Association of elevated blood serum high-sensitivity C-reactive protein levels and body composition with chronic kidney disease

A population-based study in Taiwan

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Abstract

Chronic kidney disease (CKD) is a risk factor for cardiovascular diseases and is associated with an increase in all-cause mortality. Studies regarding association among various body compositions in different inflamed states and the risk of CKD were rare. We aimed to evaluate the relationship among body composition, high-sensitivity C-reactive protein (hsCRP) level, and the risk of CKD. This was a retrospective cross-sectional study using annual health examination data from 2 medical centers in northern and southern Taiwan between January and December 2015. We performed a variance analysis of the estimated glomerular filtration rate (eGFR) distribution in groups based on hsCRP and body fat percentage (BFP), and a multivariate logistic regression model was used to assess the relationship among BFP, hsCRP levels, and CKD.

A total of 10,287 subjects aged ≥18 years undergoing health examination were analyzed. In our study, overweight/obese patients were associated with increased risk of CKD. Nevertheless, in subjects with elevated hsCRP level, overweight/obese group with a higher BFP had a lower risk of CKD as compared with overweight/obese with normal BFP group (for BMI ≥ 23 kg/m², high BFP/high hsCRP: odds ratio [OR] for CKD 1.86, 95% confidence interval [CI] = 1.10–3.17, P = .02; normal BFP/high hsCRP group: OR 2.32, 95% CI = 1.23–4.37, P = .01) after adjusting for various confounders.

Our findings suggest that various body compositions in different inflamed states may interfere with the risk of CKD. These results provide an important method for the early detection of impaired renal function by identifying various body compositions and inflammation states to detect CKD at an earlier stage.

Abbreviations: BFP = body fat percentage, BIA = body impedance analysis, BMI = body mass index, BP = blood pressure, CI = confidence interval, CKD = chronic kidney disease, Cr = Creatinine, eGFR = estimated glomerular filtration rate, ESRD = end-stage renal disease, FPG = fasting plasma glucose, HDL-C = high-density lipoprotein cholesterol, hsCRP = high-sensitivity C-reactive protein, IL-6 = interleukin-6, MDRD = Modification of Diet in Renal Disease, MetS = metabolic syndrome, OR = odds ratio, TChol = total cholesterol, TG = triglyceride, TNF = tumor necrosis factor, WC = waist circumference.

Keywords: body composition, body fat percentage, chronic kidney disease, estimated glomerular filtration rate, high-sensitivity C-reactive protein, inflammation

1. Introduction

Obesity and chronic kidney disease (CKD) are both important public health issues in primary care worldwide. Obesity is often associated with the presence of hypertension and diabetes, which are common leading causes of end-stage renal disease (ESRD). Nonetheless, of the risk factors for CKD, obesity is potentially reversible. According to the 2013 United States Renal Data System report, Taiwan had the highest prevalence of...
ESRD worldwide, with 2584 cases per million population.\textsuperscript{32} Because most ESRD patients died from other causes before they reached for scheduled dialysis,\textsuperscript{4,5} early recognition and management to prevent the occurrence of CKD and its progression are of particular importance.

A higher body mass index (BMI) was associated with CKD in many large-scale epidemiologic studies.\textsuperscript{51} The pathophysiology of CKD and its association with obesity, a chronic inflammatory state,\textsuperscript{7} is possible through glomerular hyperfiltration, monocyte influx, the proliferation of macrophages, and matrix expansion.\textsuperscript{8,9} Adipose tissue can release inflammatory mediators such as interleukin (IL)-6 and tumor necrosis factor (TNF)-\alpha,\textsuperscript{10,11} which may contribute to the deterioration of renal function.\textsuperscript{12,13} However, little is known about the association between body composition and chronic inflammation that leads to impaired renal function.

Different body compositions such as the ratio between and distribution of lean mass and adipose tissue compartments may be associated with metabolic risks.\textsuperscript{14–16} However, the BMI does not differentiate lean mass from fat mass.\textsuperscript{17} To circumvent this limitation, other measures for estimating adiposity have been proposed, including body fat percentage (BFP) or waist circumference (WC). Many studies have indicated that WC, BFP, and triceps skinfold, which serve as surrogates of visceral and subcutaneous fat, have a similar or even stronger association with survival, as compared with BMI. Several diagnostic modalities including dual-energy x-ray absorptiometry, computed tomography, and magnetic resonance imaging could be useful for assessing BF and body compartments. However, their use in large epidemiologic studies is limited because of higher costs and the required technical expertise. Body impedance analysis (BIA) is another non-invasive, simple, and inexpensive tool to evaluate changes in body composition. To date, little has been studied on whether inflammation modifies the role of BFP regarding the risk of CKD.

We designed a study to assess the relationship between body composition including BMI and BFP and the association of reduced estimated glomerular filtration rate (eGFR). Moreover, we intended to evaluate whether different serum levels of high-sensitivity C-reactive protein (hsCRP), an acute-phase protein that indicates the degree of systemic inflammation affects the relationship in a relatively healthy adult population in Taiwan.

2. Methods

2.1. Subjects

This was a retrospective cross-sectional study that enrolled subjects aged ≥18 years who underwent an annual health check-up between January and December 2015. Informed consents were obtained from all participants. The study protocol was approved by the institutional review board. Subjects who did not complete a questionnaire; who did not respond to questions regarding their medical history, cigarette smoking, or medications used; or whose data were incomplete were excluded from the study. Subjects who had the following conditions that might alter their metabolic state or kidney function were excluded: thyroid diseases, hypothalamic diseases, adrenal disease, renal cancer, glomerulonephritis, liver cirrhosis, pregnancy, receiving dialysis, or diuretics use.

2.2. Data collection

Trained nurses performed the anthropometric measurements for all participants in accordance with standard operating procedures. All participants were provided questionnaires regarding individual information including smoking and alcohol drinking habits, medical history, and current medications. Blood pressure (BP) was measured with an automatic sphygmomanometer (Welch Allyn, Skaneateles Falls, New York); if greater than 120/80 mm Hg, the BP measurement was repeated 2 to 3 times after 10 minutes of rest. Body height and weight were measured using an automatic scale with a 0.1-kg sensitivity and 0.1-cm resolution. BMI was calculated as the weight in kilograms divided by the square of the height in meters. BFP was measured using a bioelectrical impedance analysis (InBody 3.0 model; BioSpace, Urbandale, Iowa), and all subjects were told not to perform any physical exercise or consume alcohol for at least 24 hours before the examination. The WC was measured by 2 trained examiners using a measuring tape placed horizontally around a subject’s abdomen at the midpoint between the lower border of the rib cage and the upper iliac crest.

2.3. Biochemical measurements

Venous blood samples were obtained through venepuncture and collected in vacuum tubes in the morning after a 12-hour fast; the samples were stored at 4°C in a refrigerator prior to analysis by the laboratory of the hospital. All blood analyses were performed at the clinical laboratory; both laboratories are certified by the College of American Pathologists. Urine specimens were obtained in the morning and scheduled to avoid menstrual periods. Laboratory measurements included hsCRP, fasting plasma glucose (FPG), total cholesterol (TChol), triglyceride (TG), and high-density lipoprotein cholesterol (HDL-C) levels. Creatinine (Cr) and hsCRP levels were measured using a Hitachi 7600 Modular Chemistry Analyzer (Hitachi, Tokyo, Japan). FPG was measured using a hexokinase method. TChol and TG levels were measured using an enzymatic colorimetric test. HDL-C was measured using a selective-inhibition method. Urinary protein excretion was evaluated using a dipstick urine test (Multistix 10 SG, Siemens Healthcare Diagnostics, Erlangen, Germany) and graded: negative, trace, 1+ (25 mg/dL), 2+ (75 mg/dL), 3+ (150 mg/dL), or 4+ (500 mg/dL).

2.4. Definition of measurement cut-offs and calculations

BMIs were categorized according to ranges established for Asian populations,\textsuperscript{18,19} that is, normal if <22.9 kg/m²; overweight if between 23.0 and 24.9 kg/m²; and obese if ≥25 kg/m². A BFP of >25% in men or >35% in women was defined as high based on the standard of the National Institutes of Health.\textsuperscript{20} The WC cut-off for abdominal obesity was ≥90 cm for men and ≥80 cm for women, using the Asian-specific cut-off points established by the International Diabetes Federation.\textsuperscript{21} The eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) equations for Chinese patients.\textsuperscript{22} It had been reported that the Chinese version of the MDRD equation is a superior screening tool for CKD among middle-aged Taiwanese than the original MDRD and Cockcroft–Gault equations.\textsuperscript{23,24} CKD was defined according to the definition of the Kidney Disease Outcomes Quality Initiative,\textsuperscript{41} as an eGFR of <60 mL/min per 1.73 m² of body surface area and/or the presence of 1+ or greater proteinuria on urinalysis. A high serum hsCRP level was defined as exceeding the upper quartile level, which was 1.95 μg/dL in our study. Diagnostic criteria for metabolic syndrome (MetS) were adapted from the Asian modification of the United States National Cholesterol Education Program criteria,\textsuperscript{24} which required 3 or
more of the following: a high BP (systolic BP ≥ 130 mm Hg; and diastolic BP ≥ 85 mm Hg); a high serum TG (≥ 150 mg/dL); a decreased HDL-C (< 40 mg/dL for males or < 50 mg/dL for females); hyperglycaemia (FPG ≥ 100 mg/dL); and abdominal obesity.

2.5. Statistical analysis

Continuous variables are presented as medians (interquartile range [IQR]), and categorical variables are presented as percentages. For comparisons of the differences in continuous variables among the groups, the Mann–Whitney U and Kruskal–Wallis tests were used.

Table 1

Baseline characteristics of study subjects aged ≥ 18 years who underwent annual health checkups from January to December 2015 in northern and southern branches of medical centers (N = 10,267).

| Characteristics                      | Normal percent body fat BF ≤ 25% in male; ≤ 35% in Female (n = 2579) | High percent body fat BF - 25% in male; > 35% in Female (n = 7688) | P Value |
|--------------------------------------|---------------------------------------------------------------------|-------------------------------------------------------------------|--------|
| Age (years)                          | 38 (33, 44)                                                         | 40 (35, 46)                                                       | <.001* |
| Gender (n, %)                        |                                                                    |                                                                  | <.001* |
| Female                               | 2470 (95.8)                                                        | 39 (0.5)                                                          |        |
| Male                                 | 109 (4.2)                                                          | 7649 (99.5)                                                       |        |
| Smoking (n, %)                       |                                                                    |                                                                  |        |
| Current or past smokers              | 145 (5.6)                                                          | 2540 (33.0)                                                       | <.001* |
| None smokers                         | 2434 (94.4)                                                        | 5148 (67.0)                                                       |        |
| BMI (kg/m²)                          | 21.77 (19.80, 24.39)                                               | 25.10 (23.13, 27.43)                                             | <.001* |
| Waist circumference (cm)             | 72 (67, 78)                                                        | 86 (80, 92)                                                       | <.001* |
| SBP (mmHg)                           | 112 (103, 112)                                                     | 79 (72, 86)                                                       | <.001* |
| DBP (mmHg)                           | 70 (64, 77)                                                        | 189 (169, 211)                                                    | <.001* |
| Total cholesterol (mg/dL)            | 180 (160, 202)                                                     | 111 (78, 160)                                                    | <.001* |
| Triglycerides (mg/dL)                | 68 (51, 97)                                                        | 47 (41, 54)                                                       | <.001* |
| HDL-cholesterol (mg/dL)              | 57 (50, 67)                                                        | 4.06 (3.38, 4.81)                                                | <.001* |
| Chol /HDL                             | 3.05 (2.66, 3.63)                                                  | 78 (83, 99)                                                       | <.001* |
| Fasting glucose (mg/dL)              | 84 (79, 89)                                                        | 88 (61, 0.98)                                                    | <.001* |
| Creatinine (mg/dL)                   | 0.61 (0.54, 0.68)                                                  | 0.69 (0.61, 0.98)                                                | <.001* |
| eGFR (mL/min/1.73m²)                  | 133.95 (116.58, 154.95)                                            | 104.71 (92.30, 118.05)                                           | <.001* |
| hsCRP (µg/mL)                        | 0.63 (0.25, 1.50)                                                  | 1.06 (0.52, 2.09)                                                | <.001* |
| Homocysteine (µmol/L)                | 3.70 (7.50, 10.20)                                                 | 11.00 (6.00, 12.70)                                              | <.001* |
| MetS (n, %)                          | 2388 (92.6)                                                        | 6117 (79.6)                                                       |        |
| Present                              | 191 (7.4)                                                          | 1571 (20.4)                                                       |        |

Continuous data are reported as median (interquartile range) for non-normal distribution data and compared using the Mann–Whitney U Test; categorical data are shown as number (percentage) and compared using the Chi-square test.

* Indicates a significant difference between normal percent body fat and high percent body fat groups.

BMI = body mass index, CKD = chronic kidney disease, DBP = diastolic blood pressure, eGFR = estimated glomerular filtration rate, HDL = high density lipoprotein lipase cholesterol, hsCRP = high-sensitivity C-reactive protein, MetS = metabolic syndrome, FBFI = percent body fat, SBP = systolic blood pressure.
as appropriate, and the χ² test was used to examine categorical variables. If significant differences were noted among groups, post hoc analyses were performed using a Bonferroni correction. Multivariate logistic regression models were established to determine the risk estimates for CKD among the groups of different BFPs with a normal or high hsCRP level based on different BMIs after adjusting for various confounding variables. SPSS software package, version 20.0 (IBM corporation, Chicago, Illinois), was used for the statistical analysis. All statistical tests were 2-tailed and a P value of <.05 indicated significance.

3. Results

3.1. Baseline characteristics between different percent body fat groups

A total of 10,267 subjects were included with a median age of 40 (34, 46) years, male gender rate of 75.6%, and median eGFR of 110.19 (95.94, 127.86) mL/min/1.73 m². Among all participants, 25.1% had a normal BMI and 74.9% had a high BMI. The CKD prevalence was 3.7%. All participants were categorized into 2 groups based on BMI: normal (n = 2579) and high BMI (n = 7688).

The flow diagram of study protocol was demonstrated as Figure 1.

There were significant differences in demographic and cardiometabolic risk factors between the 2 groups (Table 1). Subjects in the high BMI group were older and had a higher systolic and diastolic BP, higher serum TChol, FPG, Cr, homocysteine, and hsCRP levels; and a lower serum HDL-C level and eGFR. In addition, the prevalence of MetS was higher in the high BMI group than the low BMI group (20.4% vs 7.4%, respectively; OR 3.21, 95% CI 2.74–3.76, P < .001). (A supplementary file was also attached to demonstrate the comparisons of general characteristics based on gender and BMI, n = 10,267, http://links.lww.com/MD/C446)

3.2. Different baseline characteristics based on quartiles of hsCRP levels

We further stratified participants into 4 quartile groups based on the serum hsCRP levels and compared the differences in characteristics among the groups. Significant differences in age, cigarette smoking, BMI, WC, systolic and diastolic

### Table 2

| hsCRP quartile | Group I (n=2516) | Group II (n=2527) | Group III (n=2527) | Group IV (n=2507) | P Value |
|----------------|-----------------|-----------------|-----------------|----------------|---------|
| Age            | 37 (32, 44)     | 40 (35, 46)     | 40 (35, 46)     | 40 (35, 45)     | <.001   |
| BMI (kg/m²)    | 22.01 (20.19, 24.03) | 24.10 (22.14, 26.02) | 25.22 (23.21, 27.51) | 26.50 (24.23, 29.48) | <.001 |
| BP (%)         | 27.88 (18.56, 32.31) | 32.30 (27.62, 35.58) | 33.91 (30.68, 37.25) | 34.93 (30.66, 38.82) | <.001 |
| WC (cm)        | 75.5 (69.0, 82.0) | 82.0 (76.0, 88.0) | 86.0 (79.0, 91.0) | 88.5 (82.0, 95.5) | <.001 |
| SBP (mmHg)     | 117 (108, 126) | 122 (113, 132) | 125 (116, 134) | 127 (117, 136) | <.001 |
| DBP (mmHg)     | 72 (66, 79)     | 76 (70, 83)     | 78 (71, 85)     | 80 (72, 87)     | <.001 |
| Total cholesterol (mg/dL) | 179 (160, 201) | 187 (167, 208) | 191 (169, 214) | 191 (170, 214) | <.001 |
| Triglycerides (mg/dL) | 72.50 (54.00, 104.00) | 97.00 (88.00, 141.00) | 113.00 (77.25, 162.00) | 117.00 (81.00, 172.00) | <.001 |
| HDL-cholesterol (mg/dL) | 55.5 (47.0, 64.0) | 50.0 (43.0, 54.0) | 47.0 (41.0, 54.0) | 45.0 (39.0, 52.0) | <.001 |
| HDL-cholesterol (mg/dL) | 3.17 (2.71, 3.83) | 3.74 (3.11, 4.43) | 4.05 (3.35, 4.83) | 4.25 (3.51, 5.00) | <.001 |
| Fasting glucose (mg/dL) | 85.00 (80.00, 90.00) | 87.00 (82.00, 93.00) | 88.00 (83.00, 94.75) | 89.00 (83.00, 97.00) | <.001 |
| Creatinine (mg/dL) | 0.79 (0.64, 0.91) | 0.85 (0.73, 0.95) | 0.86 (0.74, 0.96) | 0.85 (0.73, 0.96) | <.001 |
| eGFR (mL/min/1.73m²) | 116.01 (101.14, 135.41) | 108.63 (95.20, 124.84) | 107.68 (93.56, 124.22) | 108.37 (93.88, 125.88) | <.001 |
| hsCRP (μg/mL) | 0.24 (0.19, 0.33) | 0.65 (0.53, 0.79) | 1.34 (1.13, 1.62) | 3.18 (2.45, 5.19) | <.001 |
| Homocysteine (μmol/L) | 10.00 (8.50, 11.80) | 10.50 (9.80, 12.30) | 10.60 (9.10, 12.40) | 10.70 (9.10, 12.40) | <.001 |
| MetS (n %)     | 2422 (28.8)    | 2347 (26.4)     | 2018 (23.7)     | 1818 (21.4)     | <.001 |
| eGFR<60 (n %)  | 2464 (24.0)    | 2503 (25.3)     | 2468 (25.0)     | 2456 (24.8)     | <.001 |
| eGFR<60 and/or presence of 1+ or greater proteinuria on urinalysis | 52 (13.8) | 60 (18.4) | 104 (27.7) | 151 (40.2) | <.001 |

Grouping was based on the quartile of serum hsCRP levels. Continuous data are reported as median (interquartile range) for non-normal distribution data and compared using the Kruskal–Wallis Test; categorical data are shown as number (percentage) and compared using the Chi-square test.

1 indicates a significant difference between as compared to the Group I (1st quartile).
2 indicates a significant difference between as compared to the Group II (2nd quartile).
3 indicates a significant difference between as compared to the Group III (3rd quartile).

BFP = body fat percentage, BMI = body mass index, GFR = estimated glomerular filtration rate, HDL = high density lipoprotein (low density lipoprotein), hsCRP = high-sensitivity C-reactive protein, MetS = metabolic syndrome, SBP = systolic blood pressure, WC = waist circumference.
BP, FPG, TChol, HDL-C, Cr, eGFR, homocysteine, MetS, and CKD distribution were observed among the groups (for trend, all \(P<.001\)) (Table 2). All anthropometric indices including BFP, BMI, and WC increased in parallel with elevated serum hsCRP levels among the groups (\(P<.05\) in pairwise comparisons). The percentage of CKD increased in parallel with increased hsCRP levels among the groups (all \(P<.05\) in pairwise comparisons). The quartile group of subjects with the highest hsCRP levels had the highest BFP, BMI, WC, systolic and diastolic BP, TG, and FPG; the lowest HDL-C levels; and the highest prevalence of CKD and MetS. All indices were significantly different, as compared with the other quartile groups (Table 2).

### 3.3. Comparisons of combined BFP with hsCRP level and eGFR in normal and overweight/obese subjects

We further categorized participants into groups according to normal BFP/normal hsCRP, normal BFP/high hsCRP, high BFP/normal hsCRP, and high BFP/high hsCRP. We also analyzed and compared the differences of baseline characteristics in the 4 groups based on BFP and serum hsCRP level in Table 3.

The eGFR levels for the 4 groups of subjects with normal BMI are shown in Figure 2A. In pairwise comparisons of the high hsCRP groups, the eGFR level for the high BFP group was significantly lower than that of the normal BFP group (\(P<.05\)). The same difference was observed in pairwise comparisons of the normal hsCRP groups with normal and high BFPs (\(P<.05\)). The eGFR level was significantly decreased in the high BFP/his CRP group, as compared with the normal BFP/high hsCRP group (\(P<.05\)).

Figure 2B shows the eGFR levels of the overweight and obese subjects (i.e., BMI ≥ 23 kg/m²) categorized into groups comprising normal BFP/normal hsCRP, normal BFP/high hsCRP, high BFP/normal hsCRP, and high BFP/high hsCRP. The eGFR level was significantly lower in the high BFP/high hsCRP in a pairwise comparison with the normal BFP/high hsCRP and normal BFP/normal hsCRP groups (both \(P<.05\)). Likewise, the eGFR level was significantly decreased in the high BFP/normal hsCRP group, as compared with the normal BFP/normal hsCRP and normal BFP/ high hsCRP groups (both \(P<.05\)). The changes observed in these groups were similar to those of the normal weight subjects. However, in overweight and obese subjects, the eGFR levels seemed higher in the high hsCRP groups than the normal hsCRP groups for the same BFP categories, although the difference was not significant.

| Table 3
| Comparisons of baseline characteristics among the four groups categorized by high-sensitivity C-reactive protein levels and body fat percentage (\(N=10,267\)).

| Normal hsCRP/Normal BFP (\(n=2066\)) | Normal hsCRP/High BFP (\(n=5594\)) | High hsCRP/Normal BFP (\(n=513\)) | High hsCRP/ High BFP (\(n=2094\)) | \(p\) Value |
|---|---|---|---|---|
| **Age**<br>38 (32, 44) | 40 (35, 46)* | 39 (34, 45)* | 40 (35, 46)* | \(<0.001\) |
| **Gender (n, %)**<br>Female 1968 (78.4) | 9 (0.4) | 502 (20.0) | 30 (1.2) | \(<0.001\) |
| Male 98 (1.3) | 558 (27.0) | 11 (0.1) | 2064 (26.6) | \(<0.001\) |
| **BMI (kg/m²)**<br>21.26 (19.55, 23.41) | 24.57 (22.75, 26.65)* | 25.23 (22.42, 28.44)* | 26.82 (24.59, 29.84)* | \(<0.001\) |
| **BP %**<br>18.76 (16.03, 22.37) | 33.68 (30.83, 36.60)* | 24.02 (20.53, 27.89)* | 36.42 (33.31, 39.80)* | \(<0.001\) |
| **WC (cm)**<br>71.0 (66.5, 75.5) | 84.0 (79.0, 90.0)* | 79.8 (77.0, 83.0)* | 84.0 (80.0, 87.0)* | \(<0.001\) |
| **SBP (mmHg)**<br>111 (103, 125) | 125 (117, 133)* | 118 (107, 129)* | 129 (119, 137)* | \(<0.001\) |
| **DBP (mmHg)**<br>69 (63, 76) | 78 (71, 85)* | 75 (66, 82)* | 82 (74, 88)* | \(<0.001\) |
| **Total cholesterol (mg/dL)**<br>178 (159, 200) | 189 (168, 210)* | 187 (166, 209)* | 192 (171, 216)* | \(<0.001\) |
| **Triglycerides (mg/dL)**<br>65.0 (49.9, 89.0) | 70.5 (56.0, 90.0) | 79.0 (63.0, 95.0) | 84.0 (67.0, 102.0) | \(<0.001\) |
| **HDL cholesterol (mg/dL)**<br>53.0 (48.0, 58.0) | 51.0 (46.0, 55.0)* | 48.0 (42.0, 53.0)* | 45.0 (39.0, 50.0)* | \(<0.001\) |
| **Chol/HDL**<br>2.97 (2.61, 3.46) | 3.55 (3.00, 4.33)* | 3.55 (3.00, 4.33)* | 4.39 (3.70, 5.10)* | \(<0.001\) |
| **Fasting glucose (mg/dL)**<br>83.0 (79.0, 88.0) | 88.0 (83.0, 94.0)* | 90.0 (81.0, 93.0)* | 90.0 (84.0, 97.0)* | \(<0.001\) |
| **Creatinine (mg/dL)**<br>0.61 (0.54, 0.68) | 0.89 (0.81, 0.98)* | 0.81 (0.74, 0.87)* | 0.89 (0.80, 0.90)* | \(<0.001\) |
| **eGFR (mL/min/1.73m²)**<br>134.10 (116.58, 155.48) | 104.88 (92.61, 117.73)* | 133.00 (116.58, 152.89)* | 104.04 (91.55, 118.56)* | \(<0.001\) |
| **hsCRP (µg/mL)**<br>0.44 (0.20, 0.90) | 0.74 (0.40, 1.19)* | 3.36 (2.59, 5.52)* | 3.13 (2.43, 5.03)* | \(<0.001\) |
| **Homocysteine (µmol/L)**<br>8.7 (7.5, 10.1) | 11.0 (9.5, 12.7) | 8.8 (7.5, 10.3) | 11.1 (9.7, 12.9)* | \(<0.001\) |
| **MetS (n, %)**<br>Absent 1991 (96.4) | 4696 (63.9)* | 397 (77.4) | 1421 (67.9)* | \(<0.001\) |
| Present 75 (3.6) | 1886 (26.1*) | 116 (22.6) | 673 (32.1)* | \(<0.001\) |
| **KD (n, %)**<br>**eGFR<60**<br>2015 (97.5) | 5420 (69.6)* | 482 (94.0)* | 1974 (94.0)* | \(<0.001\) |
| **eGFR<60 and/or proteinuria**<br>of 1+ or greater proteinuria <br>on urinalysis 51 (2.5) | 174 (3.1) | 31 (6.0) | 120 (5.7) | \(<0.001\) |

*Indicates a significant difference between as compared to the normal hsCRP/normal BFP group.

**Indicates a significant difference between as compared to the normal hsCRP/high BFP group.

†Indicates a significant difference between as compared to the high hsCRP/normal BFP group.

‡Indicates a significant difference between as compared to the high CRP/high BFP group.

BFP = body fat percentage; BMI = body mass index; CKD = Chronic kidney disease; DPB = diastolic blood pressure; eGFR = estimated glomerular filtration rate; HDL = high density lipoprotein; JACE = estimated glomerular filtration rate; hsCRP = high-sensitivity C-reactive protein; MetS = metabolic syndrome; SBP = systolic blood pressure; WC = waist circumference.

Grouping was based on the serum hsCRP levels and body fat percentage. High hsCRP was defined as serum level of hsCRP ≥ 1.95 µg/mL. High body fat percentage was defined as body fat >25% in men or >35% in women. Continuous data are reported as median (interquartile range) for non-normal distribution data and compared using the Kruskal-Wallis Test; categorical data are shown as number (percentage) and compared using the Chi-square test.
### 3.4. Association of body fat percentage and hsCRP levels with estimated CKD risk based on BMI categories

Table 4 shows the OR of CKD for the normal BFP/normal hsCRP, normal BFP/high hsCRP, high BFP/normal hsCRP, and high BFP/high hsCRP groups of subjects with a normal or increased BMI. We used a multivariate logistic regression model to adjust for age, gender, smoking status, history of hypertension, diabetes, and serum TChol/HDL-C. Compared with the normal BFP/normal hsCRP group for overweight or obese subjects, the risk of CKD was higher in the normal BFP/high hsCRP and high BFP/high hsCRP groups, but not the high BFP/normal hsCRP group. However, the risks for CKD in normal BMI subjects with various combinations of BFP/hsCRP levels showed no significant difference, as compared with the normal BFP/normal hsCRP group.

#### 4. Discussion

We found that a high BFP and elevated serum hsCRP levels were both associated with a reduced eGFR in our subjects. Contrary to previous studies showing that obesity is associated with an increased risk of CKD and its progression,[3,16,25,26] our results suggest that a high BFP in the setting of acute inflammation (represented with elevated hsCRP level) might reduce the risk of CKD, especially in overweight or obese patients.

To date, numerous studies have demonstrated that excess weight, including higher BMI and greater WC, were significantly associated with increased risk for the prevalence and progression of CKD.[3,6,25,26] Possible mechanisms of chronic renal injury resulting from excess body weight include the adverse effects of adaptations to increased body mass load due to glomerular hyperfiltration, obesity, hypertension, and insulin resistance.[27,28] Furthermore, the adipose tissue, represented as an endocrine organ itself, releases several bioactive mediators,[29] many of which are associated with inflammation[30] and an increase in endogenous production of pro-inflammatory cytokines.[31–34] These inflammatory cytokines may then play a crucial pathogenic role in chronic kidney injury[7] by possibly dysregulation of renal cells and subsequent tissue injury secondary to increased oxidative stress and endothelial dysfunction. This in turn stimulates glomerular cell production and reduces degradation of extracellular matrix protein, leading to glomerular hypertension, tubulointerstitial fibrosis, and renal scarring,[35,36] and hence resulted in chronic kidney injury.

Nevertheless, nowadays more and more studies suggested that the adipose tissue, on the contrary, plays an important role in maintaining energy homeostasis, and thus protects the body from

#### Table 4

**Association analysis of percent body fat and high-sensitivity C-reactive protein based on categories of body mass index for chronic kidney disease (N = 10,267).**

| BMI < 23 | BMI ≥ 23 |
|----------|----------|
| **Odds Ratio** | **95% CI** | **P value** | **Odds Ratio** | **95% CI** | **P value** |
| Normal hsCRP/ Normal BFP | 1 | | 1 | |
| Normal hsCRP/ High BFP | 0.88 | 0.54–1.34 | .592 | 1.06 | 0.63–1.79 | .818 |
| High hsCRP/ Normal BFP | 1.83 | 0.75–4.43 | .182 | 2.32† | 1.23–4.37 | .010† |
| High hsCRP/ High BFP | 0.59 | 0.18–1.93 | .382 | 1.86† | 1.08–3.17 | .022† |

*Indicates a significant difference compared with the reference group.

† The models were adjusted for age, gender, smoking, history of hypertension, diabetes and serum total cholesterol/ high-density lipoprotein cholesterol.

BFP = body fat percentage, BMI = body mass index, CI = confidence interval, hsCRP = high sensitivity C-reactive protein.
injury in certain circumstances, such as acute inflammatory state, low temperature, critical illness, or acute infection. In some experimental studies, blockade of mineralocorticoid receptors in obese diabetic mice decreased the expression of pro-inflammatory factors in adipocytes and increased the expression of adiponectin, a potent protective mediator in health outcomes. Other studies demonstrated that inflammation might modify the association between BMI and mortality in ESRD patients through altering adipose tissue in the critically ill. The abovementioned findings indicated that inflammation might play a role in adipocyte and adipokine transformation in obese patients with CKD.

Furthermore, the traditional role attributed to adipose tissue is energy storage, and many studies have shown that energy stores were important for a survival advantage in acute illness, severe inflammation, or external stress. Because these adipocytes have an increased ability to store glucose and TGs, they may possibly reduce the detrimental effects of high levels of these circulating metabolites.

In addition, the biological function of brown adipose tissue is heat production that confers the beneficial effects of adiposity, insulin resistance, and hyperlipidemia in experimental studies in mice. Increasing evidence has indicated that the browning of white adipose tissue in hypermetabolic conditions might reduce adverse effects and help improve metabolic health. In humans, the browning of white adipose tissue plays a major role in energy homeostasis and protects the body from injury in certain situations such as critical illness or acute infection.

Recently, the opposite epidemiology was found in some studies showing that adipose tissue is protective in certain chronic diseases. This phenomenon has been termed the “obesity paradox” in which obese and overweight patients with chronic diseases have higher survival rates. The underlying pathophysiology may be related to the browning of white adipose tissue or the theory of protein energy reserve. Studies found that obesity-related preserved protein energy stores that might hypothetically result in a protective effect in an advanced CKD population, especially in patients with inflammation. However, the underlying pathophysiology and causal relationship resulting in changes in a reduction in the risk of CKD necessitate further study. Whether a paradoxical association between high body fat and CKD exists for patients with inflammation necessitates long-term study to verify the causal relationship. Future research is needed to clarify the underlying mechanisms and to determine the therapeutic targets associated with the reduction in the CKD risk.

To our knowledge, our study was the first to analyze the association among body composition, inflammation, and CKD risk in healthy Asian adults. Because BMI is a poor reflection of actual body composition, some studies reported that body composition or central fat distribution is considered a more important risk factor for CKD and eGFR than BMI, and reliance on BMI alone might underestimate the associated risk. Our study results also verified the concepts and pointed out that BFP distribution, beyond BMI, might influence eGFR in relatively healthy adults in Asian population. This might provide an aid for physician to early recognize the risks of CKD progression in management of clinical practice.

This study had some limitations. First, our study subjects were young or middle-aged, predominantly male, and relatively healthy without significant comorbidities and used of different standard of BMI or BFP would affect the results. The abovementioned characteristics enable the present findings to apply only to the specific population, rather than the overall population. Second, because this was a retrospective analysis using data of subjects undergoing annual health exam, further longitudinal analysis to verify the causal relationship was needed. Third, the BIA can reflect the estimated body composition, instead of the actual lean or fat mass amount and the regional distribution of the adipose tissue such as central or peripheral fat mass. Whether the distribution of adipose tissue could influence disease risk necessitates additional study.

This study enrolled a large sample size of Asian population where prevalence of ESRD remained high around the world. Through the evaluation of relationship among BMI, BFP and CKD in various hsCRP state may provide information in clinical management of chronic kidney disease progression.

5. Conclusion

Our findings provide an important method for the early detection of impaired renal function by identifying overweight or obese subjects with various body compositions and inflammatory states to prevent CKD at an earlier stage.

Acknowledgments

YLCh and SSC are in equal contribution to this work. The research team would like to thank the staff of the Family Medicine, Health, and Management and Emergency Department in the Keelung, Taoyuan, Linkou, and Chiayi branches of Chang Gung Memorial Hospital who participated in data collection. This study had no funding source. Thanks also to Chang Gung Memorial Hospital for the research resources.

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