94 (2.23–3.87) | <0.001 | 2.93 (2.22–3.86) | <0.001 |
| P (percentage body fat in top 40%) | 2.40 (1.21–4.76) | 0.012 | 1.62 (0.81–3.26) | 0.174 | 1.60 (0.80–3.22) | 0.188 |
| O + W | 34.69 (21.50–55.96) | <0.001 | 28.16 (17.16–46.21) | <0.001 | 27.77 (16.90–45.62) | <0.001 |
| O + F | 5.63 (2.66–11.94) | <0.001 | 3.68 (1.72–7.91) | <0.001 | 3.74 (1.74–8.03) | <0.001 |
| O + P | 8.97 (1.78–45.11) | 0.008 | 3.84 (0.72–20.55) | 0.116 | 3.60 (0.66–19.54) | 0.137 |
| W + F | 23.32 (17.48–30.48) | <0.001 | 20.23 (15.34–26.68) | <0.001 | 20.12 (15.25–26.54) | <0.001 |
| W + P | 13.78 (8.94–21.25) | <0.001 | 12.50 (7.94–19.48) | <0.001 | 12.36 (7.84–19.48) | <0.001 |
| P + F | 6.07 (3.99–9.24) | <0.001 | 3.74 (2.43–5.77) | <0.001 | 3.82 (2.47–5.89) | <0.001 |
| O + W + F | 47.19 (34.47–64.60) | <0.001 | 36.73 (26.59–50.75) | <0.001 | 36.25 (26.21–50.12) | <0.001 |
| O + W + P | 21.42 (13.55–33.86) | <0.001 | 16.14 (9.95–26.17) | <0.001 | 15.93 (9.80–25.88) | <0.001 |
| O + F + P | 17.93 (9.17–35.06) | <0.001 | 10.52 (5.29–20.93) | <0.001 | 10.65 (5.34–21.24) | <0.001 |
| W + F + P | 27.90 (20.70–37.60) | <0.001 | 21.82 (15.93–29.88) | <0.001 | 21.74 (15.87–29.78) | <0.001 |
| O + W + F + P | 51.34 (39.36–66.97) | <0.001 | 38.03 (28.91–50.04) | <0.001 | 38.26 (29.07–50.36) | <0.001 |

Table 4. Association between various combinations of obesity phenotypes and the presence of MetS. *Adjusted covariates: Model 1 = age. Model 2 = Model 1 + proteinuria, serum total cholesterol, uric acid, creatinine, AST, albumin, hsCRP. Model 3 = Model 2 + history of smoking, drinking.
triglyceride levels (TG): higher than 150 mg/dL; (3) reduced high-density lipoprotein cholesterol (HDL-C) levels: less than 50 mg/dL in women and 40 mg/dL in men; (4) increased blood pressure (BP): 130/85 mmHg or higher; and (5) elevated fasting plasma glucose (FPG): 100 mg/dL or higher based on the Harmonized criteria for MetS in 2009 with the Asian cut-off for WC39,40.

Definition of type 2 DM. As reported by the American Diabetes Association criteria, subjects with one of the following components were diagnosed of T2DM: (1) fasting plasma glucose ≥126 mg/dL (2) hemoglobin A1c test ≥6.5% (3) random plasma glucose ≥200 mg/dL (4) past history of diabetes status, or use of antidiabetic agents41.

Definition of HTN. Participants who had HTN was diagnosed by the guidelines of the Taiwan Society of Cardiology and the Taiwan Hypertension Society for the management of hypertension (1) blood pressure was higher than 140/90 mmHg (2) subjects were taking antihypertensive agents42.

Covariates measurement. BMI was calculated by a formula that the weight of the subject in kilograms divided by the square of the height in meters (kg/m²). WC was measured at the mid-level between the iliac crest and the lower border of the 12th rib. Biochemistry data was collected by drawing blood samples from subjects after fasting for at least 8 hours. Serum profiles included total cholesterol (TC), uric acid (UA), creatinine (Cr), aspartate aminotransferase (AST), albumin, and C-reactive protein (CRP) were analyzed by using standard methods.

Statistical analysis. Statistical estimations used in the study were performed by the Statistical Package for the Social Sciences, version 18.0 (SPSS Inc., Chicago, IL, USA) for Windows. The differences among these obesity phenotypes in terms of demographic information and biochemistry data were examined by analysis of variance and chi-square test. A two-sided p-value of ≤ 0.05 was regarded as the threshold for statistical significance. Extend-model approach was performed in the study with multivariable adjustment for pertinent clinical variables. ORs of different obesity phenotype combinations for the presence of DM and HTN were performed by a multivariate logistic regression.
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**Author Contributions**
Yuan-Yuei Chen contributed to the design of the study, was responsible for the management and retrieval of data, contributed to initial data analysis and interpretation, drafted the initial manuscript. Yuan-Yuei Chen, Wen-Hui Fang, Chung-Ching Wang, Tung-Wei Kao, Yaw-Wen Chang, Hui-Fang Yang, Chen-Jung Wu, Yu-Shan Sun, and Wei-Liang Chen decided upon the data collection methods. Yuan-Yuei Chen and Wei-Liang Chen were also responsible for the data analysis decisions. Wei-Liang Chen conceptualized and designed the study, supervised all aspects of the study, critically reviewed and revised the manuscript, and approved the final manuscript as submitted. All authors meet the ICMJE criteria for authorship.

**Additional Information**

**Competing Interests:** The authors declare no competing interests.

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