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Impact of age on epicardial and pericoronary adipose tissue volume

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Abstract. – OBJECTIVE: The aim of the present study was to investigate the impact of age on epicardial and pericoronary adipose tissue volume.

PATIENTS AND METHODS: Eighty healthy individuals with normal body mass index underwent multi-slice computed tomography (MSCT) with coronary computed tomography angiography, and their scanning images were stored and analysed. Among them, 62 subjects were male, and 18 subjects were female. The patients were grouped by age: 10 subjects were < 35 yrs, 20 were 35-44 yrs, 20 were 45-54 yrs, 20 were 55-64 yrs, and 10 were > 65 yrs. Pericoronary adipose tissue (PCAT), and the volume and the thickness of epicardial adipose tissue (EAT) were measured.

RESULTS: The correlation analysis showed that age was positively correlated to EAT volume. Moreover, spearman correlation analysis showed that the volumes of PCAT in the left main-left anterior descending artery (LM-LAD) and right coronary artery (RCA) gradually increased with increasing age, but not with the left circumflex artery (LCX) and EAT thickness ($p > 0.05$).

CONCLUSIONS: These findings suggest that the volumes of EAT and the adipose tissue surrounding the LM-LAD and RCA increase with increasing age.

Key Words:
Age, Epicardial adipose tissue, Pericoronary adipose tissue.

Introduction

With the improvement of medical care and living standards, the proportion of elderly individuals in China's population is growing every year. With increasing age, the functions of various organs and tissues in elderly individuals change, showing a gradually reduced proportion of muscle and a gradually increased proportion of fat in the body[1]. This increase in adipose tissue plays a pathophysiological role in some geriatric diseases[2]. Epicardial and pericoronary adipose tissue are part of visceral adipose tissue, which is closely related to the coronary artery with respect to anatomy[3,4]. The elderly population is susceptible to coronary heart disease. This study was performed to investigate the relationship between epicardial and pericoronary adipose tissue and increasing age.

Patients and Methods

Patients

Inclusion criteria. In January-December 2012, 80 healthy individuals with normal body mass index (BMI) underwent multi-slice computed tomography (MSCT) with coronary computed tomography angiography (coronary CTA), and their scanning images were stored and complete. Among them, 62 subjects were male, and 18 subjects were female. The patients were grouped by age: 10 subjects were < 35 years old, 20 subjects were 35-44 years old, 20 subjects were 45-54 years old, 20 subjects were 55-64, and 10 subjects were > 65 years old.

Exclusion criteria. (1) a BMI ≤ 18 or ≥ 25; (2) an abdominal circumference ≥ 90 cm for males or ≥ 85 cm for females; (3) a history of cancer; (4) acute infection; (5) moderate or severe renal insufficiency (a glomerular filtration rate GFR < 60 ml/min); (6) autoimmune disease; (7) diabetes mellitus; (8) thyroid disease; (9) lipid metabolic disorders; (10) arrhythmia; or (11) coronary stenosis or coronary revascularisation found in the coronary CTA.

Clinical Data

1) General information. The heights (m^2) and weights (kg) of subjects were measured to calculate BMI (kg/m^2); smoking history as well as the

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medical history of hypertension, coronary heart disease, diabetes, and thyroid disease were also obtained.

2) Metabolic indicators. Venous blood was collected from all patients after fasting for 8 hours to determine fasting blood glucose (FBG), uric acid (UA), total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), and low density lipoprotein cholesterol (LDL-C) levels. The blood fat, blood glucose, and uric acid were detected with an automatic biochemical analyser.

MSCT Method

Patient preparation. The patients were orally administered metoprolol tartrate tablets (12.5 mg) twice daily for 3 days before the examination, and chewable metoprolol tartrate (0-100 mg) was administered 0.5 hours before the examination. Heart rate was controlled at < 70 beats/min.

Imaging of the coronary CT scan. Light Speed HDCT 64-MSCTwas utilised with a scanningrange from 1 cm below the tracheal bifurcation to 2 cm under the diaphragm. A dynamic scan was performed at the same layer of the aortic root to detect the peak time of the contrast agent. The non-ionic contrast agent (iopamidol 300, 15 ml + saline 15 ml iopamidol) was injected into the cubital vein using a binocular high-pressure syringe with a flow rate of 4.0-5.0 ml/s. The delay time of scanning was determined (22-36s) based on the time-density curve. Using prospective or retrospective electrocardiography (ECG) gating, the iodide contrast agent (60-80 ml + 20 ml saline) was injected at a rate of 4.0-5.0 ml/s. The scanning scope was from the level of the tracheal carina to 2 cm below the diaphragmatic surface of the heart, and the scanning direction was from the feet to the head. The scanning parameters were as follows: tube voltage 120-140 kv, tube current 350-750 mA, thickness 0.625 mm, pitch 0.26, and rotation time 0.35s.

Measurement of the volume and thickness of epicardial adipose tissue (EAT). EAT volume was measured with GE ADW4.5 processing and analysis software. EAT was defined as the adipose tissue between the visceral pericardium and the myocardium. The measurement range was from the pulmonary artery bifurcation to the apex. In the measurement, the area containing EAT was manually cropped from the multiplanar reconstruction (MPR) image. The adipose tissues in the medi-

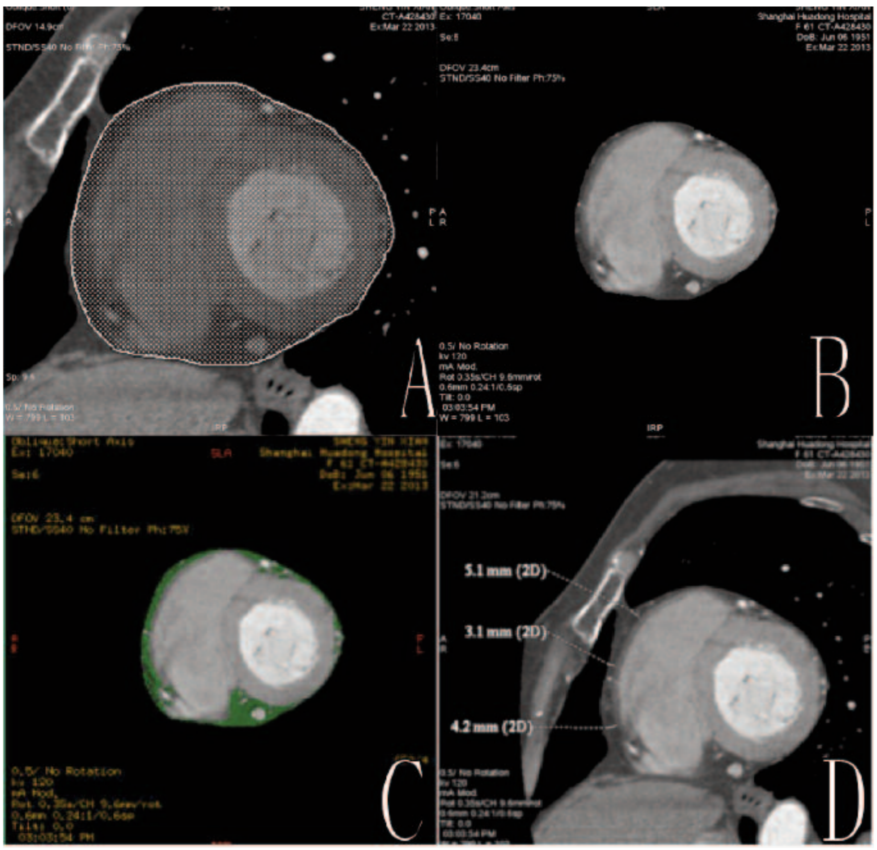

Figure 1. Determination of EAT volume and thickness. ***A,*** The area containing EAT to be manually cropped from the multiplanar reconstruction image; ***B,*** The EAT-containing area after cropping; ***C,*** The components within the specified region of -200 to -30 HU and the EAT volume were automatically calculated using the volume measurement function of the software; ***D,*** With the dissociation levels of 25%, 50% and 75% in the right ventricular wall as boundaries, the thicknesses of EAT in the anterior, middle and posterior segments were measured.

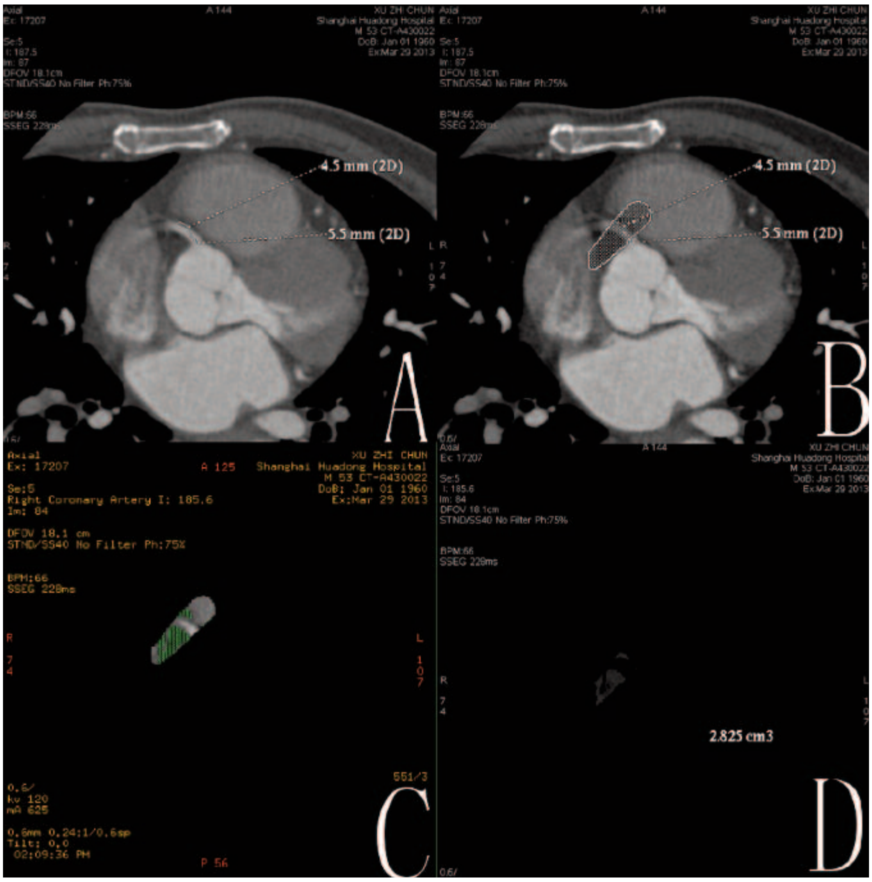

Figure 2. PCAT determination. ***A,*** The coronary artery was measured in 10-mm segments; ***B,*** The short axis of each vessel segment was reconstructed by MPR, and a region of interest containing the adipose tissue in the vessel segments and pericoronary area was manually cropped; ***C,*** The threshold was setas -200 to -30 HU; ***D,*** The PCAT volume of each segment was determined using automatic volume measurement software.

astinum and outside of the pericardium were removed. Using the method of threshold determination, the EAT was specified as the content within the region of -200 to -30HU. The components with CT values outside of the specified scope, such as the intracardiac contrast agent, vessel wall, and myocardium, were automatically removed by the software. Finally, the EAT volume was automatically calculated using the volume measurement function of the software. The EAT thickness was defined as the thickness of the adipose tissue in the right ventricular dissociated wall. The short axis images of the left and right ventricles were automatically obtained by the software Cardiac Reformat. With the dissociation levels of 25%, 50% and 75% in the right ventricular wall as boundaries, the EAT thicknesses in the anterior, middle and posterior segments were measured, and the average value of the three measurement was calculated for the statistical analysis (Figure 1).

Measurement of the pericoronary adipose tissue (PCAT). Using Auto Coronary Analysis software, VR (volume rendering) and MPR were performed for the coronary artery, and the shape of the coronary artery was determined using the vascular automatic analysis function to measure its exact length. The left main-the left anterior descending artery (LM-LAD), left circumflex artery (LCX), and right coronary artery (RCA) were continuously partitioned from the opening with 10 mmin each segment, and 5 segments of each coronary artery branch were measured. The measurement results for the 50 mm from the opening were sequentially labelled asLM-LAD1-5, LCX1-5, and RCA1-5. The short axis of each vessel segment was reconstructed by MPR, and the region of interest containing the adipose tissue in the vessel segments and pericoronary area was manually cropped. Using threshold measurements (the threshold was set as -200 to -30 HU) and automatic volume measurement software, the PCAT volume of each segment was determined, and the sum of the PCAT volumes for the 5 segments of each coronary artery was calculated to serve as the near middle PCAT of this coronary artery (Figure 2).

Statistical Analysis

Data were analysed by using SPSS Statistical Package version 16 (SPSS Inc., Chicago, IL, USA). Normally distributed data were expressed as mean

Table I. Comparison of the clinical data of patients in each group.

Age group	< 35 (n=10)	35-44 (n=20)	45-54 (n=20)	55-64 (n=20)	> 65 (n=10)	*p* value
Age (years)	32.4±1.95	40.6±2.44	49.4±3.60	60.00±3.00	70.00±2.16	0.000**
Gender (male/female)	8/2	16/4	15/5	16/4	7/3	0.969
BMI (kg/m^2)	22.81±0.78	22.45±1.37	22.81±1.22	23.09±0.98	23.09±0.98	0.572
Hypertension (number of cases)	2	11	11	16	8	0.014*
Smoking history (number of cases)	6	9	6	12	3	0.252
UA (mmol/dl)	317.70±70.52	336.65±53.65	366.45±40.40	338.10±61.72	340.90±62.13	0.218
TC (mmol/dl)	4.58±0.38	4.61±0.45	4.64±0.34	4.81±0.46	4.55±0.43	0.411
TG (mmol/dl)	1.14±0.34	1.04±0.28	1.21±0.24	1.17±0.36	1.10±0.36	0.462
HDL-C (mmol/dl)	1.21±0.11	1.25±0.10	1.13±0.08	1.19±0.14	1.13±0.10	0.004**
LDL-C (mmol/dl)	2.88±0.23	2.85±0.25	2.58±0.42	2.78±0.32	2.77±0.30	0.074

*$p < 0.05$; **$p < 0.01$.

± standard deviation and were compared using *t*-tests between two independent samples. Count data were compared using the chi-square test. Linear correlation analysis was conducted to manage the indicators using the Spearman correlation. $p < 0.05$ was considered statistically significant.

Results

Comparison of the Clinical Data

The general clinical data of the patients in different age groups are shown in Table I. Among the five age groups, no significant difference was found in the BMI and history of smoking ($p > 0.05$), and the UA, TC, TG, and LDL-C levels were not significantly different ($p > 0.05$). Compared to the 55-64 yrs and > 65 yrs groups, the number of hypertension cases in the < 35 yrs group was significantly lower, and the difference was statistically significant ($p < 0.05$). In addition, the HDL-C levels among the 5 groups were not the same; pairwise comparisons showed that the HDL-C levels of the 35-44 yrs group were higher than those of the 45-54 yrs and > 65 yrs groups, and the differences were statistically significant ($p < 0.05$).

Comparison of the EAT Volume and Thickness in Different Age Groups

As shown in Table II, the EAT volume gradually increased with increasing age, which occurred in the following order: > 65 yrs group > 55-64 yrs group > 45-54 yrs group > 35-45 yrs group > the < 35 yrs group (211.53 ± 14.03 cm^3 > 176.25 ± 21.63 cm^3 > 157.13 ± 27.24 cm^3 > 141.15 ± 26.93 cm^3 > 107.86 ± 14.31 cm^3), with statistically significant differences between the five groups ($p < 0.05$); the EAT thickness of the patients in the < 35 yrs group was significantly lower than the those of other four age groups, and the differences were statistically significant ($p < 0.05$), while no significant difference was found among the other four age groups ($p > 0.05$).

Comparison of PCAT in Different Age Groups

The PCAT volumes of different age groups are shown in Table III. The volumes of the PCAT in the LM-LAD and RCA gradually increased with increasing age. The volume of the PCAT in the LCX of the < 35 yrs group was significantly lower than that of the other four groups, while no significant difference was found among the other four groups ($p > 0.05$) (Figures 3 to 5).

Table II. Comparison of EAT volume and thickness in each group.

Age group	< 35 (n=10)	35-44 (n=20)	45-54 (n=20)	55-64 (n=20)	> 65 (n=10)	*p* value
EAT volume (cm^3)	107.86 ± 14.31	141.15 ± 26.93	157.13 ± 27.24	176.25 ± 21.63	211.53 ± 14.03	0.00**
EAT thickness (mm)	2.59 ± 0.27	3.37 ± 1.05	3.29 ± 0.42	3.34 ± .057	3.31 ± 0.44	0.03*

*$p < 0.05$; **$p < 0.01$.

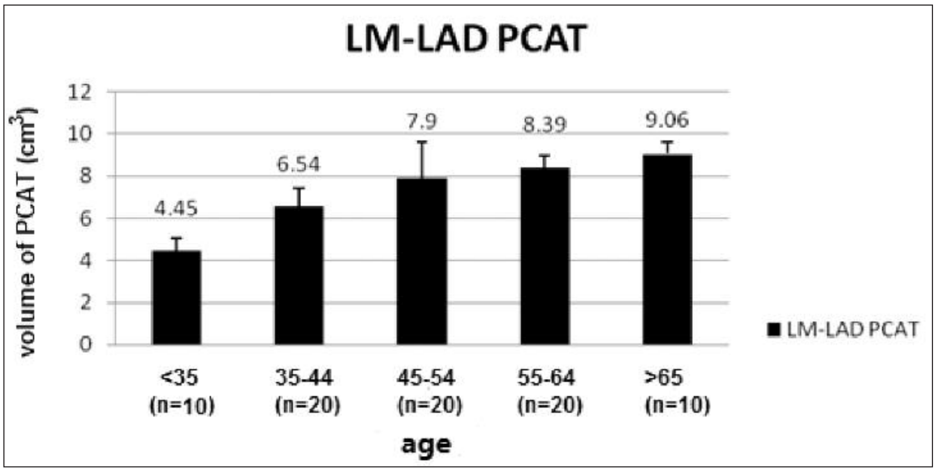

Figure 3. Comparison of the LM-LAD PCAT volume in different age groups.

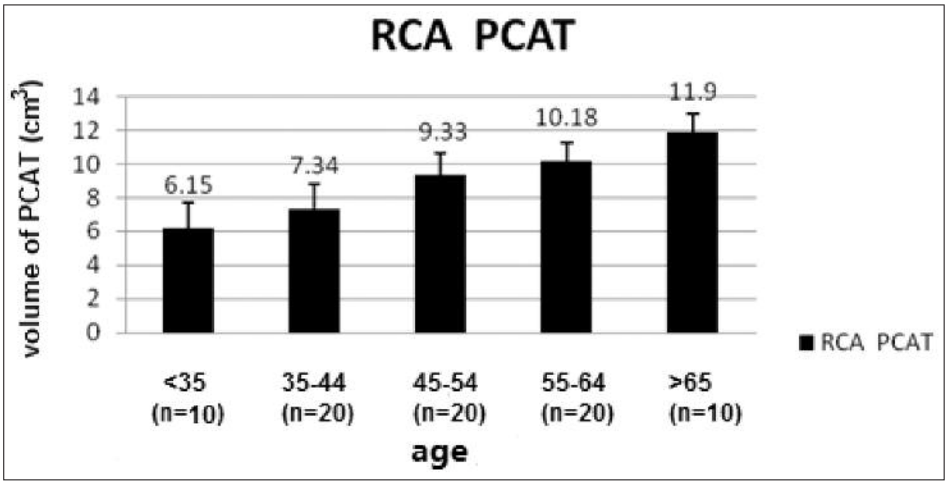

Figure 4. Comparison of the RCA PCAT volume in different age groups.

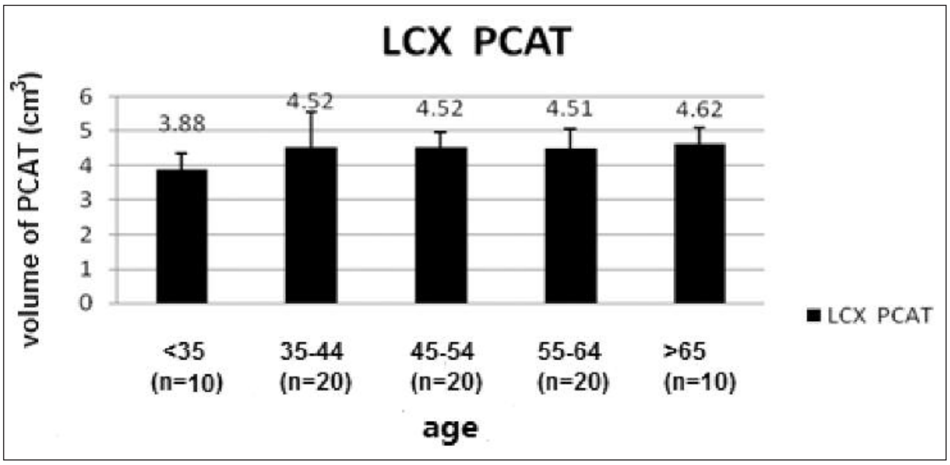

Figure 5. Comparison of the LCX PCAT volume in different age groups.

Table III. Comparison of the PCAT volume in each group.

Age group	< 35 (n=10)	35-44 (n=20)	45-54 (n=20)	55-64 (n=20)	> 65 (n=10)	*p* value
LM-LAD PCAT (cm^3)	4.45 ± 0.60	6.54 ± 0.86	7.90 ± 1.70	8.39 ± 0.60	9.06 ± 0.54	0.000^{**}
LCX PCAT (cm^3)	3.88 ± 0.48	4.52 ± 1.03	4.52 ± 0.44	4.51 ± 0.56	4.62 ± 0.50	0.102
RCA PCAT (cm^3)	6.15 ± 1.56	7.34 ± 1.48	9.33 ± 1.30	10.18 ± 1.07	11.90 ± 1.07	0.000^{**}

$^{*}p < 0.05$; $^{**}p < 0.01$.

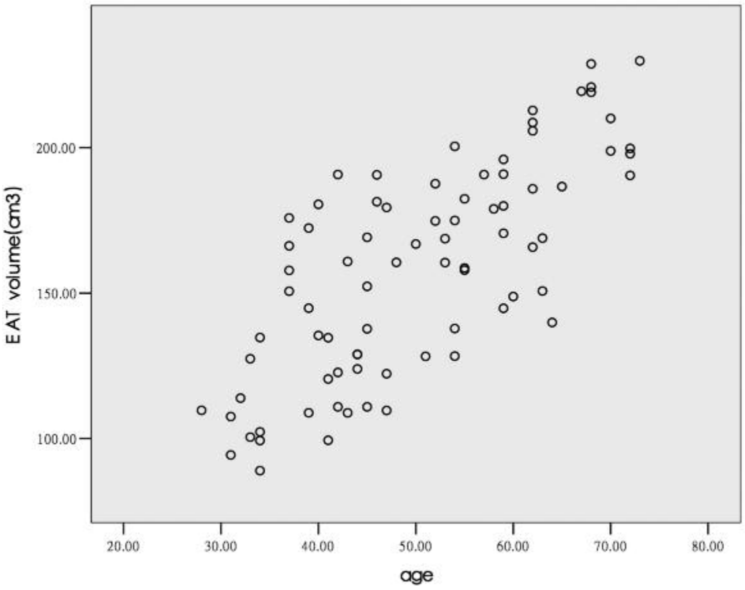

Figure 6. The correlation of age and EAT volume (r = 0.749, $p < 0.05$).

The Impact of Age on EAT and PCAT

The results of Spearman correlation analysis are shown in Table IV. Age was correlated with EAT volume, LM-LAD, and RCA PCAT ($p < 0.01$) but not with LCX PCAT and EAT thickness ($p > 0.05$) (Figures 6 to 10).

Table IV. Correlation analysis of age with EAT and PCAT.

	Age (correlation coefficient)	*p* value
EAT volume	0.749	0.000**
EAT thickness	0.14	0.215
LM-LAD PCAT	0.694	0.000**
LCX PCAT	0.183	0.104
RCA PCAT	0.709	0.000**

**$p < 0.01$.

Discussion

Muscle tissue is gradually lost with increasing age, and this situation may occur even in the rela-

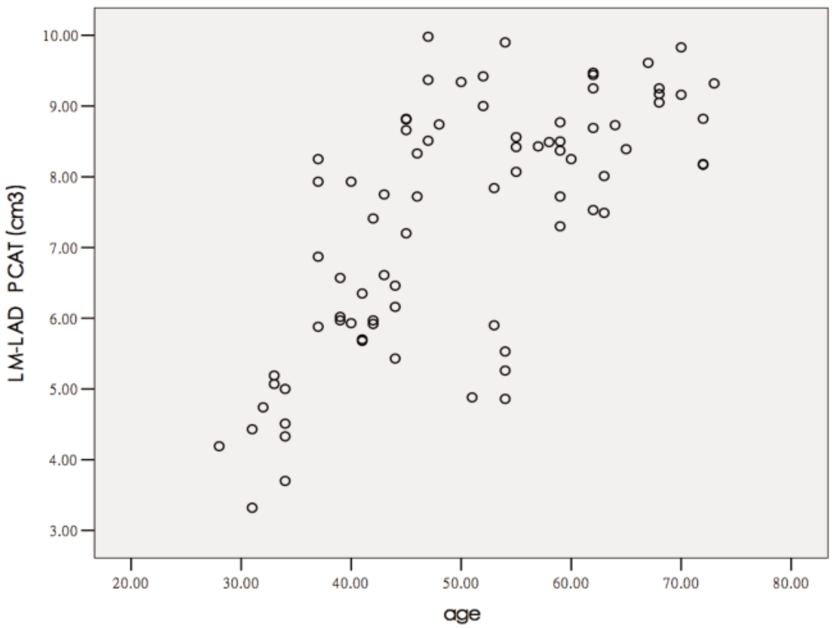

Figure 7. The correlation of age and LM-LAD PCAT volume (r = 0.694, $p < 0.05$).

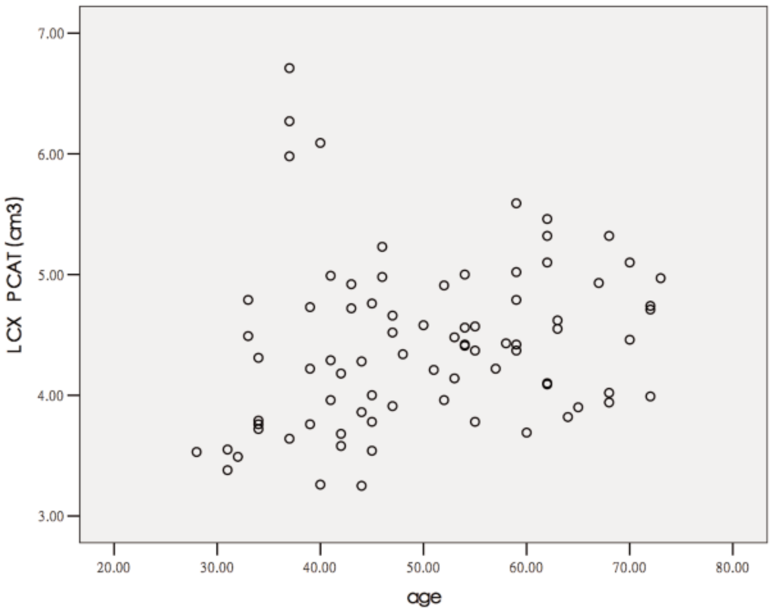

Figure 8. The correlation of age and LCX PCAT volume (r = 0.183, $p > 0.05$).

tively healthy elderly population[5]. After 50 years of age, 1%-2% of muscle is lost each year, and after age 60, the rate increases to 3%. Concurrent with the muscle loss with increasing age, the amount of fat in the body increases. The fat tissue of an adult aged 30-60 years increases annually by approximately 0.45 kg. The adipose tissue is mainly increased by two approaches: one is fat intake, and the other is the increase in the number of preadipocytes that are subsequently differentiated into fat to achieve the proliferation of adipose tissue[6]. In adulthood, although the increase in fat tissue under normal circumstances is mainly due to the changes in cell volume, the adipocytes still retain their differentiation ability and continue to produce new fat cells[7].

Adipose tissue is widely distributed in various parts of the body, with fatty tissue covering the

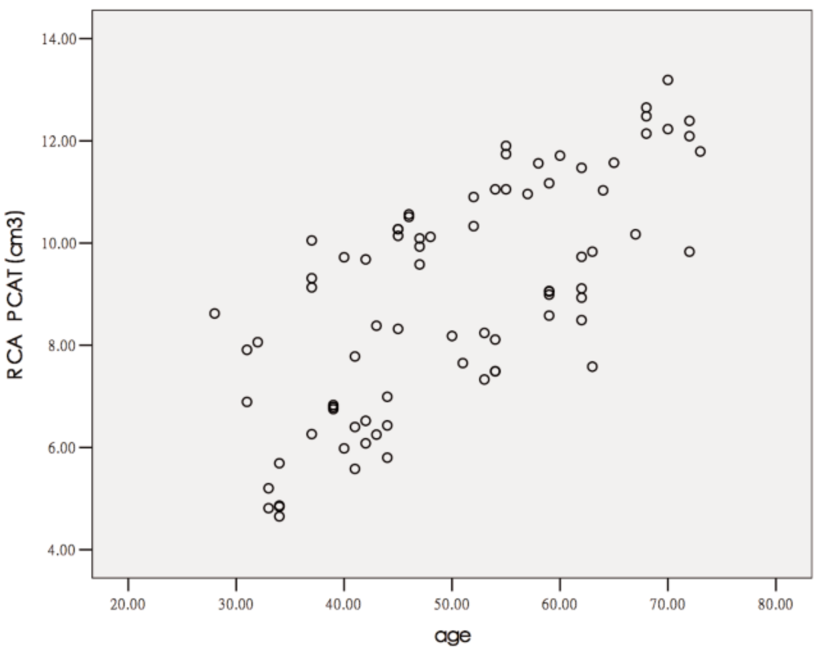

Figure 9. The correlation of age and RCA PCAT volume (r = 0.709, $p < 0.05$).

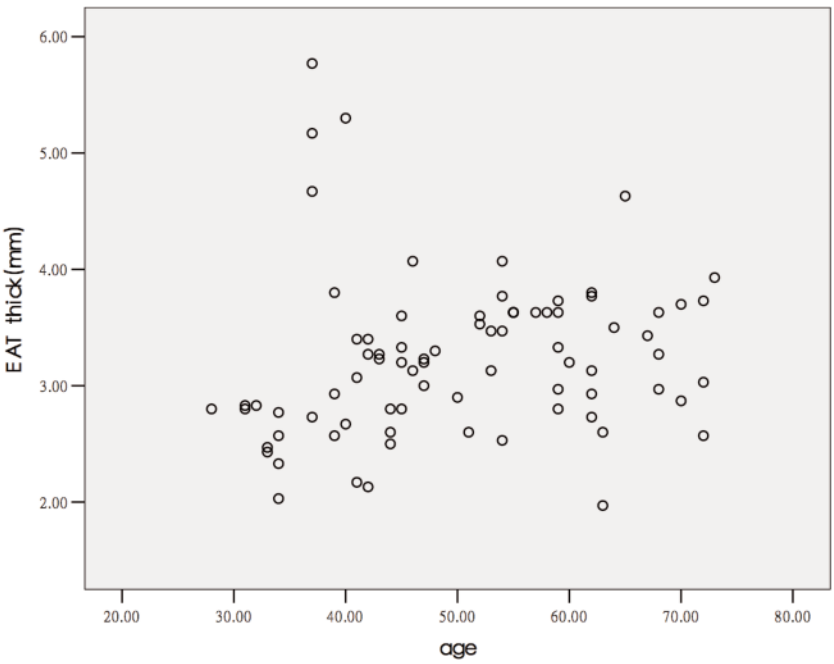

Figure 10. The correlation of age and EAT thickness (r = 0.14, $p > 0.05$).

surface of the limbs, trunk, and internal organs. With increasing age, the distribution of adipose tissue in the body presents a centripetal tendency to aggregate, showing an increase in visceral fat accumulation and a reduction in subcutaneous fat[8]. Through bioelectrical impedance analysis, Chen et al[9] showed that visceral fat is increased with increasing age, and its growth rate is significantly greater than that of the increase in total body fat.

EAT is a special type of thoracic visceral fat deposited in the epicardium and wrapped around the myocardial tissue and coronary artery[10]. In an animal study, Fei et al[11] found that with increasing age, the volume of the adipose tissue on the surface of the epicardium in rats was significantly increased, suggesting that EAT is also involved in the age-related redistribution of adipose tissue. The results of this study showed that EAT volume gradually increased with age (> 65 yrs group > 55-64 yrs group > 45-54 yrs group > 35-45 yrs group > the < 35 yrs group). The correlation analysis showed that age was positively correlated to EAT volume, confirming the impact of aging on EAT volume in humans. However, in this study, we found that only EAT thickness, which reflects the dissociated thickness of the right ventricular wall, in the < 35 yrs group was significantly lower than that in the other four groups ($p = 0.03$), with no significant difference among the other four groups ($p > 0.05$), suggesting that the adipose tissue in the right ventricular dissociated wall may not change significantly in the aging process. Therefore, the adipose tissue thickness in the right ventricular dissociated wall is not a very sensitive indicator for the evaluation of EAT.

According to their different anatomical structures, EAT can be further divided into cardiac adipose tissue on the myocardial surface and the PCAT that surrounds the coronary artery or adheres to the epicardium[12]. Because the PCAT directly covers the surface of the coronary arteries, it may have a direct impact on the physiological and pathological processes of the coronary arteries. However, studies on PCAT are currently rarely conducted[13-16].

In this study, we found that the volumes of the adipose tissue around the left main-left anterior descending artery and the right coronary artery of the 3 major coronary arteries gradually increased with increasing age in the following order: > 65 yrs group > 55-64 yrs group > 45-54 yrs group > 35-44 yrs group > the < 35 yrs group. The correlation analysis also showed that age and LM-LAD PCAT volume are positively correlated, suggesting that LM-LAD and RCA PCAT were involved in the redistribution of adipose tissue in the aging process. However, our study also found that only the LCX PCAT volume of the < 35 yrs group was significantly lower than those of the other four groups ($p < 0.05$), with no significant difference among the other four groups ($p > 0.05$), which may be due to the small amount of the adipose tissue around the circumflex artery itself, as well as the small number of included subjects in this study.

Conclusions

The volumes of EAT and the adipose tissue surrounding the LM-LAD and RCA increase with increasing age. Whether the age-induced increase of EAT and PCAT is associated with the age-related gradual increase in coronary atherosclerosis awaits confirmation by further investigation.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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