Original Research

Relationship of Coronary Artery Disease with Pericardial and Periaortic Adipose Tissue and Their Volume Detected by MSCT

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Key words: **Multislice computed tomography, coronary arteriosclerosis, adipose tissue.**

Introduction: The relationship of pericardial and periaortic adipose tissue with coronary artery disease (CAD) and the significance of this relationship were investigated.

Methods: The present study included 323 subjects, with or without cardiac symptoms, who underwent multislice computed tomography coronary angiography between May 2009 and January 2013. Patients were divided into two groups according to the mean values of pericardial adipose tissue volume (PCFV) and periaortic adipose tissue volume (PAFV). In the grouping based on PCFV, subjects with PCFV<157.7 cm^3 comprised Group 1, and those with PCFV≥157.7 cm^3 comprised Group 2. According to PAFV values, Group 1 consisted of subjects with PAFV<24.3 cm^3, and Group 2 subjects with PAFV≥24.3 cm^3. The relationship of CAD with each of PCFV and PAFV was investigated.

Results: Based on PCFV measurements, there were 79 (43.6%) and 113 (79.6%) patients with CAD in Groups 1 and 2, respectively. Based on PAFV measurements, Group 1 comprised 90 (48.1%) and Group 2 comprised 102 (75%) CAD patients.

Conclusions: In both groupings, the prevalence of CAD was significantly higher in Group 2 versus Group 1 ($p<0.01$ for both). There was a significant relationship between CAD and PAFV ($p<0.05$), but the relation between CAD and PCFV was more significant ($p<0.01$).

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Visceral adipose tissue is not merely a passive store of lipids, but it is an active endocrine organ that secretes active peptides, called adipokines.[1,2] Although subcutaneous adipose tissue accounts for a substantial proportion of total body adipose tissue, visceral adipose tissue has secretory functions associated with the pathophysiology of atherosclerosis.[3-6] There has been gradually increasing evidence that specific adipose tissue deposits are related with cardiovascular diseases.[7,8] Pericardial and periaortic adipose tissue is a part of visceral adipose tissue that surrounds the muscular organs in the body.[9] Pericardial adipose tissue is located in close proximity to the coronary arteries and may enhance the local effects of cells and cytokines with proatherogenic inflammatory effects.[10,11] Perivascular adipose tissue is also known to be metabolically active and may be a mediator of local vascular diseases.[12-15] Perivascular adipose tissue hypertrophy, in particular, may cause hypoxia, inflammation and oxidative stress as the result of physiological interaction with vascular tone.[16]

Multislice computed tomography (MSCT) coronary angiography is a non-invasive modality used in the detection and classification of coronary artery disease (CAD).[17,18] Pericardial, epicardial and periaortic adipose tissue volumes can be precisely measured from the same screening data.[19]

The aim of the present study was to compare the concurrency of CAD with pericardial and periaortic adipose tissue volumes and to determine which is more significant.

Methods

Clinical characteristics of patients

The present study included 323 subjects, with or without cardiac symptoms, who underwent MSCT angiography in our clinic between May 2009 and January 2013. The age range of the patients was 30-83 years (53.1 ± 11.2 years); 244 (75.5%) were male and 79 (24.5%) were female. Data were collected retrospectively and approval was obtained from the Ethics Committee.

All subjects were examined in terms of the traditional risk factors for CAD, including smoking, diabetes mellitus (DM), dyslipidemia, hypertension (HT), and familial CAD. Dyslipidemia was defined as a fasting serum triglyceride level ≥150 mg/dL, low-density lipoprotein (LDL) cholesterol level ≥140 mg/dL, and/or high-density lipoprotein (HDL) cholesterol level <40 mg/dL, or use of lipid modifying medication. Eighty-four (26%) of the study participants were smokers, 89 (26.9%) had HT, 50 (15.5%) had DM, 98 (30.3%) had dyslipidemia, and 68 (21.1%) had a family history of CAD.

The height (Human weighing scale, NAN TARTI A.Ş., Turkey) and weight (TANITA Body Composition Analyzer, TANITA Corporation, Japan) of the participants were measured prior to computed tomography (CT) scanning, and their body mass index (BMI) was calculated. Based on these measurements, 40 (12.4%) subjects had normal weight (BMI<25 kg/m^2), 236 (73.1%) were overweight (BMI between 25 kg/m^2 and 30 kg/m^2), and 47 (14.6%) were obese (BMI ≥30 kg/m^2).

MSCT image reconstruction, assessment of PCFV and PAFV

In the first stage, all subjects underwent non-contrast CT scanning from the carina to the sub-diaphragmatic level (Somatom Sensation 64, Siemens, Forchheim, Germany). The assessment of calcified coronary artery plaques was performed on non-contrast cardiac CT images. Tissues with an attenuation between ≤-200 and ≤-50 Hounsfield units were defined as adipose tissue. Pericardial adipose tissue volume (PCFV) and periaortic adipose tissue volume (PAFV) were measured by manually drawing a region of interest using a Leonardo workstation (Siemens) and volume analysis software (Argus; Siemens Medical Solutions). For analyzing PCFV, manual drawing was performed, covering the epicardial adipose tissue, pericoronary adipose tissue and paracardiac fat at the cardiac level (Figure 1).[20,21] For analyzing PAFV, fat tissue volume, bounded by the esophagus on the anterior, vertebral corpus margin on the posterior, the lateral part of the vertebral corpus on the right, and the costovertebral joint on the left side, was measured in the area surrounding the thoracic aorta (Figure 2).[22]

Two groupings were made for each parameter, with study groups created according to the mean values of PCFV and PAFV. The minimum and maximum values of PCFV were 43 and 359 cm^3 (mean ± SD, 157.7 ± 69.2 cm^3), whereas the corresponding values for PAFV were 1 and 102 cm^3 (24.3 ± 16.1 cm^3).

MSCT angiography and CAD evaluation

In the second phase, study participants underwent MSCT angiography, with imaging parameters as follows: 330 ms gantry rotation time, 120 kV tube voltage, 250 mA tube current and 0.6 mm detector col-

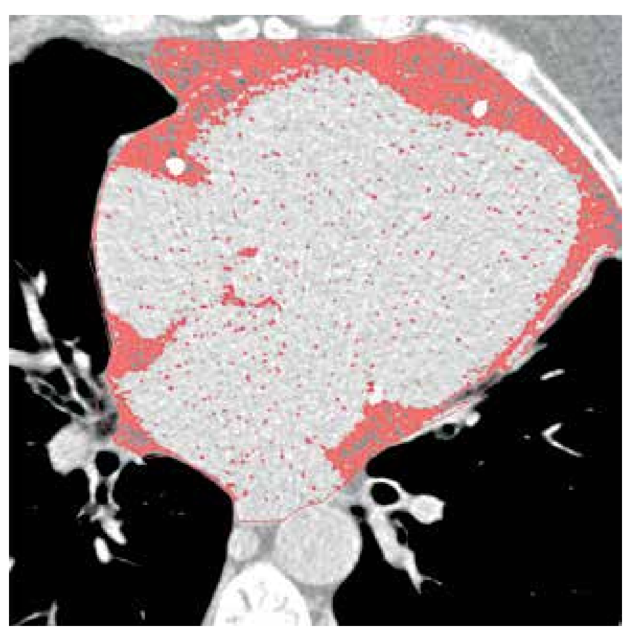
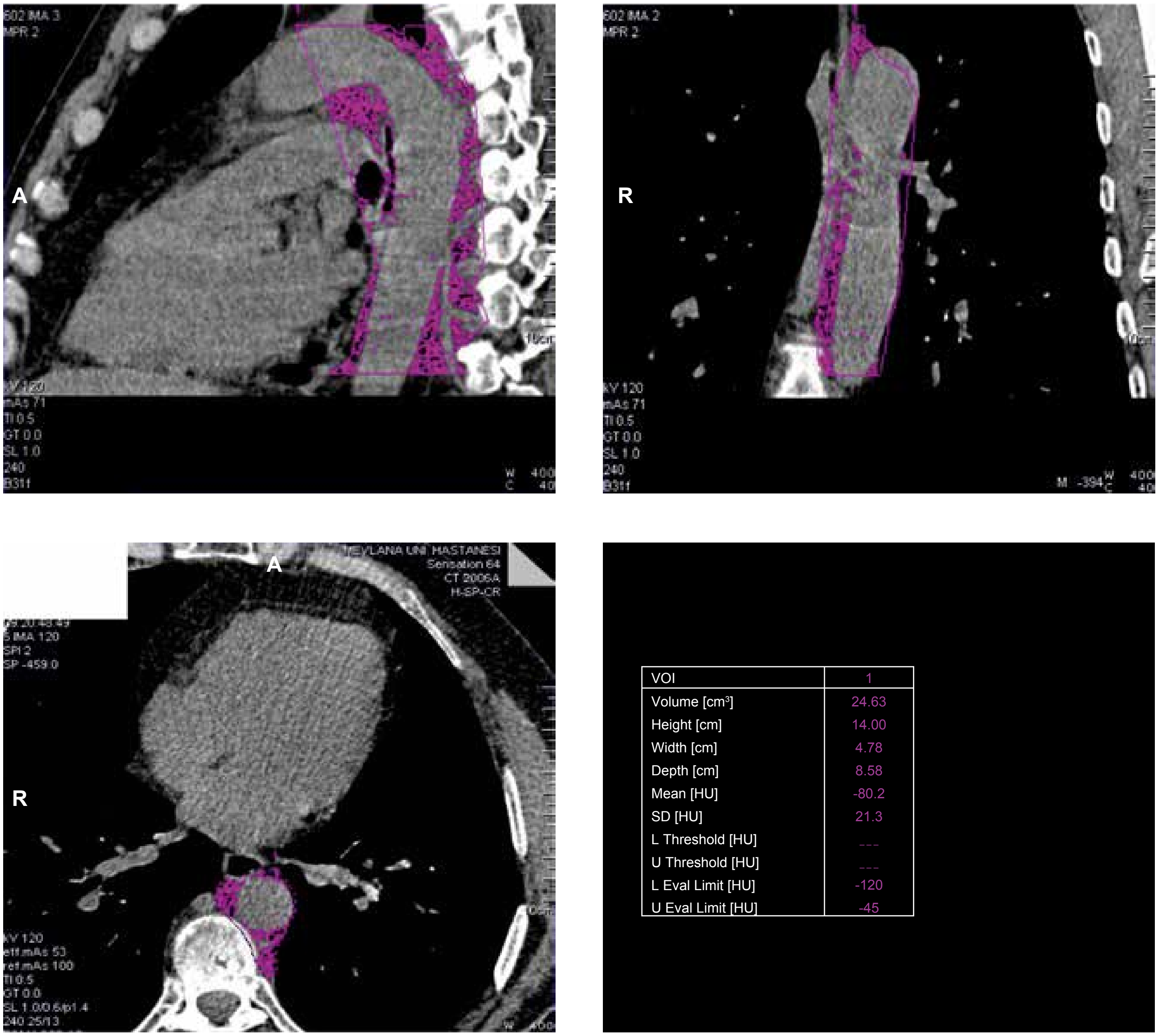


Figure 1. Pericardial fat volume in non-contrast CT images.



VOI	1
Volume [cm³]	24.63
Height [cm]	14.00
Width [cm]	4.78
Depth [cm]	8.58
Mean [HU]	-80.2
SD [HU]	21.3
L Threshold [HU]	---
U Threshold [HU]	---
L Eval Limit [HU]	-120
U Eval Limit [HU]	-45

Figure 2. Drawings showing the manual region of interest measurements of peri-aortic fat volume in non-contrast CT images.

limation. Images were obtained in the cranio-caudal direction from the carina to the diaphragmatic level, during a single breath hold for approximately 8.4-13.1 s. Depending on the patient's weight, 80-110 mL of nonionic contrast medium (Iomeron 400, Bracco s.p.a., Milan, Italy) was administered through an antecubital vein at a rate of 5.0 mL/s, followed by a bolus of 40 mL saline. The automatic peak contrast density of the ascending aorta was determined to be +140 Hounsfield units (HU). Images without artifacts were reconstructed at 0.6 mm slice thickness with an increment of 0.6 mm, according to a retrospective electrocardiographic gating technique. Multiplanar reformatted and three-dimensional volume rendered images were created from thin axial sections, and coronary artery anatomy was evaluated.

All coronary artery segments were evaluated visually. Study participants were divided into three groups according to the degree of coronary artery stenosis. Participants with no or small plaques were considered normal (Figures 3 & 4); those with at least one plaque and with luminal stenosis less than 50% were considered to have non-obstructive CAD (non-obsCAD) (Figures 5 & 6); and those with at least one atherosclerotic plaque causing ≥50% stenosis were considered to have obstructive CAD (obsCAD) (Figures 7 & 8). In addition, according to their content, coronary artery plaques were recorded as calcified or

Figure 3. Three-dimensional reconstruction image showing normal coronary arteries.

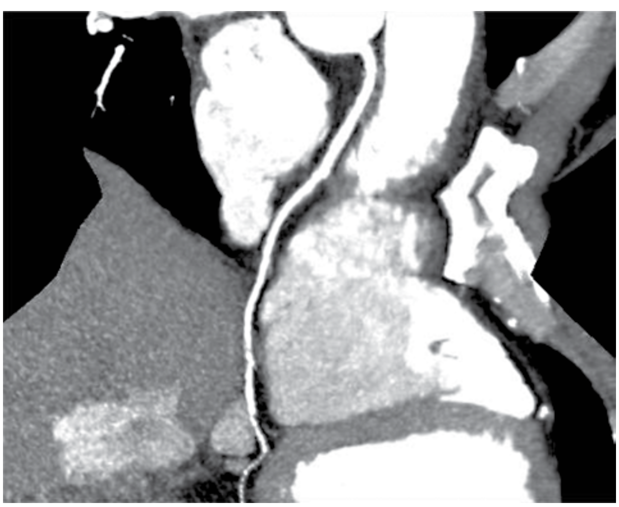


Figure 4. Multiplanar reformation image showing a normal coronary artery.

non-calcified. The MSCT angiography examination was performed by radiology and cardiology specialists.

Statistical analysis

The statistical analysis was performed using SPSS version 14 (SPSS Inc., Chicago, IL, USA). Statistical significance of nonparametric data between the groups was analyzed using Pearson's chi-square test.

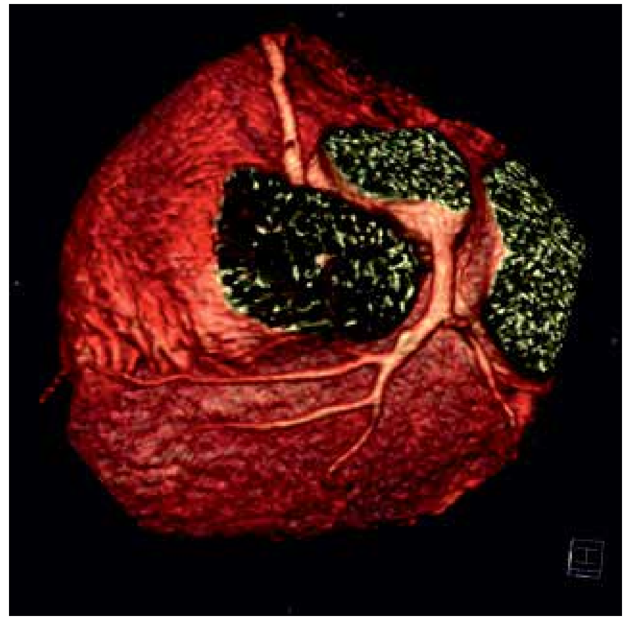


Figure 5. Three-dimensional reconstruction image showing a mildly stenotic coronary artery (non-obstructive coronary artery disease).

Figure 6. Multiplanar reformation image showing mildly stenotic calcified coronary plaque (non-obstructive coronary artery disease).

Parametric data were presented as minimum, maximum, and mean ± standard deviation, and the sta-

Figure 7. Three-dimensional reconstruction image showing severely stenotic coronary arteries (obstructive coronary artery disease).

Figure 8. Multiplanar reformation image showing severely stenotic calcified coronary plaques (obstructive coronary artery disease).

tistical significance of parametric data between the groups was analyzed using the independent Student t-test. A two-tailed p-value <0.05 was considered statistically significant. The relation of CAD with PCFV and PAFV was analyzed using binary logistic regression analysis and odds ratios were calculated.

Results

Subject characteristics

The mean PCFV was 113.9 ± 30.7 cm^3 and the mean PAFV was 23.4 ± 11.1 cm^3 in participants under the age of 40 years, whereas mean PCFV and PAFV were 210.8 ± 90.7 cm^3 and 33.1 ± 26.1 cm^3, respectively, in participants over the age of 65 years. Mean PCFV and PAFV were 170 ± 59.7 cm^3 and 26.5 ± 17.2 cm^3 in males, compared to 119.8 ± 81.9 cm^3 and 17.4 ± 9.3 cm^3 in females. Mean PCFV and PAFV were 162.5 ± 78.9 cm^3 and 17.2 ± 8.6 cm^3 in normal weight subjects, 152.4 ± 69.5 cm^3 and 23.6 ± 14.4 cm^3 in overweight subjects, and 180.5 ± 53.1 cm^3 and 33.6 ± 23.5 cm^3 in obese subjects, respectively.

The study participants were first divided into two groups according to the mean values (PCFV<157.7 cm^3 group 1, PCFV≥157.7 cm^3 group 2) and the relation of PCFV with CAD was investigated. Then the participants were again divided into two groups according to the mean PAFV values (PAFV<24.3 cm^3 group 1, PAFV≥24.3 cm^3 group 2), and the relation of PAFV with CAD was investigated.

Characteristics of the groups according to PCFV measurements

According to the PCFV measurements, Group 1 consisted of 181 (120 males, 66.3%) subjects and Group 2 consisted of 142 (124 males, 87.3%) subjects (Table 1, Figure 9).

The mean age of the males in Group 1 was 49.1 ± 10.8 years. The mean PCFV was 123.1 ± 28.6 cm^3, the mean serum C-reactive protein (CRP) level was 8.5 ± 7.3 mg/L, the mean serum triglyceride level was 187.3 ± 96.2 mg/dL, the mean serum HDL cholesterol level was 46 ± 14.7 mg/dL, and the mean serum LDL cholesterol level was 127.4 ± 32.1 mg/dL. Obesity was detected in 15 (12.5%) subjects and 26 (21.7%) subjects were diagnosed to have obsCAD.

The mean age of the females in Group 1 was 52.3 ± 11.0 years. The mean PCFV was 83.9 ± 29.3 cm^3, the mean serum CRP level was 7.2 ± 2.9 mg/L, the mean serum triglyceride level was 154.3 ± 69.8 mg/dL, the mean serum HDL cholesterol level was 49.7 ± 14.7 mg/dL, and the mean serum LDL cholesterol level was 132.5 ± 38.1 mg/dL. Obesity was detected in 4 (6.6%) and obsCAD 13 (21.3%) subjects.

The mean age of the males in Group 2 was 55.3 ± 10.1 years. The mean PCFV was 215.4 ± 45.2 cm^3, the mean serum CRP level was 8.6 ± 19.8 mg/L, the

Table 1. Association between pericardial fat volume (PCFV) and various measured parameters.

	Group 1 (n=181) (PCFV<157.7 cm^3)	Group 2 (n=142) (PCFV≥157.7 cm^3)	p
Age	50.2 ± 10.9	56.8 ± 10.5	0†
Sex (male)	120 (66.3%)	124 (87.3%)	0*
Familial history	42 (23.2%)	27 (19.0%)	0.362*
Diabetes	13 (7.2%)	38 (26.8%)	0*
Hypertension	41 (22.7%)	48 (33.8%)	0.026*
Smoking	38 (21%)	47 (33.1%)	0.014*
Obesity	19 (10.5%)	28 (19.7%)	0.020*
hsCRP (mg/L)	8 ± 6.2	8.8 ± 18.5	0.601†
Dyslipidemia	48 (26.5%)	52 (36.6%)	0.051*
Triglycerides (mg/dL)	176.2 ± 89.4	204.3 ± 88.9	0.005†
HDL-C (mg/dL)	47.2 ± 14.8	44.3 ± 9.8	0.043†
LDL-C (mg/dL)	129.1 ± 34.2	117.4 ± 30.9	0.002†
CAD:			
normal	102 (56.4%)	29 (20.4%)	
obsCAD	39 (21.5%)	75 (52.8%)	0*
obsCAD+non-obsCAD	79 (43.6%)	113 (79.6%)	

*By Pearson chi-square test; †by Student's t-test.

hsCRP – high-sensitivity C-reactive protein; HDL-C – high-density lipoprotein cholesterol; LDL-C – low-density lipoprotein- cholesterol; CAD – coronary artery disease; non-obs – non-obstructive; obs – obstructive.

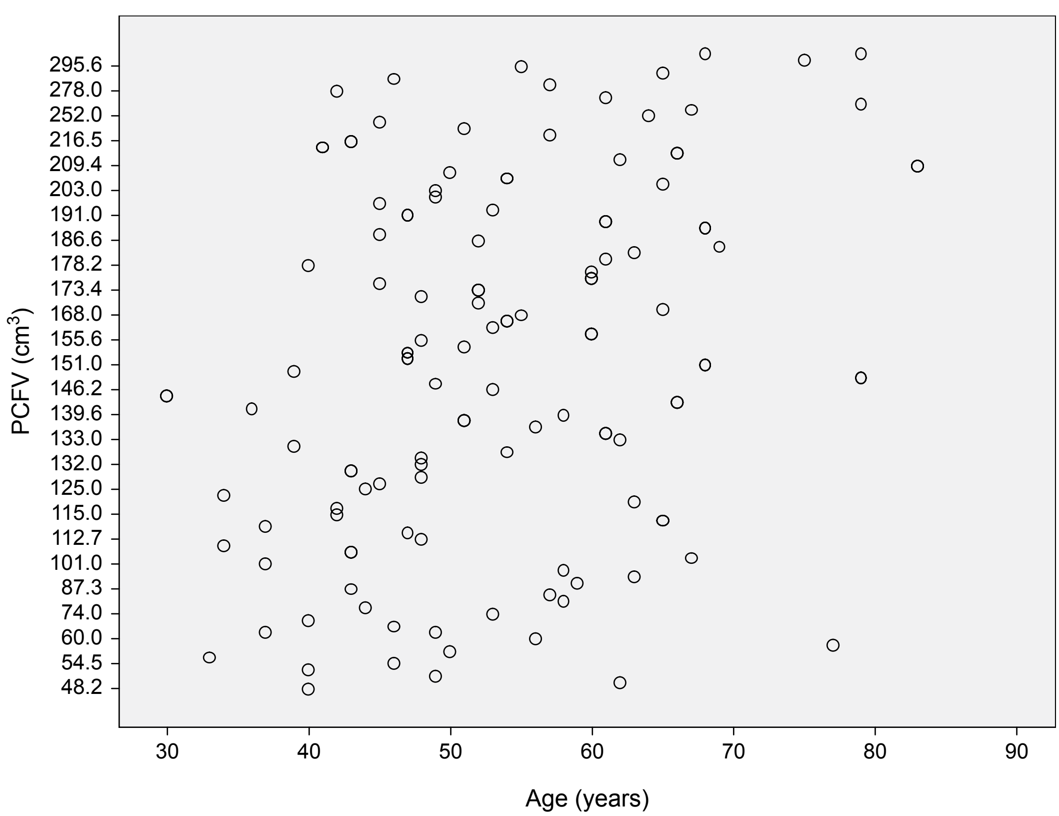


Figure 9. Scatter plot showing the distribution of pericardial fat volume (PCFV) measurements in relation to age.

Table 2. Association between periaortic fat volume (PAFV) and various measured parameters.

	Group 1 (n=187) (PAFV<24.3 cm^3)	Group 2 (n=136) (PAFV≥24.3 cm^3)	p
Age	51.7 ± 10.2	55.1 ± 12.3	0.007†
Sex (male)	123 (65.8%)	121 (89%)	0*
Familial history	38 (20.3%)	31 (22.8%)	0.592*
Diabetes	20 (10.7%)	31 (22.8%)	0.003*
Hypertension	50 (26.7%)	39 (28.7%)	0.700*
Smoking	42 (22.5%)	43 (31.6%)	0.065*
Obesity	18 (9.6%)	29 (21.3%)	0.001*
hsCRP (mg/L)	9.2 ± 16.8	7.2 ± 4.4	0.167†
Dyslipidemia	66 (35.3%)	34 (25%)	0.048*
Triglycerides (mg/dL)	190.8 ± 97.5	185.4 ± 79.2	0.600†
HDL-C (mg/dL)	45.1 ± 13.6	47 ± 11.9	0.196†
LDL-C (mg/dL)	124.9 ± 37.3	122.7 ± 26.9	0.561†
CAD:			
normal	97 (51.9%)	34 (25%)	
obsCAD	60 (32.1%)	54 (39.7%)	0*
obsCAD+non-obsCAD	90 (48.1%)	102 (75%)	

Notes and abbreviations as in Table 1.

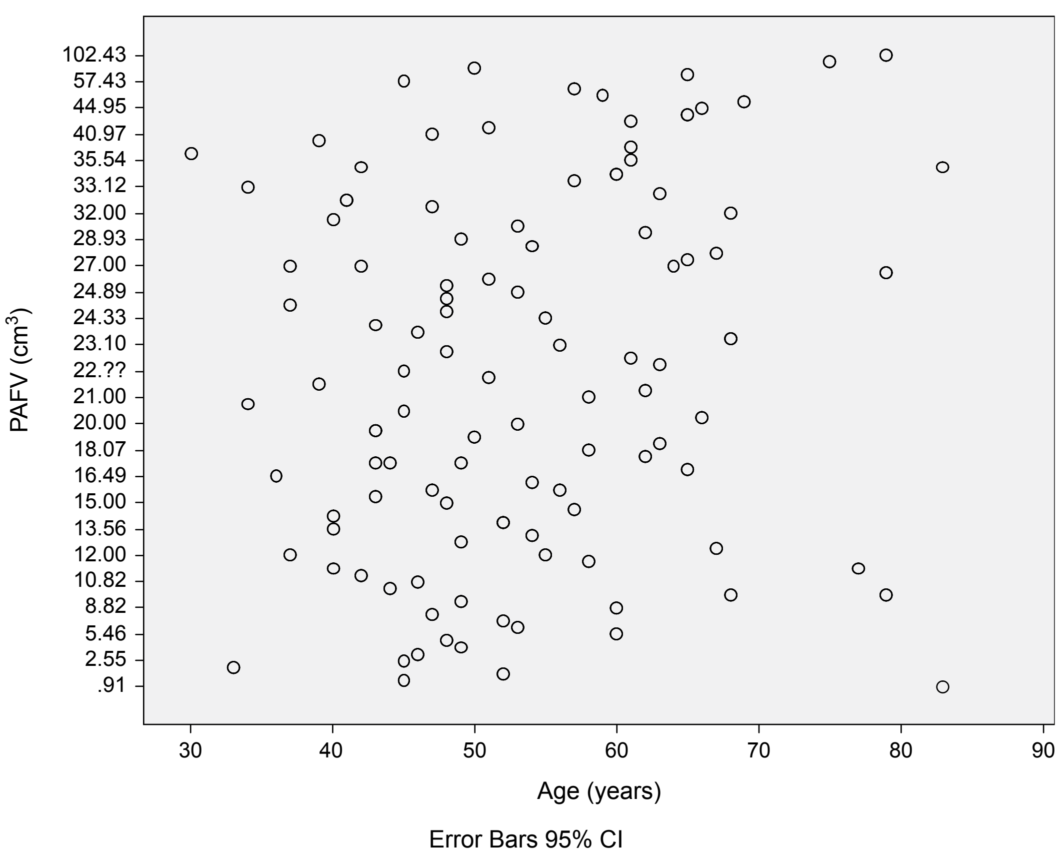


Figure 10. Scatter plot showing the distribution of periaortic fat volume (PAFV) measurements in relation to age.

Table 3. Results of binary logistic regression analysis.

	Unadjusted OR	95% CI	p	Adjusted OR	95% CI	p
Age	1.090	1.057-1.117	0.000	1.086	1.060-1.113	0.000
Sex (male)	0.973	0.488-1.938	0.937	-	-	-
Diabetes	2.873	1.262-6.539	0.012	-	-	-
Smoker	1.359	0.695-2.659	0.370	-	-	-
BMI (obesity)	0.625	0.349-1.120	0.114	-	-	-
hsCRP (mg/L)	1.015	0.977-1.054	0.446	-	-	-
Dyslipidemia	2.021	1.105-3.697	0.022	-	-	-
Total cholesterol (mg/dL)	0.996	0.985-1.007	0.518	-	-	-
Triglycerides (mg/dL)	0.999	0.996-1.003	0.748	-	-	-
HDL-C (mg/dL)	0.997	0.974-1.021	0.806	-	-	-
LDL-C (mg/dL)	0.988	0.975-1.001	0.066	-	-	-

OR – Odds Ratio; CI – confidence interval; BMI – body mass index. Other abbreviations as in Table 1.

mean serum triglyceride level was 209.4 ± 92.3 mg/dL, the mean serum HDL cholesterol level was 43 ± 9.6 mg/dL, and the mean serum LDL cholesterol level was 115.3 ± 31.3 mg/dL. Obesity was detected in 25 (20.2%) and obsCAD in 61 (49.2%) subjects.

The mean age of the females in Group 2 was 67.6 ± 5.9 years. The mean PCFV was 241.5 ± 86.4 cm^3, the mean serum CRP level was 10.1 ± 2.7 mg/L, the mean serum triglyceride level was 169.3 ± 49.4 mg/dL, the mean serum HDL cholesterol level was 47.6 ± 11.1 mg/dL, and the mean serum LDL cholesterol level was 131.7 ± 24.2 mg/dL. Obesity was detected in 3 (16.7%) subjects and 14 (77.8%) patients were diagnosed as having obsCAD.

Characteristics of the groups according to PAFV measurements

According to the PAFV measurements, there were 187 (123 males, 65.8%) participants in Group 1, and 136 (121 males, 89%) participants in Group 2 (Table 2, Figure 10).

The mean age of the males in Group 1 was 49.4 ± 8.5 years. The mean PAFV was 14.71 ± 6.6 cm^3, the mean serum CRP level was 10.1 ± 20.5 mg/L, the mean serum triglyceride level was 203.7 ± 107.3 mg/dL, the mean serum HDL cholesterol level was 43.3 ± 12.4 mg/dL, and the mean serum LDL cholesterol level was 120.8 ± 35.8 mg/dL. Obesity was determined in 14 (11.4%) and obsCAD in 39 (31.7%) subjects.

The mean age of the females in Group 1 was 56.1 ± 11.6 years. The mean PAFV was 14 ± 5.8 cm^3, the mean serum CRP level was 7.6 ± 3.1 mg/L, the mean serum triglyceride level was 166 ± 69.5 mg/dL, the mean serum HDL cholesterol level was 48.7 ± 15 mg/dL, and the mean serum LDL cholesterol level was 132.8 ± 39 mg/dL. Obesity was determined in 4 (6.3%) and obsCAD in 21 (32.8%) subjects.

The mean age of the males in Group 2 was 55.1 ± 12.2 years. The mean PAFV was 38.5 ± 16.3 cm^3, the mean serum CRP level was 7 ± 4.5 mg/L, the mean serum triglyceride level was 193.3 ± 80.1 mg/dL, the mean serum HDL cholesterol level was 46 ± 12.2 mg/dL, and the mean serum LDL cholesterol level was 121.7 ± 28.2 mg/dL. Obesity was determined in 26 (21.5%) and obsCAD in 48 (39.7%) subjects.

The mean age of the females in Group 2 was 54.6 ± 13.8 years. The mean PAFV was 32 ± 7.3 cm^3, the mean serum CRP level was 9 ± 3.2 mg/L, the mean serum triglyceride level was 122.4 ± 26.3 mg/dL, the mean serum HDL cholesterol level was 51.4 ± 7.5 mg/dL, and the mean serum LDL cholesterol level was 130.6 ± 8.7 mg/dL. Obesity was determined in 3 (20%) and obsCAD in 6 (40%) subjects.

The effect of different characteristics in the groups, including age, sex, etc., on CAD was investigated using binary logistic regression analysis. Results were considered statistically significant if the two-tailed p-value was <0.01 (Table 3).

Morphology of coronary plaques

In our study, 131 (40.6%) patients demonstrated no coronary plaques, 103 patients (31.7%) revealed calcified plaques, 55 (17,2%) cases had non-calcified plaques, and 34 (10.5%) subjects had mixed-type coronary plaques. The mean PCFV and PAFV in patients without coronary plaque were 119.1 ± 53.8 and 18.9 ± 11.4 cm^3, respectively, and the respective values in patients with coronary plaque were 184.1 ± 66.1 and 27.9 ± 17.8 cm^3. The differences between these subgroups were statistically significant ($p=0.001$ for PCFV and $p=0.048$ for PAFV). Mean PCFV values were statistically greater in patients with calcified plaque than in patients with non-calcified plaque (184.1 ± 66.2 vs. 161.5 ± 25.1, $p=0.014$). However these two groups did not demonstrate a statistically significant difference in terms of PAFV (27.9 ± 17.8 vs. 19.8 ± 10.9, $p>0.05$)

Discussion

The present study is the first to investigate the relation of CAD with pericardial and periaortic adipose tissue volumes. It revealed that the frequency of CAD was significantly higher in Group 2 versus Group 1 ($p<0.01$) in the grouping of patients according to PCFV. Likewise, in the grouping of patients according to PAFV, the frequency of CAD was significantly higher in Group 2 versus Group 1 ($p<0.01$). Whilst the relation between CAD and PAFV was statistically significant ($p<0.05$), the relation between CAD and PCFV was found to be statistically more significant ($p<0.01$).

Obesity is an important risk factor for cardiovascular diseases. However, regional fat deposition is a CAD marker that is attracting increasing attention. PCFV is considered as an independent risk factor in cardiovascular disease with respect to BMI and coronary artery plaque burden.[23] Therefore, measurement of the volume of adipose tissue around internal organs has become important for coronary atherosclerosis.[24,25] Today, magnetic resonance imaging (MRI) and CT are considered the gold-standard tools for PCFV measurement.[26] Recent studies have revealed that MSCT is more sensitive than transthoracic echocardiography in detecting PCFV and in measuring the thickness of adipose tissue.[19,28,29] Because pericardial fat tissue around the heart does not demonstrate a symmetrical three-dimensional distribution, thickness measurement from a single location would not optimally express the whole pericardial adipose tissue.[27] CT provides substantial information in detecting not only stenotic, but also subclinical coronary plaques.[19,28,29]

Two studies performed in patients with CAD demonstrated a significant relation between pericardial adipose tissue volume and the severity of CAD detected by coronary angiography.[30,34] A study performed in Japanese men found a significant relation between the severity of CAD and pericardial adipose tissue volume detected by coronary angiography.[30] Some studies found a positive relation between CAD and PCFV, supporting the results of the study conducted by Ding et al; however, other studies failed to find a significant relation.[31-32]

The amount of visceral adipose tissue is a risk factor for cardiovascular diseases; however, it is difficult to measure the amount of visceral adipose tissue. Some studies have shown that waist circumference measurement, which is commonly used, only moderately corresponds to the amount of intra-abdominal (visceral) and subcutaneous adipose tissues.[33] Mahabadi et al conducted a study using non-contrast CT in the measurement of PCFV, and reported that PCFV was correlated with CAD, after adjustment for age, gender, BMI and waist circumference, but that intrathoracic fat volume was not correlated with CAD.[33] Consistent with the results of the present study, some population-based studies and a few small-scale studies reported a relation between adipose tissue volume and thickness and certain risk factors of CAD, including development of calcified coronary artery plaques, blood pressure, LDL cholesterol, HDL cholesterol and glucose.[26]

Kilicaslan et al found a significant correlation between CRP and epicardial fat thickness. Sung et al showed high CRP levels in women of normal weight. However, there are studies showing elevated CRP levels in individuals with coronary artery disease (CAD).[35] In our study, no statistically significant difference in CRP levels was found in either the PCFV or the PAFV group.

Study limitations

In the present study, most of the participants were subjects who underwent MSCT with a prior diagnosis of CAD. Therefore, epidemiological studies are needed to verify our results. All of the participants were Caucasians and do not represent other races. In some patients, the degree of stenosis could hardly be determined on MSCT angiography because of dense calcified plaques. It was difficult to differentiate respiratory artifacts from potential coronary artery soft plaques in subjects with respiratory problems.

Conclusions

The present study determined a significant relation between pericardial and periaortic adipose tissue volumes measured by MSCT and the presence of coronary artery disease. Since the level of significance was $p<0.05$ for PAFV and $p<0.01$ for PCFV, it is reasonable to say that the relation between PCFV and CAD is stronger. These findings suggest that measurement of adipose tissue volume using a thoracic CT scan, performed for various purposes, may be used as a guide in determining the presence of coronary artery disease.

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