Correlation of CT Epicardial Adipose Tissue (EAT) Thickness with Cardiovascular Risk Using the Framingham Risk Score*

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Abstract

Background. Epicardial adipose tissue (EAT) thickness as a marker of cardiovascular risk has not been extensively studied. Though readily seen in CT images, it is often overlooked due to limited information of its significance. This study aims to determine the correlation of CT EAT thickness with cardiovascular risk using the Framingham Risk Score in adult Filipino patients.

Methodology. This study is a cross-sectional study involving 44 Filipinos, 21 to 70 years, who underwent chest CT scan, CT aortogram, CT calcium score, CT coronary angiogram and CT pulmonary angiogram in our institution from January 2017 to June 2018. After undergoing CT scan, patients are recruited to participate in which their Framingham Risk Score (FRS) was determined. EAT thickness measurements will be measured in the right ventricular anterior free wall along the axial plane. Correlation between EAT thickness and FRS will be analyzed using Pearson's Product – Moment Correlation.

Results. Findings suggest that FRS has a moderate correlation with EAT thickness ($r = 0.6287$, $p = <0.001$).

Conclusion. CT measured EAT shows moderate correlation with Framingham Risk Score.

Key words: Epicardial Adipose Tissue Thickness, Framingham Risk Score.

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INTRODUCTION

Cardiovascular disease is a global concern and has long become the number one cause of mortality in the Philippines. According to 'The 2013 Philippine Health Statistics' of the Department of Health National Epidemiology Center, 'Disease of the Heart' is the top cause of mortality in both sexes, hence emphasizing how much importance we must put on cardiovascular care (1). Obesity is highly predictive of cardiovascular events and contributes to diastolic dysfunction (2, 3). Fat, which is mainly accumulated in subcutaneous tissue, is also deposited around visceral organs in the abdominal or thoracic regions (3). One of which is the epicardial adipose tissue which is the fat located between the myocardium and visceral layer of the pericardium (3). Adipose tissues, especially visceral adipose tissue, are highly associated with coronary artery disease and cardiovascular events (2). Several studies also show that adipose tissues also produce many adipokines which affects the cardiovascular system (3).

The Framingham Risk Score (FRS) is a gender-specific algorithm used to estimate the 10-year cardiovascular risk of an individual (4). It has been a widely accepted method in determining patients of high risk for heart disease. On the other hand, Epicardial Adipose Tissue (EAT) thickness, as a marker of cardiovascular risk, has not been extensively studied. Though readily seen and measurable in CT images, it is often overlooked due to the limited information of its significance (5). It is a readily derivable information in chest CT scans, however, its utility is still not well studied. CT scan, together with MRI, provide accurate assessment of epicardial adipose tissue thickness and regarded as the gold standard diagnostic methods for evaluating epicardial fat (3).

Few studies have been done to document the value of EAT thickness and their correlation with cardiovascular risk. In a retrospective review of 356 assymptomatic patients done by Nelson et. al., the study concluded that echocardiographically measured EAT thickness is weakly correlated to FRS ($r=0.21$, $P <0.0001$). In a cross-sectional observational study done by Cetin et. al. involving 127 untreated hypertensive patients, it also reported a positive correlation in EAT thickness and FRS ($r = 0.414$, $p < 0.001$). This study aims to determine the correlation of CT derived Epicardial Adipose Tissue thickness with Framingham Risk Score in adult Filipino patients.

MATERIALS AND METHODS

Institutional Review Board (IRB) approval was obtained prior to the initiation of the study. Informed consent was obtained from all participants of the study. The research is a cross-sectional study done in the CT MRI Division of our institution. Participants were chest CT scan, CT aortogram, CT calcium score, CT coronary angiogram and CT pulmonary angiogram patients from January 2017 to June 2018.

Adult Filipinos aged 21 – 70 years old, either inpatient or outpatient, were included in the study. Exclusion criteria were as follows: (1) substantial motion artifacts in CT scan that render inaccurate measurement of the EAT, (2) previous percutaneous transluminal coronary angioplasty, coronary artery bypass grafting, implanted pacemaker, artificial valves or any other artifact-generating metal objects, (3) cardiac or mediastinal lesions that may render poor delineation of EAT (e.g. myxoma, rhabdomyosarcoma, angiosarcoma), (4) thoracic abdominal aneurysm that may interfere in the visualization of the EAT, and (5) previous myocardial infarction or diagnosed heart disease.

Images of the heart were obtained using either a Philips 256- or 40- slice channel configuration. Subjects were scanned in supine position. Participants were then recruited for the study after scanning. Framingham Risk Score was then obtained. Epicardial adipose tissue thickness was measured by the investigator. Three measurements were obtained at the 25%, 50% and 75% levels of the right ventricular anterior free wall along the axial plane (Figure1). EAT was measured from the visceral epicardium to the outer aspect of the myocardium and perpendicular to the surface of the heart. The mean of these measurements were used for analysis. Randomly selected cases were reassessed by another radiologist and T- test was done to establish interobserver variability.

Figure 1. Anterior RV wall levels where epicardial adipose tissue thickness was measured.

Sample size calculation was done using Epi Info version 7, the minimum sample size requirement is at least 44 based on the correlation between EAT thickness and FRS = 0.414(3) with alpha level = 5% and power = 80%.

Data analysis was performed in stata SE version 13. Quantitative variables were summarized as mean and standard deviation, while qualitative variables were tabulated as frequency and percent. Correlation between epicardial adipose tissue thickness and Framingham's Risk Score was analyzed using Pearson's Product – Moment Correlation and was graphically presented in a scatterplot. The level of significance was set at 5%.

Results

The baseline characteristics of the study population (n = 44) is described in Table 1. The population has slightly more males than females. The mean BMI of the participants is on the overweight range and the mean FRS is 9.23 $\pm$ 6.72 which place the population in a higher risk for cardiovascular disease.

Age	47.43 + 13.26
Sex	
Male	29 (65.91)
Female	15 (34.09)
Height (m)	1.60 + 0.10
Weight (kg)	66.98 + 13.98
BMI	25.95 + 3.74
Blood Pressure	
Systolic	128.41 + 19.40
Diastolic	77.73 + 7.74
Mean Arterial Pressure	94.57 + 10.52
Lipid Profile	
Total Cholesterol	190.68 + 49.15
Triglycerides	123.23 + 39.30
HDL	51 + 14.93
LDL	115.95 + 40.98
Framingham Risk Score	9.23 + 6.72
EAT (mm)	3.05 + 2.13
Co-morbidities	
Hypertension	16 (36.360
Diabetes Mellitus	6 (13.64)
PTB	7 (15.91)
CA	0
CAD	7 (15.91)
Breast CA	2 (4.55)
Papillary Thyroid CA	1 (2.27)
Non-Hodgkins Lymphoma	1 (2.27)
Pulmonary abscess	1 (2.27)
CDK	1 (2.27)
PTB/Lung CA (including mets)	7 (15.91)
Gallstones	1 (2.27)
Hypercholesterolemia	9 (20.45)
AAA	1 (2.27)
Neurofibromatosis	1 (2.27)
Aneurysm	1 (2.27)
Arthritis	1 (2.27)
Colon CA	1 (2.27)
Chronic Limn Ischemia	1 (2.27)
Lung Adenocarcinoma	1 (2.27)
Medication	
ACE Inhibitor	2 (4.55)
ARB	8 (18.18)
Beta Blockers	4 (9.09)
CCB	5 (11.36)
Angiotensin II receptor Blocker + CCB	1 (2.27)
Beta-Blocker + Diuretic	1 (2.27)

There is a moderate direct correlation of CT measured EAT with FRS (r=0.6287, p= <0.0001) as shown in Figure 2.

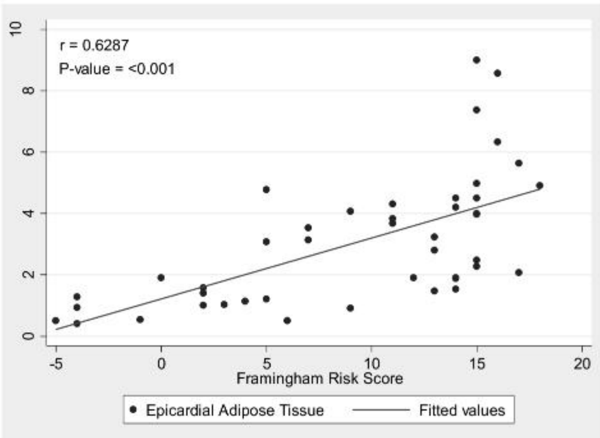

Figure 2. Scatter plot of Epicardial Adipose Tissue versus Framingham

Bland-Altman test was used to demonstrates the interobserver difference done by two radiologist in measuring the epicardial adipose tissue thickness. The test shows good interrater agreement with a p-value of 0.016 (Figure 3).

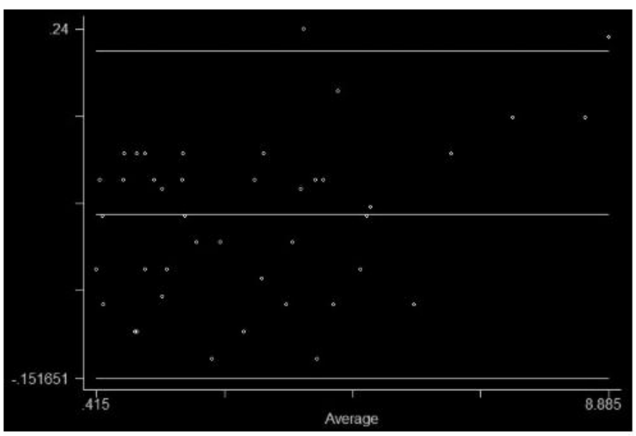

Figure 3. Inter-rater agreement of two Radiologist on Epicardial Adipose

Discussion

This study demonstrates that CT measured EAT thickness is moderately correlated with FRS. Few other studies documented this correlation using 2D- echocardiography derived EAT thickness. In a retrospective review of 356 asymptomatic patients done by Nelson et. al., they reported that 2D echo measured EAT thickness is weakly correlated to FRS (r = 0.21, P <0.0001) (2). In a cross- sectional observational study done by Cetin et. al., involving 127 untreated hypertensive patients, they reported a much higher correlation of EAT thickness, obtained by 2D echo, with FRS (r = 0.414, p < 0.001) (3).

According to Cetin et. al., EAT thickness is a stronger predictor of coronary artery disease than visceral adipose tissues located in other parts of the body. Embryologically, EAT is similar to abdominal visceral adiposity (3). It is a special fat depot which is related more to visceral fat than total adiposity and shares the same microcirculation with myocardial tissue (3). They also reported that EAT may be a source of several pro-inflammatory and pro-atherogenic cytokines. In addition, they also theorized that EAT may contribute to enhance myocardial hypertrophy, myocardial fibrosis, and perivascular fibrosis. Furthermore, EAT is also associated with diastolic dysfunction, non-dipper status, increased left atrial size and lower ejection fraction, arterial stiffness, higher coronary calcium score, and reduced regional systolic motion (3).

CT scan provides very good anatomic depiction of the epicardial adipose tissue. EAT thickness is readily identifiable and measurable in any CT scans that include the heart. EAT measurements is easy to do and reproducible. This study shows that EAT thickness may provide information regarding a patient's cardiovascular risk.

This study is limited by the time period through which the study was undertaken. Increasing the number of participants may further establish the value of EAT thickness with regards to its correlation in assessing cardiovascular risk. To further determine the significance of EAT thickness, one can correlate it to stratified data providing more specific information.

Conclusion

CT measured EAT thickness is moderately correlated with Framingham Risk Score.

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Appendices

Table 2. Age scoring. Framingham Risk Score for males.

Age, y	Points
20-34	-9
35-39	-4
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	11
70-74	12
75-79	13

Table 3. Cholesterol scoring. Framingham Risk Score for males

	Points				
Total Cholesterol mg/dL	Age 20-39 y	Age 40-49 y	Age 50-59 y	Age 60-69 y	Age 70-79 y
<160	0	0	0	0	0
160-199	4	3	2	1	0
200-239	7	5	3	1	0
240-279	9	6	4	2	1
x280	11	8	5	3	1

Table 4. HDL scoring. Framingham Risk Score for males.

HDL, mg/dL	Points
x60	-1
50-59	0
40-49	1
<40	2

Table 5. Blood pressure scoring. Framingham Risk Score for males.

Systolic BP, mmHg	If Untreated	If Treated
<120	0	0
120-129	0	1
130-139	1	2
140-159	1	2
x160	2	3

Table 6. Final scoring. Framingham Risk Score for males.

Point Total	10-Year, %
<0	<1
0	1
1	1
2	1
3	1
4	1
5	2
6	2
7	3
8	4
9	5
10	6
11	8
12	10
13	12
14	16
15	20
16	25
x17	x30

Table 7. Age scoring. Framingham Risk Score for females.

Age, y	Points
20-34	-7
35-39	-3
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	12
70-74	14
75-79	16

Table 8. Cholesterol scoring. Framingham Risk Score for females.

	Points				
Total Cholesterol mg/dL	Age 20-39 y	Age 40-49 y	Age 50-59 y	Age 60-69 y	Age 70-79 y
<160	0	0	0	0	0
160-199	4	3	2	1	1
200-239	8	6	4	2	1
240-279	11	8	5	3	2
x280	13	10	7	4	2

Table 9. HDL scoring. Framingham Risk Score for females.

HDL, mg/dL	Points
x60	-1
50-59	0
40-49	1
<40	2

Table 10. Blood pressure scoring. Framingham Risk Score for Females

Systolic BP, mmHg	If Untreated	If Treated
<120	0	0
120-129	1	3
130-139	2	4
140-159	3	5
x160	4	6

Table 11. Final Scoring. Framingham Risk Score for females.

Point Total	10-Year, %
<9	<1
9	1
10	1
11	1
12	1
13	2
14	2
15	3
16	4
17	5
18	6
19	8
20	11
21	14
22	17
23	22
24	27
x25	x30