

The Association between Three-Dimensional Pericardial Adiposity Measures, Life Quality Scores and Physical Functional Status beyond Anthropometrics in Men

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Abstract

Background: Previous studies demonstrated visceral adiposity in relation to metabolic disorder may mediate systemic inflammation and predict cardiovascular outcomes. However, data regarding visceral adipose tissue burden and quality of life or physical performance remains largely unknown.

Methods: We studied participants who underwent non-contrast enhanced 16-slice multi-detector cardiac Computed Tomography (CT) scanning for cardiovascular health survey. Three-Dimensional (3D) visceral adipose volumes, including both Pericardial Fat (PCF) and Thoracic Peri-Aortic Fat (TPAF), were obtained. We further related these measures to high sensitivity C-Reactive Protein (hs-CRP) levels and questionnaires regarding life quality and physical performance assessments (SF-36).

Results: Among 306 men (mean age: 49.4 ± 7.6 years) in our study, we observed that items of decreased physical functioning scoring were significantly associated with both increased PCF (β -

coefficient: -4.20, $P = 0.010$) and TPAF (β -coefficient: -2.86, $P = 0.036$). Interestingly, these associations remained unchanged even after adjusting for clinical variables and hs-CRP (both $p < 0.05$).

Conclusion: Increased pericardial and thoracic aortic fat burden may play a role via multiple potential mechanisms in worsening physical function, which may be less relevant to common cardiovascular disease pathophysiologies related to systemic inflammation.

Keywords: Life Quality; Pericardial Fat; Thoracic Peri-Aortic Fat; Cardiovascular Disease; SF-36

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Background

The prevalence of obesity increase gradually, even among the aging group. The long-term deleterious consequences of excessive adiposity have great clinical importance. Abundant evidence demonstrates that overweight or obesity lead to impaired physical function and decreased life quality, along with increased risk of various chronic diseases and reduced life expectancy [1-3]. In recent years, increasing interest has been raised regarding the impact of body fat composition or distribution to alterations in cardiac structure and function [4]. Abdominal obesity which is characterized as increased adipose tissue surrounding the intra-abdominal organs is also referred to as visceral or central obesity [5]. Central obesity is also independently associated with Left Ventricular (LV) diastolic dysfunction [6, 7].

As a hormonally active tissue, Visceral Adipose Tissue (VAT) release different bioactive molecules and hormones mediating metabolic derangements and atherogenic inflammatory cytokines such as interleukin 6 and tumor necrosis factor- α . These inflammatory cytokines result in chronic cellular dysfunction and injury [8]. VAT such as Pericardial Fat (PCF) and Thoracic Peri-Aortic Fat (TPAF), namely the adipose tissues surrounding the myocardium, coronaries and thoracic aorta, are associated with inflammatory cell infiltration and higher production of NF- κ B-dependent cytokines compared to subcutaneous adipose tissue [9, 10]. The more evidences demonstrated that excessive PCF may exert its toxic effect on adjacent cardiac structures [11, 12] and even associated with autonomic dysfunction and poor cardiopulmonary fitness [13]. These evidences all suggest that excessive PCF may be tightly associated with exercise intolerance and physical activity limitations. In our study, we aimed to investigate whether PCF, TPAF are associated with physical activity in our subjects. We further wished to examine the relationship between systemic inflammatory marker, PCF, TPAF and physical activity.

Methods

Study participants

A total of 350 men were consecutively enrolled using a cardiovascular health survey in Mackay Memorial Hospital (MMH). Baseline demographics and medical history were obtained using questionnaires, with blood counts, biochemistry and biomarker data obtained upon initial examination. All

subjects who were free from angina symptoms during exercise and excluded those who suffered any known cardiovascular diseases such as previous myocardial infarction, coronary arterial disease, stroke, atrial fibrillation, or peripheral arterial disease. Those with overt renal failure, with a serum creatinine level ≥ 2.5 , or who were currently undergoing hemodialysis were also excluded. Detailed physical examinations were performed for each participant as well as a thorough review of baseline demographics and medical history including alcohol consumption, smoking, and physical activity status from structured questionnaires. All baseline characteristics and anthropometric measures including age, body height, body weight, body Waist Circumference (WC), and buttocks circumference were collected, and the Body Mass Index (BMI) was calculated. Standardized sphygmomanometer cuff-defined blood pressure was measured under resting status by medical staff blinded to other test results. This study was approved by MMH, international ethical review committees (MMH-I-S-023).

Biochemical data acquisition and analysis

All sample collection and analytic principles were based on the standard requirements according to the Clinical Laboratory Standards Institute guidelines (Specimen Choice, Collection, and Handling; Approved Guideline H18-A3). To ensure accuracy, samples were tested twice in their original tubes on the same day to avoid sample mix-up. Fasting and post-prandial glucose levels (hexokinase method), total cholesterol, triglyceride, and uric acid, blood urea nitrogen, creatinine level (kinetic colorimetric assay), and all lipid profiles (homogeneous enzymatic colorimetric assay) were obtained using a Hitachi 7170 Automatic Analyzer (Hitachi Corp. Hitachinaka Ibaraki, Japan). Hs-CRP levels were determined using the highly sensitive, latex particle-enhanced Immunoassay, Elecsys 2010 (Roche, Mannheim, Germany).

Quantification of PCF and TPAF

All study participants underwent non-contrast enhanced cardiac Computed Tomography (CT) in our center. PCF and TPAF volumes were measured on cardiac CT scans that were used to assess coronary calcification. Cardiac CT was performed using a 16-slice Multi-Detector CT (MDCT) scanner (Sensation 16, Siemens Medical Solutions, Forchheim, Germany) with 16×0.75 mm collimation, rotation time of 420 ms, and tube voltage of 120 kV. In one breath-hold, images were acquired from landmark

above the level of tracheal bifurcation to below the base of the heart using prospective electrocardiogram triggering with the center of the acquisition at 70% of the R-R interval. By using the raw data, the images were reconstructed into 3D-based volume data with standard kernel in 3-mm-thick axial, non-overlapping slices, and 25-cm field of view. All image analyses were performed on a dedicated workstation (Aquarius 3D Workstation, TeraRecon, San Mateo, CA, USA). PCF and TPAF volumes were quantified using a dedicated workstation (Aquarius 3D Workstation, TeraRecon, San Mateo, CA, USA). By using this semi-automatic segmentation technique, we are able to quantify fat volumes. We traced the region of interest manually and defined the amount of fat tissue as the number of pixels within a window of -195 HU to -45 HU and a window center of -120 HU. PCF was defined as any adipose tissue located within the pericardial sac. TPAF was defined as all of the adipose tissue surrounding the thoracic aorta which extended 67.5 mm from the level of the bifurcation of pulmonary arteries with cranial-caudal coverage of the thoracic aorta. This approach has previously been validated [14, 15] with intra-observer and inter-observer coefficients of variation in a subset of 40 subjects in our previous report [14].

Quality of life survey

The SF-36 [16] questionnaire has long been used in a number of cardiac rehabilitation studies as well as in additional studies related to cardiovascular diseases including coronary arterial disease. The questionnaire is composed of 8 concepts: physical functioning (pf), role-physical (rp) limitations due to physical health, bodily pain (bp), general health (gh) perceptions, vitality (vt), social functioning (sf), role limitations due to emotional problems (role-emotional: re), and general mental health (mh). Subsequently, 2 summary measures of physical and mental health are constructed from the 8 scales. The quality of life of the study participants was assessed using the SF-36 questionnaire. Each subscale ranges from 0 to 100 scores, with zero indicating the worst and 100 the best [17]. In addition, 2 summary scale scores (physical component summary and mental component summary) can be calculated by normalizing Taiwan population means, so that the average score is 50, and the Standard Deviation (SD) is 10. Higher scores on the physical component summary and the mental component summary indicate better quality of life.

Statistical Analysis

Continuous data were expressed as the mean and SD with categorical data expressed as the frequency and proportion of occurrence. The correlation of PCF and TPAF with hs-CRP was assessed using Pearson's correlation analysis. A partial correlation was further carried out to examine correlations after adjusting for age, hypertension, hyperlipidemia, diabetes, smoking, BMI, and WC. Considering that the values of the 3 serum biomarkers PCF, TPAF, and hs-CRP were not normally distributed, a log transformation was used. To investigate the association of PCF, TPAF, and hs-CRP with quality of life, multivariable linear regression was carried out. The regression coefficients were based on a model adjusted for age, BMI, WC, smoking status, drinking status, exercise habit, education level, marriage status, and medical history. As some medical histories were less common, frequencies below ten ($n < 10$) were categorized as other disease.

Results

Baseline demographic information and anthropometric data of all participants

Of all 350 men who participated in the cardiovascular health survey, 306 completed a quality of life questionnaire available for subsequent analysis. The mean age of the 306 participants was 49.4 ± 7.6 years. Approximately half of the participants completed their college education ($n = 90$, 29%), and most were married ($n = 286$, 96%), non-smokers ($n = 219$, 72%), non-drinkers ($n = 260$, 87%), non-betel users ($n = 292$, 98%), and had exercise habits ($n = 223$, 73%). The average weight, height, BMI, WC, and hip circumference were 70.6(kg), 169.0 (cm), 24.7 (kg/m²), 85.9 (cm), and 96.5 (cm), respectively. The mean values of PCF, TPAF, and hs-CRP were 77.0mL, 8.4mL and 0.21 mg/L, respectively. Other serum lipid measurements are summarized in Table 1.

Correlation of PCF and TPAF with baseline demographic data, anthropometrics, biochemical profiles, and hs-CRP levels

As shown in Table 2, a correlation analysis was performed to assess the correlation of PCF and TPAF with several baseline demographics, body anthropometrics, biochemical data, and hs-CRP levels. There was strong correlation between PCF and TPAF ($r=0.62$, $p<0.001$), with good association between BMI and both visceral fat measures ($r=0.52$ & 0.59 , both $p<0.001$, Figure 1).

We observed that aging, increased body weight; BMI, larger waist and hip circumferences, as well as higher fasting glucose and triglyceride levels were all positively associated with both higher PCF and TPAF (all $P < 0.001$). In addition, HDL levels were inversely correlated with PCF and TPAF (both $P < 0.001$). Moreover, we observed a negative relationship between PCF and renal function as assessed by the estimated glomerular filtration rate ($r = -0.13$, $P = 0.02$), with a borderline relationship noted between renal function and TPAF ($r = -0.11$, $P = 0.065$). In addition, there was significant correlation between PCF and hs-CRP, regardless of the adjustment for age, hypertension, hyperlipidemia, diabetes, and smoking (Pearson's correlation coefficient = 0.15, $P = 0.024$ and partial correlation coefficient = 0.14, $P = 0.044$). A similar correlation was found between TPAF and hs-CRP (Pearson's correlation coefficient = 0.19, $P = 0.003$ and partial correlation coefficient = 0.18, $P = 0.008$). These results indicate that both PCF and TPAF are positively correlated with hs-CRP levels.

Distribution of overall quality of life scoring for all participants

The scores of the quality of life questionnaire (SF-36) are summarized in Figure 2. The mean value of each subscale ranged from 66.7 to 94.1 with a standard variation range of 8.8 to 21.0. The summary score of the physical component, which consists of physical functioning, role-physical limitation due to physical problems, bodily pain, and general health perception was 50 (SD = 9.5). The remaining 4 subscales accounted for the mental component and had a summary score of 50 (SD = 10.1).

The association between quality of life scoring, PCF, TPAF, anthropometrics, biochemical profiles, and hs-CRP levels

In Table 3, the univariable and multivariable regression models for PCF, TPAF, hs-CRP, and overall quality of life scoring are shown. By univariable analysis, we observed a significant negative association between physical functioning scoring and PCF (log value) (coefficient = -3.41 , $P = 0.02$), with a borderline negative association between physical functioning and TPAF (log value) (coefficient = -2.12 , $P = 0.081$). In addition, general health perception scoring had a significant negative association with TPAF (log value) (coefficient = -5.78 , $P = 0.011$) and a borderline negative association with PCF (log value) (coefficient = -5.00 , $P = 0.068$). In addition, there was

significantly negative association between bodily pain and hs-CRP (log value) (coefficient = -2.49 , $P = 0.007$). Furthermore, there was no association between physical functioning and BMI, WC ($B = -0.204$, $P = 0.299$, $B = -0.120$, $P = 0.618$, respectively) after adjustment for PCF and TPAF.

By multivariable analysis, again no association was observed between the SF-36 quality of life scoring subscales and PCF or TPAF, except for physical functioning and general health perception. Negative associations between PCF and physical functioning was observed, with an increase in PCF and TPAF significantly associated with decreases in physical functioning by 4.14 and 3.05, respectively ($P = 0.014$ and 0.04 , respectively). The regression coefficient between TPAF and general health was -4.1 ($P = 0.046$), suggesting that higher TPAF levels are significantly associated with lower general health scores.

The association between each item of physical functioning, PCF, TPAF, and hs-CRP

In addition to total physical functioning scores, we also estimated the relationship between the each item of physical functioning and PCF, TPAF and hs-CRP (Table 4). As shown in table 4, the univariable analysis, a significant negative correlation of PCF with item 1 (vigorous activities) and item 6 (bend, kneel) was observed (coefficient = -0.396 , $P < 0.001$; coefficient = -0.169 , $P = 0.003$); while that of TPAF with item 1 and item 4 (climb several flights) was also observed (coefficient = -0.237 , $P = 0.004$; coefficient = -0.108 , $P = 0.031$). By multivariable analysis, an increase in PCF significantly associated with decreases in item 1 and item 6, respectively (coefficient = -0.447 , $P < 0.001$; coefficient = -0.241 , $P < 0.001$). Similarly, TPAF was independently negatively associated with item 1 and item 6, respectively (coefficient = -0.320 , $P = 0.002$; coefficient = -0.174 , $P = 0.002$). However, there also was no correlation between each item of physical functioning and hs-CRP.

Discussion

The main results of this study demonstrated a negative correlation between physical functioning scores and both PCF and TPAF independent of body anthropometrics in terms of BMI, obesity-related disorders or cardiovascular risk factors (including age, diabetes, hypertension, hyperlipidemia, and cigarette smoking) or co-morbidities (including hepatitis, fatty liver, peptic ulcer disease, and gout).

Recent studies [18] suggest that the association between physical activity and BMI is weak in non-obese individuals. We observed a significant positive correlation between BMI, WC and PCF, TPAF. However, there was no association between physical functioning and BMI ($B = -0.204$, $P = 0.299$) or WC ($B = 0.120$, $P = 0.618$) after adjustment for PCF and TPAF. It seems that the term “central obesity,” in reference to visceral fat accumulation in either lean or obese individual, might identify those at risk for chronic disease better than the commonly used definitions of obesity by body mass index (BMI) [19].

In the each component of physical functioning scores, we particularly observed that the ability of vigorous activity or body flexibility (bend or kneel) had significant negative correlation with PCF and TPAF. The more evidences have demonstrated that an amount of Inter-Muscular Adipose Tissue (IMAT) or epicardial fat has stronger positive associations with increase age [20]. Aging-related progression of sarcopenia [21] and degenerative joint disease is exacerbated by Inter-Muscular Adipose Tissue (IMAT) inflammation mediated. High levels of leg IMAT are associated with decreased muscle strength and muscle quality. A vicious cycle is established when such individuals become less physically able, progressing to the inability to perform simple activities of daily living [22, 23]. Our study also demonstrated an increase in PCF, TPAF deposition significantly associated with aging. Simultaneously, we particularly observed that a growing amount of PCF and TPAF pay strong negative impact on the strenuous exercise or body flexibility. Underlying mechanisms may be increased PCF and TPAF accompanied IMAT increased, thereby decreasing muscle strength and reducing exercise capacity and physical function. Additionally, PCF and TPAF accumulation might be associated with causing skeletal muscle damage mechanisms mediated. These need further research to clarify.

In addition to musculoskeletal dysfunction, the potential mechanisms of PCF, TPAF may adversely affect physical activity mediated multiple organ dysfunctions. The specific effects of pericardial fat on LV structural remodeling in terms of greater concentricity and functional disturbances that may be mediated by various mechanisms including mechanical, paracrine, and systemic processes have been suggested [24]. Furthermore, direct compression of the heart by this enveloping fat deposit may cause

impaired LV diastolic filling, leading to atrial remodeling and enlargement. Interestingly, the exact pathophysiological role of pericardial adiposity remains controversial so far [25].

Additionally, PCF lies in close proximity to the pulmonary outflow tract and lungs may adversely affect the lung function through following the potential mechanisms [26]. Firstly, PCF may mechanistically influence pulmonary function and a restrictive lung pattern through compression of the pulmonary artery. Secondly, PCF shares the same blood supply as the lung and exert a locally adverse effect on lung function through the expression of inflammatory cytokines.

Moreover, PCF has been found to correlate with autonomic dysfunction and poor cardiopulmonary fitness, which may impact exercise intolerance [13]. These evidences all recommend that excess accumulation of PCF and TPAF could lead to multiple organs dysfunction and further deteriorate exercise capacity and physical function status.

However, the systemic inflammatory mechanisms that link VAT (such as PCF and TPAF) accumulation with poor physical activity or exercise intolerance are still not well understood. Most studies have used high-sensitivity C-reactive protein (hs-CRP) to represent the extent of vascular and systemic inflammation response. It has also been widely advocated as a novel risk factor of CVD [27]. Although there was positive correlation between PCF, TPAF and hs-CRP in our research, our analysis demonstrated the physical activity was reversely related to PCF and TPAF, but was not correlated with hs-CRP. Therefore, the PCF, TPAF adversely affecting exercise capacity or physical function through systemic inflammation mediated was not confirmed in our study. There is limited evidence at present that raising HDL-C has a benefit on CVD prevention independent of lowering LDL-C particularly in patients with metabolic syndrome [28]. However, there was no correlation between HDL-C and physical functioning (coefficient=0.077, $P=0.180$) in our current cohort. These results suggest that PCF and TPAF may play a more direct role in worsening physical function, which may be less relevant to a common hypothetical CVD pathophysiology related to systemic inflammation. The potential key role of PCF, TPAF in decreased physical function remains to be further clarified.

Regardless of the mechanisms whereby the accumulation of PCF and TPAF will worsen exercise capacity and physical function, it is not known whether increasing exercise will reduce VAT (such as PCF, TPAF), and thus improve life quality. Recent researches have shown that aerobic exercise has significant effects not only on body weight loss but also reducing abdominal subcutaneous fat, VAT and thus improve insulin sensitivity, muscle strength, and physical function [29, 30]. In the future, longitudinal cohort study is important to verify what type the exercise and which intensity and frequency will reduce the PCF, TPAF, thereby increasing physical functional status in the men population.

Limitations

There are several limitations in our study. First, this survey is retrospective and cross-sectional study. We had various confounders in the multivariate analysis including hepatitis, fatty liver, hypertension, hyperlipidemia, peptic ulcer disease, gout, or other disease as well as lifestyle factors like exercise, smoking and alcohol. However, some factors such as diet and drug therapies are literally not included in our study. Longitudinal study is required to further follow up or validation with clinical outcomes. Secondly, physical activity is a more complex behavior cannot be accurately reflected in a questionnaire. Further study, calculated exercise capacity is necessary to quantify physical activity. Third, our database has no coronary CT angiogram results. It could not provide the correlation of coronary artery stenosis, quality of life and physical function in men population. Finally, our study only analyzed male participants and is therefore not representative of the overall population.

Conclusion

In our study, we observed that VAT (as assessed by PCF and TPAF) is an independent measure, beyond the commonly used anthropometric parameters for abdominal obesity, and had a negative correlation with physical functional status. Several possible mechanisms may contribute to VAT accumulation to poor physical function and exercise intolerance. However, these mechanisms are not based on the conventional conceptual link

between systemic inflammation and CVD. Nonetheless, the results of studies that examined the impact of excessive adiposity on impaired physical function remain inconclusive and longitudinal cohort studies are required to validate clinical outcomes.

References

1. Shimabukuro M. Cardiac adiposity and global cardiometabolic risk: new concept and clinical implication. *Circ J*. 2009;73(1):27–34.
2. Wilson PW, D’Agostino RB, Sullivan L, et al. Overweight and obesity as determinants of cardiovascular risk: the Framingham experience. *Arch Intern Med*. 2002;162(16):1867–1872.
3. Mathus VEM. Prevalence, pathophysiology, health consequences and treatment options of obesity in the elderly: a guideline. *Obes Facts* 2012;5: 460-483.
4. Lauer MS, Anderson KM, Kannel WB, et al. The impact of obesity on left ventricular mass and geometry. The Framingham Heart Study. *JAMA* 1991;266:231– 236.
5. Shuster A, Patlas M, Pinthus JH, et al. The clinical importance of visceral adiposity: a critical review of methods for visceral adipose tissue analysis *Br J Radiol*. 2012 ;85(1009):1-10.
6. Russo C, Jin Z, Homma S, et al. Effect of obesity and overweight on left ventricular diastolic function: a community-based study in an elderly cohort. *J Am Coll Cardiol* 2011;57:1368–1374.
7. Canepa M, Strait JB, Abramov D, et al. Contribution of central adiposity to left ventricular diastolic function (from the Baltimore Longitudinal Study of Aging). *Am J Cardiol*. 2012;109:1171-1178.
8. Despres JP, Lemieux I, Bergeron J, et al. Abdominal obesity and metabolic syndrome: contribution to global cardiometabolic risk. *Arterioscler Thromb Vasc Biol*. 2008;28(6):1039–1049.
9. Tadros TM, Massaro JM, Rosito GA, et al. Pericardial fat volume correlates with inflammatory markers: the Framingham Heart Study. *Obesity*. 2010;18(5):1039–1045.
10. Iacobellis G, Bianco AC. Epicardial adipose tissue: emerging physiological, pathophysiological and clinical features. *Trends Endocrinol Metab*. 2011 Nov;22(11):450-457.

11. Iacobellis G, Ribaudo MC, Zappaterreno A, et al. Relation between epicardial adipose tissue and left ventricular mass. *Am J Cardiol*. 2004 Oct15;94(8):1084–1087.
12. Konishi M, Sugiyama S, Sugamura K, et al. Accumulation of pericardial fat correlates with left ventricular diastolic dysfunction in patients with normal ejection fraction. *J Cardiol*. 2012;59(3):344–351.
13. Kim MK, Tanaka K, Kim MJ, et al. Epicardial fat tissue: relationship with cardiorespiratory fitness in men. *Med Sci Sports Exerc*. 2010;42(3):463–469.
14. Yun CH, Lin TY, Wu YJ et al. Pericardial and thoracic adipose tissues contribute to systemic inflammation and calcified coronary atherosclerosis independent of body fat composition, anthropometric measures and traditional cardiovascular risks. *Eur J Radiol*. 2012;81(4):749–756.
15. Lehman SJ, Massaro JM, Schlett CL, et al. . Peri-aortic fat, cardiovascular disease risk factors, and aortic calcification: the Framingham Heart Study. *Atherosclerosis*. 2010;210(2):656–661.
16. Ware JE, Kosinski MK, Keller SD. SF-36 Physical and Mental Health Summary Scales: A User's Manual. Boston: The Health Institute, New England Medical Center; 1994.
17. Tseng HM, Lu JF, Tsai YJ. Assessment of health-related quality of life in Taiwan (II): norming and validation of SF-36 Taiwan Version. *Taiwan Journal of Public Health*. 2003;22:512–518.
18. Hemmingsson E, Ekelund U. Is the association between physical activity and body mass index obesity dependent? *Int J Obes*. 2007;31(4):663–668.
19. Hamdy O, Porramatikul S, Al-Ozairi E. Metabolic obesity: the paradox between visceral and subcutaneous fat. *Curr Diabetes Rev*. 2006;2(4):367–373.
20. Guglielmi V, Maresca L, D'Adamo M, et al. Age-Related Different Relationships between Ectopic Adipose Tissues and Measures of Central Obesity in Sedentary Subjects. *PLoS One*. 2014 Jul 22;9(7):e103381.
21. Cominacini L, Harris TB, Zamboni M, et al. Adipose tissue infiltration in skeletal muscle of healthy elderly men: relationships with body composition, insulin resistance, and inflammation at the systemic and tissue level *J Gerontol A Biol Sci Med Sci*. 2010 Mar;65(3):295-299.
22. Zamboni M, Mazzali G, Fantin F, et al. Sarcopenic obesity: a new category of obesity in the elderly. *Nutr Metab Cardiovasc Dis* 2008; 18: 388–395.
23. Schrager MA, Metter EJ, Simonsick E, et al. Sarcopenic obesity and inflammation in the InCHIANTI study. *J Appl Physiol* 2007; 102: 919–925.
24. Turkbey EB, McClelland RL, Kronmal RA, et al.. The impact of obesity on the left ventricle: the Multi-Ethnic Study of Atherosclerosis (MESA). *J Am Coll Cardiol Img* 2010;3:266–274.
25. Lai YH, Liu CC, Kuo JY, et al. Independent effects of body fat and inflammatory markers on ventricular geometry, midwall function, and atrial remodeling. *Clin Cardiol* 2014;37:172-177.
26. Hickson DA, Liu J, Bidulescu A, et al .Pericardial fat is associated with impaired lung function and a restrictive lung pattern in adults: the Jackson Heart Study *Chest*. 2011 Dec;140(6):1567-1573.
27. Libby P, Ridker PM. Novel inflammatory markers of coronary risk: theory versus practice. *Circulation*. 1999;100:1148-1150.
28. Katabami T, Murakami M, Kobarashi S, et al. Efficacy of low-dose rosuvastatin in patients with type 2 diabetes and hypo high-density lipoprotein cholesterolaemia. *J Int Med Res* 2014;42:457-467.
29. Stessman J, Hammerman-Rozenberg R, Cohen A, et al. Physical activity, function, and longevity among the very old. *Arch Intern Med*. 2009;169(16):1476–1483.
30. Hamer M, Venuraju SM, Urbanova L, et al. Physical activity, sedentary time, and pericardial fat in healthy older adults. *Obesity*. 2012 20(10):2113-2117.

Table 1 Baseline demographic information, anthropometric data, and biochemical profiles for the 306 study participants

Variable	<i>n</i> (%) or Mean $\pm$ SD
Demographical characteristics	
Age (yr)	49.4 $\pm$ 7.6
Completed college, %	90 (29%)
Married, %	286 (96)
Current or former smoker, %	85 (28)
Current or former alcohol consumption, %	39 (13)
Current or former betel consumption, %	6 (2)
Exercise (more than 1 hour per week), %	223 (73)
Systolic BP (mmHg)	127.9 $\pm$ 17.7
Diastolic BP (mmHg)	75.4 $\pm$ 11.8
Anthropometric characteristics	
Body weight (kg)	70.6 $\pm$ 9.8
Height (cm)	169.0 $\pm$ 5.8
BMI (kg/m ²)	24.7 $\pm$ 3.0
Waist circumference (cm)	85.9 $\pm$ 7.8
Hip circumference (cm)	96.5 $\pm$ 5.6
Biochemical Data	
Fasting glucose (mg/dL)	101.0 $\pm$ 15.7
Triglyceride (mg/dL)	147.6 $\pm$ 89.5
HDL-C (mg/dL)	48.0 $\pm$ 12.1
LDL-C (mg/dL)	128.6 $\pm$ 30.4
Cholesterol (mg/dL)	204.2 $\pm$ 36.2
eGFR (mL/min/1.73 m ²)	85.3 $\pm$ 13.2
hs-CRP (mg/L)	0.21 $\pm$ 0.42
Visceral Adiposity	
PCF (mL)	77.0 $\pm$ 25.9
TPAF (mL)	8.4 $\pm$ 3.5

Note: Continuous variables were presented as mean and standard deviation; BP = blood pressure; BMI = body mass index; eGFR = estimated glomerular filtration rate; PCF = pericardial fat; TPAF = thoracic peri-aortic fat; HDL-C = high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; hs-CRP, high sensitivity C-reactive protein; SD = standard deviation.

Table 2 Correlation between VAT, including PCF and TPAF, and baseline demographic information, body anthropometrics, serum biochemical profiles, and serum hs-CRP level

	PCF		TPAF	
	<i>r</i>	<i>P value</i>	<i>r</i>	<i>P value</i>
Demographics				
Age (yr)	0.3	<0.001	0.26	<0.001
Body weight (kg)	0.44	<0.001	0.52	<0.001
Height (cm)	0.004	0.95	−0.001	0.99
BMI (kg/m ²)	0.52	<0.001	0.59	<0.001
Waist circumference (cm)	0.54	<0.001	0.63	<0.001
Hip circumference (cm)	0.4	<0.001	0.47	<0.001
Biochemical Data				
Fasting glucose (mg/dL)	0.19	<0.001	0.25	<0.001
Triglyceride (mg/dL)	0.25	<0.001	0.3	<0.001
HDL-C (mg/dL)	−0.26	<0.001	−0.33	<0.001
LDL-C (mg/dL)	0.08	0.17	0.05	0.42
Cholesterol (mg/dL)	0.06	0.28	0.04	0.52
eGFR (mL/min/1.73 m ²)	−0.13	0.02	−0.11	0.065
hs-CRP(mg/L)				
Pearson's correlation coefficient	0.15	0.024	0.19	0.003
Partial correlation coefficient ^a	0.14	0.044	0.18	0.008

Note: All values were log transformed; ^aAdjustment was made for age, hypertension, hyperlipidemia, diabetes, and smoking; BMI = body mass index; eGFR = estimated glomerular filtration rate; PCF = pericardial fat; TPAF = thoracic peri-aortic fat; HDL-C = high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; hs-CRP, high sensitivity C-reactive protein.

Table 3 Univariable and multivariable regression models for associations of (PCF), TPAF, and hs-CRP with SF-36 scores for all 306 study participants

Univariable Model Component of SF-36	PCF (log)		TPAF (log)		hs-CRP (log)	
	Coef.	P value	Coef.	P value	Coef.	P value
Physical functioning	-3.41	0.02	-2.12	0.081	0.32	0.555
Role limitation due to physical problem	-0.15	0.963	-1.89	0.481	0.502	0.703
Role limitation due to emotional problem	0.57	0.87	-1.36	0.642	0.38	0.791
Social functioning	0.68	0.713	0.58	0.707	-0.53	0.475
Bodily pain	-1.23	0.614	-0.71	0.726	-2.49	0.007
Mental health	-0.001	0.99	-0.15	0.937	0.74	0.392
Vitality	-0.37	0.886	-2.17	0.316	-0.19	0.853
General health	-5	0.068	-5.78	0.011	-1.8	0.089
Physical component summary	-2.07	0.19	-1.7	0.195	-0.47	0.452
Mental component summary	0.42	0.797	-0.45	0.74	-0.05	0.934
Multivariable Model Component of SF-36	PCF (log)		TPAF (log)		hs-CRP (log)	
	Coef.	P value	Coef.	P value	Coef.	P value
Physical functioning	-4.14	0.014	-3.05	0.04	0.31	0.591
Role limitation due to physical problem	-1.06	0.769	-4.4	0.167	0.43	0.747
Role limitation due to emotional problem	0.58	0.885	-2.13	0.545	0.17	0.911
Social functioning	-0.3	0.889	0.75	0.689	-0.49	0.534
Bodily pain	-2.29	0.414	-0.41	0.824	-2.73	0.005
Mental health	0.93	0.709	0.24	0.913	0.84	0.351
Vitality	-0.14	0.961	-3.9	0.123	-0.24	0.818
General health	-2.3	0.456	-4.1	0.129	-1.35	0.225
Physical component summary	-3.03	0.097	-2.55	0.113	-0.54	0.416
Mental component summary	1.35	0.466	-0.08	0.96	0.04	0.955

Table 4 Univariable and multivariable regression models for associations of (PCF), TPAF, and hs-CRP with each item of physical functioning (PF) for all 306 study participants

Univariable Model	PCF (log)		TPAF (log)		hs-CRP (log)	
	Coef.	P	Coef.	P	Coef.	P
Item of physical functioning						
Item 1 Vigorous activities	-0.396	<0.001	-0.237	0.004	0.011	0.765
Item 2 Moderate activities	-0.077	0.216	-0.030	0.552	0.024	0.275
Item 3 Lift, carry groceries	-0.038	0.425	-0.003	0.933	0.001	0.938
Item 4 Climb several flights	-0.091	0.136	-0.108	0.031	-0.001	0.978
Item 5 Climb one flight	0.007	0.771	0.021	0.288	0.005	0.567
Item 6 Bend, kneel	-0.169	0.003	-0.082	0.080	0.029	0.181
Item 7 Walk mile	0.034	0.469	0.002	0.961	-0.006	0.722
Item 8 Walk several blocks	-0.008	0.815	-0.010	0.726	-0.008	0.520
Item 9 Walk one block	0.008	0.692	0.009	0.571	-0.002	0.797
Item 10 Bathe , dress	0.009	0.361	0.009	0.285	0.000	1.000
Multivariable Model	PCF (log)		TPAF (log)		hs-CRP (log)	
	Coef.	P	Coef.	P	Coef.	P
Item of physical functioning						
Item 1 Vigorous activities	-0.447	<0.001	-0.320	0.002	0.015	0.711
Item 2 Moderate activities	-0.114	0.107	-0.087	0.169	0.024	0.301
Item 3 Lift, carry groceries	-0.071	0.190	-0.041	0.395	-0.003	0.883
Item 4 Climb several flights	-0.072	0.296	-0.103	0.089	0.000	0.990
Item 5 Climb one flight	-0.010	0.726	0.013	0.600	0.003	0.776
Item 6 Bend, kneel	-0.241	<0.001	-0.174	0.002	0.017	0.449
Item 7 Walk mile	0.010	0.850	-0.028	0.550	-0.012	0.521
Item 8 Walk several blocks	-0.003	0.946	0.002	0.944	-0.009	0.507
Item 9 Walk one block	0.005	0.827	0.014	0.492	-0.003	0.663
Item 10 Bathe , dress	0.015	0.205	0.017	0.105	0.000	1.000

Note: All serum lipid values were log transformed; B = regression coefficient; In multivariable models, adjustment was made for age (≥ 60), BMI (≥ 25), smoke (yes vs. no), alcohol (yes vs. no), exercise habit (yes vs. no), education level (graduate vs. college or below), and marriage status (married vs. single or divorced), and disease (hepatitis, fatty liver, hypertension, hyperlipidemia, peptic ulcer disease, Gout, or other disease). All the control variables were coded as dummy variables.

PCF = Pericardial Fat; TPAF = Thoracic Peri-Aortic Fat.

Figure 1 The linear correlation between PCF and TPAF ($r=0.62$, $p<0.001$), and the positive association between body size (BMI) and both visceral adiposity (PCF and TPAF).

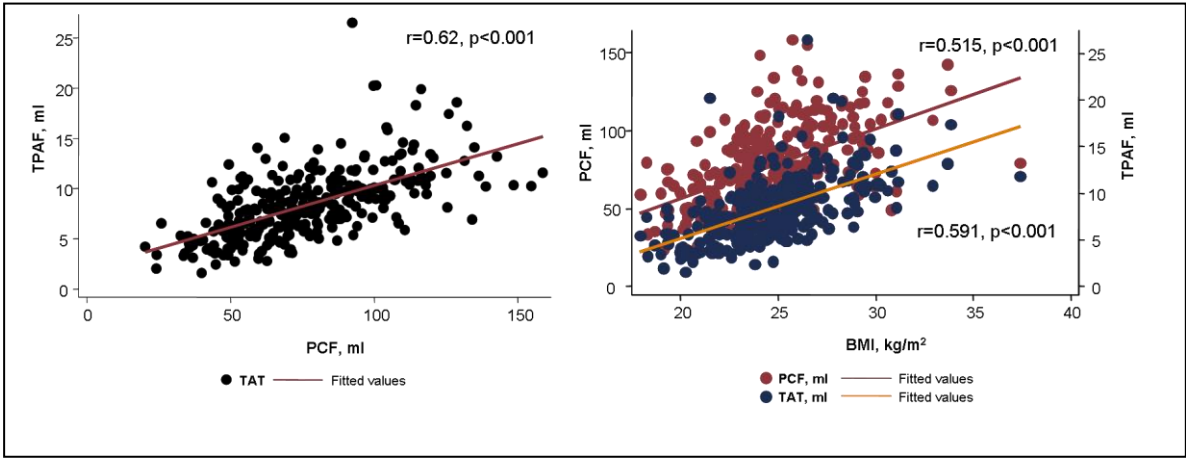


Figure 2 The SF-36 scores among the 306 study participants with mean and standard deviation presented. Physical functioning (pf), role-physical (rp) limitations due to physical health, bodily pain (bp), general health (gh) perceptions, vitality (vt), social functioning (sf), role limitations due to emotional problems (role-emotional: re), and general mental health (mh) were displayed.

