British Journal of Medicine & Medical Research
11(7): 1-10, 2016, Article no.BJMMR.20546
ISSN: 2231-0614, NLM ID: 101570965

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Epicardial Adipose Tissue (EAT) Thickness and Its Association with BMI and Waist Circumference in Healthy Adults and Coronary Artery Disease (CAD) Patients

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Authors' contributions

This work was carried out in collaboration between all authors. Author SS designed the study, wrote the protocol and designed the manuscript. Author NH reviewed the whole manuscript. Authors MABA and AM supervised the sampling and author NZ helped in statistical analysis. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2016/20546
Editor(s):
(1) Franciszek Burdan, Experimental Teratology Unit, Human Anatomy Department, Medical University of Lublin, Poland and Radiology Department, St. John's Cancer Center, Poland.
Reviewers:
(1) Andrea Borghini, Institute of Clinical Physiology, CNR, Pisa, Italy.
(2) Dhastagir sheriff, Benghazi University, Libya.
(3) Marco Matteo Ciccone, University of Bari, Italy.
(4) Pietro Scicchitano, Hospital "F. Perinei"–Altamura (Bari), Italy.
Complete Peer review History: http://sciencedomain.org/review-history/11731

Original Research Article

Received 31st July 2015
Accepted 19th September 2015
Published 7th October 2015

ABSTRACT

Introduction: Coronary Artery Disease (CAD) risk factors clustering has increases the morbidity and mortality of CAD. These factors are responsible for insulin resistance; it leads to the development of Metabolic Syndrome (MS), which later leads to the development of CAD. Endothelial dysfunction leads to CAD. EAT is the visceral adipose tissue (VAT) around the heart. It plays a major role in the development of MS. The aim of this study was to measure the EAT thickness through echocardiography in healthy adults and coronary artery disease patients and to determine its association with Body Mass Index (BMI) and waist circumference.

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Methodology: 156 diagnosed cases of CAD and age matched 157 asymptomatic individuals were recruited from Cardiology Department of Ziauddin Hospital for this case control study. Waist circumference and BMI were measured. Echocardiography was done for EAT thickness.
Results: CAD group had significantly higher EAT thickness as compared to controls. There was no significant difference of EAT thickness with BMI. A weak positive association of EAT thickness with BMI was found. A significant difference of EAT thickness with waist circumference was found. There was weak association of EAT with waist circumference in CAD.
Conclusion: The mean EAT thickness is significantly higher in CAD group of Karachi population. EAT thickness has weak positive association with BMI and waist circumference. Therefore, we can conclude that BMI and Waist Circumference are the indicators of generalized obesity while EAT thickness may be considered to be a true indicator of visceral obesity.

Keywords: Coronary artery disease; epicardial adipose tissue; visceral adipose tissue echocardiography; cardiac adiposity.

1. INTRODUCTION

Epicardial Adipose Tissue thickness (EAT) is an independent risk factor in the development of coronary artery disease [1]. It is responsible for fatal and nonfatal coronary artery events in general population irrespective of cardiovascular risk factors [2]. EAT is the visceral fat depot of the heart [3]. It is a metabolically active organ with anatomical and functional contiguity to the myocardium [4]. EAT has the most significant independent correlation with myocardial fat [5]. Epicardial adipose tissue has anatomic and functional proximity to the myocardium and has intense metabolic activity. Therefore, some interactions between heart and its visceral fat depot have been suggested [6].

Epicardial adipose tissue has endocrine and paracrine activity [7,8]. It secretes proinflam-matory and anti- inflammatory cytokines and chemokines [9,10]. It has been suggested that these chemicals promote the development of coronary artery atherosclerosis [11,12,13].

Epicardial adipose tissue thickness increases with age. The reason for this gradual increase in EAT thickness with age is that there is a decrease in lean body mass and increase in fat mass, with fat tissue redistribution to the trunk and viscera [14]. Epicardial adipose tissue is more abundant in the elderly and is correlated to visceral adipose tissue depots, indicating a higher cardio metabolic risk [15]. There was no consensus in the previous literature on the association of gender with the thickness of EAT.

Previous studies done internationally have shown strong positive association of waist circumference with EAT thickness [16,17,18]. Waist circumference is widely accepted as a marker of high cardiovascular risk in subjects with adverse metabolic profile, although it has been positively correlated with abdominal fat content and not with Visceral Adipose Tissue (VAT) [19,20,21].

Determination of normal EAT thickness has now become essential for prediction of developing coronary artery disease in future [22]. Epicardial adipose tissue has been identified to play a crucial role in the pathogenesis of coronary artery disease [23]. Epicardial adipose tissue thickness may serve as a new index of cardiac and visceral adiposity with potential as a diagnostic tool and therapeutic target in myocardial infarction. Increased epicardial adipose tissue thickness may be associated with poor prognosis in patients with acute coronary syndrome [24]. To the best of our knowledge there is no data available on EAT thickness in Karachi population. The objectives of this study were to determine EAT thickness in a subset of Karachi population and also to determine the effects of BMI and waist circumference on EAT thickness.

2. METHODOLOGY

This was a case-control study carried out from September 2014 to March 2015. A total of 313 individuals were recruited in the study and underwent through echocardiographic examination at Echocardiography Department of Ziauddin Hospital, Clifton Campus, Karachi. The study was conducted after approval from Ethic Review Committee of Ziauddin University. Samples were collected after taking a written informed consent. Proforma regarding subject's history and demographic profile was filled. All those healthy individuals with incidental findings of coronary artery disease, or any other cardiac pathology on echocardiography, hypertension,

any major cardiac surgical history, pregnancy and diabetes were excluded. Subject's history of alcohol use, chest irradiation, and chest deformity, anti hypertensive, anti arrhythmic drugs and oral corticosteroid drugs were also excluded from the study. Echo machine Toshiba model NemioXG with cardiac probe frequency of 3.5 MHz was used to determine EAT thickness. Participants were examined in supine position, with pillow under their shoulders. EAT thickness was measured by sub costal view, parasternal long axis view and parasternal short axis view. The mean EAT by all three views was then calculated.

2.1 Statistical Analysis

A sample size of 313 was calculated by using sample size estimation calculator for unmatched case and control study available on Open Epi [25]. Sample size was assumed at α = .05 (significant level) with power = 80% using a 1:1 ratio of cases to controls while looking for an odds ratio of 2. Total sample was calculated to be 156 for cases and 157 for controls. Samples were collected through non-probability convenience sampling. Data was entered on SPSS version 20 for statistical analysis. Means and standard deviations were derived for numerical variables. Paired t-test was used to compare the difference of EAT with BMI and waist circumference. Independent T-test was applied to calculate association of EAT with BMI and waist circumference. P- Value of < 0.05 was considered to be significant.

3. RESULTS

A total of 313 individuals participated in this study. Among this study group 156 were controls (males=78 and females=78), while 157 were cases (males=78, females=79). All the study participants had risk factors for CAD. Among these risk factors highest risk factor in control group was smoking, while in CAD group highest risk factor was IHD (Table 6).

Mean age of the study group was from forty one year to sixty eight years. Mean BMI of the control group was higher than CAD group. Mean waist circumference of CAD group was higher than control group (Table 1). Mean EAT thickness of CAD group was higher than controls group (Table 1). Significant difference (P-value = <0.002) of mean EAT thickness was found between CAD group and controls (Table 2). No significant difference (p=0.142) of EAT thickness with BMI was found in control and CAD groups (P=0.208) (Table 3). Weak positive(r=0.014) association of EAT thickness with BMI was found in control and in CAD groups (r=0.010) (Figs. 1 and 2). The mean waist circumference of the control group was less than the CAD group (Table 4). We found a significant difference (P=0.025) of waist circumference in control and CAD groups (p=0.002) (Table 4). There was weak association (r=0.032) of waist circumference in control and CAD groups (r=0.063) (Figs. 3 and 4).

Table 1. Demographic data of study participants

	N (%)	Mean age (yrs)	Mean BMI (kg/m^2)	Mean waist circumference (cm)
Case				
Males	78 (50)	55.16±13.79	27.98±6.78	102.15±16.30
Females	78 (50)			
Control				
Males	78 (50)	55.16±13.79	29.47±6.71	98.19±13.91
Females	79 (50.31)			

Table 2. Mean epicardial adipose tissue thickness in cases and controls

	N (313)	EAT thickness (mm) mean ± SD	P- value
Case control	156	16.77±9.8	<0.002
	157	14.13±4.5	

Table 3. Epicardial adipose tissue thickness with mean BMI in cases and controls

	N (313)	EAT thickness (mm) mean ± SD	BMI (kg/m^2) mean ± SD	P- value	R
Case control	156	16.77±9.8	27.98±6.78	<0.142	0.010
	157	14.13±4.5	29.47±6.71	<0.208	0.14

Table 4. Epicardial adipose tissue thickness with mean waist circumference in cases and controls

	N (313)	EAT thickness (mm) mean ± SD	Mean waist circumference (mm) ± SD	P- value	R
Case control	156	16.77±9.8	102.15±16.30	0.002	0.063
	157	14.13±4.5	98.19±13.91	0.025	0.032

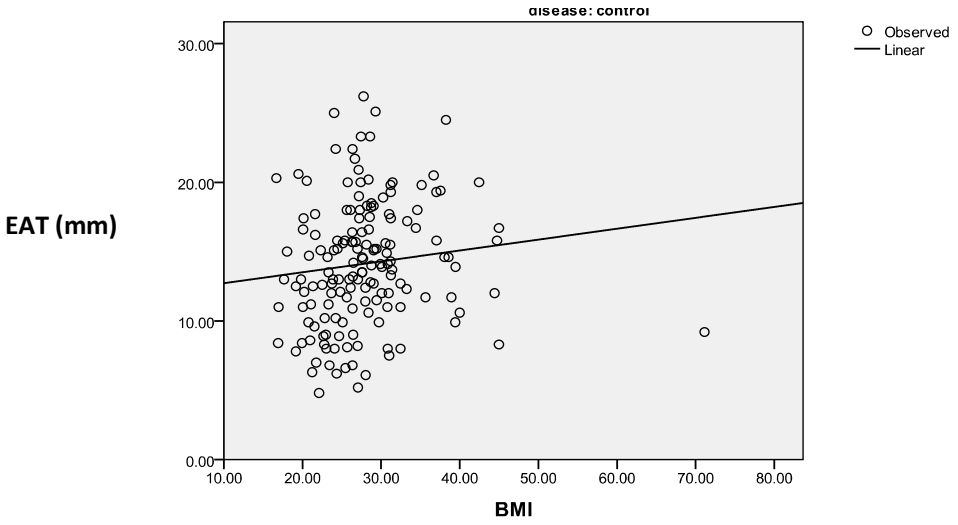

Fig. 1. Association of epicardial adipose tissue thickness with BMI in control group

This scatter plot shows that most of the participants in the control group had a BMI between range of 20-40 Kg/m^2 and a EAT thickness in the range of 5-20mm. There is a weak insignificant positive correlation between EAT thickness and BMI in control group. (P=0.208, R=0.14)

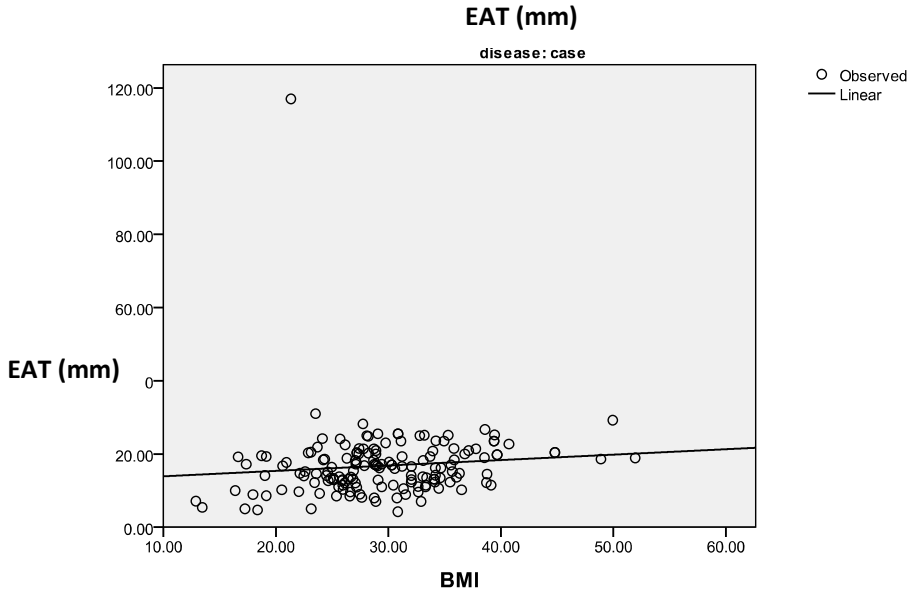

Fig. 2. Association of epicardial adipose tissue thickness with BMI in CAD group

This scatter plot shows that most of the participants in the CAD group had a BMI between range of 20-40 Kg/m^2 and a EAT thickness in the range of 8-20 mm. There is a weak insignificant positive correlation between EAT thickness and BMI in CAD Group (0.142, R=0.010)

4. DISCUSSION

Many studies has been done on the normative data of EAT thickness worldwide, but unfortunately we could not find our own data on EAT thickness. It has been studied that in low and middle income countries nearly 80% of deaths occur due to cardiovascular diseases [26]. Therefore, it is very important to have the reference range of the EAT thickness for our population and its association with BMI and Waist Circumference especially for the early diagnosis and prevention of coronary artery disease. EAT has been identified to play a crucial role in the pathogenesis of coronary artery disease [23]. EAT thickness may serve as a new index of cardiac and visceral adiposity with potential as a diagnostic tool and therapeutic target in myocardial infarction. Increased EAT thickness may be associated with poor prognosis in patients with acute coronary syndrome [24]. Therefore, it is important to determine the reference range of

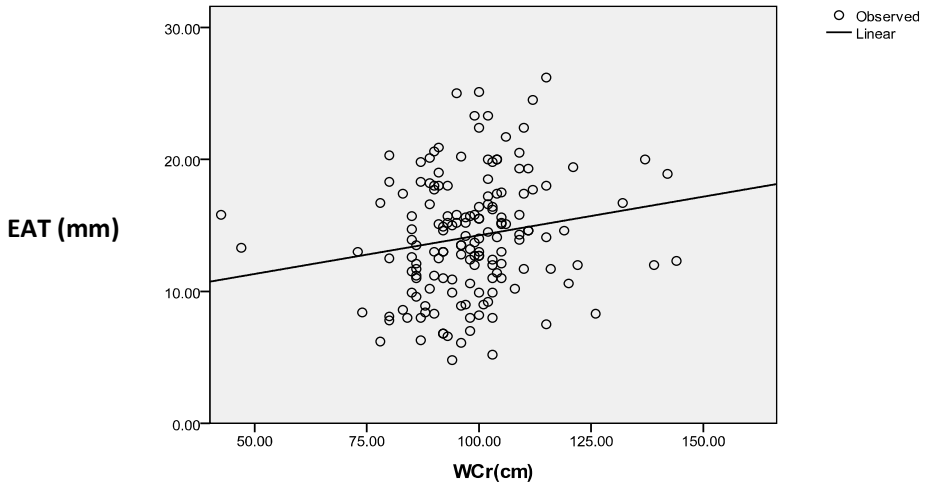

Fig. 3. Association of epicardial adipose tissue thickness with waist circumference in control group

This scatter plot shows that most of the participants in the control group had a waist circumference between ranges of 75-125 cm and EAT thickness in the range of 5-20 mm. There is a significant weak positive correlation between EAT thickness and BMI in control group (P=0.025, R= 0.032)

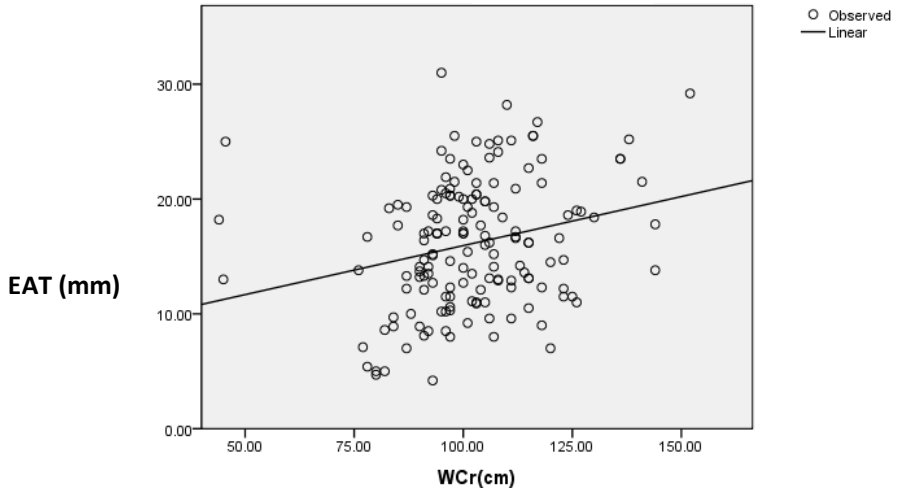

Fig. 4. Association of epicardial adipose tissue thickness with waist circumference in CAD group

This scatter plot shows that most of the participants in the CAD group had a waist circumference between ranges of 75-125 cm and EAT thickness in the range of 5-25 mm. There is a significant weak positive correlation between EAT thickness and waist circumference in CAD group. (P=0.002, R=0.063)

EAT and its association with anthropometric measurements for a specific population especially for early diagnosis and prevention of coronary artery disease. Therefore, the present study was designed to determine the EAT thickness in a subset of Karachi population.

Mean EAT thickness in our healthy adult group was found to be 14.13±4.5 mm. Many studies have been done on the measurement of EAT thickness in different regions of the world like South Korea [27], Rome [28] and Italy [29], Turkey [30], Croatia [31] and India [16]. Among these studies the mean EAT thickness in healthy adult of South Korea [27], Rome [28] and Italy [29] was found to be close to the mean results of EAT thickness in our control group. The reason for this similarity of result is probably the similarity in life style of our population with these populations, but the mean EAT thickness in Turkey [30] and Croatia [31] was found to be very low. The reason for this low value is unknown. When we compared our results with our neighboring country India [16], we found that India has significantly low values of EAT thickness. The reason for this dissimilarity of result is perhaps because they are purely vegetarians while we use more meat and transformed fat in our diet.

Mean EAT thickness in CAD group was found to be 16.77±9.80 mm. It is significantly higher than that of the control group. Similar studies on EAT thickness in CAD patients were done in South Korea [27], Turkey [30], Croatia [31], and USA [32]. Our results of EAT thickness in CAD patients were found to be significantly higher than those of the other studies, and this is an alarming sign. There is growing evidence that excessive visceral adipose tissue (including abdominal, pericardial, and thoracic peri-aortic adipose tissue) is linked to abnormal lipid profile, enhanced systemic inflammation, diabetes and cardiovascular diseases [33,34]. Our CAD group and healthy adult group has significant difference (P=<0.002) of EAT thickness. Therefore, by these results it is suggested that an increase in EAT thickness may be considered to be an indicator for future incidence of CAD development.

In our study mean BMI of control group was 27.98±6.7 kg/m^2 and mean BMI of CAD group was 29.47±6.71 kg/m^2. We could not find significant difference (p=0.142) in EAT thickness with BMI in control and CAD groups (P=0.208). Weak positive(r=0.014) association of EAT thickness with BMI was found in both control and CAD groups (r=0.010). Previous studies have demonstrated direct correlation between EAT and BMI [35,36,16,27,29,21,18]. It has been reported that a person with BMI ≥ 30 kg/m^2 has a greater risk of death caused by cardiovascular diseases [37,38]. Our results of BMI were not in accordance with those of previous studies. Some recent studies on Asian populations have shown that low BMI increases the incidence of cardiovascular diseases [39,40]. The reason for weak association of EAT with BMI in our study might be the different proportion of the EAT to a total amount of VAT according to BMI. In the high BMI group, the EAT might make up a smaller proportion of the total VAT compared to the non-high BMI group [41].

Table 5. Association of epicardial adipose tissue thickness with BMI, Waist circumference and age

	R	B	P-value	95.0% Confidence interval for B	
				Lower bound	Upper bound
BMI		-.005	.928	-.108	.099
WCr(cm)	0.206	.066	.038	.004	.129
Age		.087	.006	.026	.149

Table 6. Risk factors in healthy adults and coronary artery disease patients group

Risk factors	Control group			CAD group			
	Yes (N/%)	No (N/%)	Total	Yes (N/%)	No (N/%)	Total	P-vale
IHD	47/14.9	112/35.6	159/50.5	156/49.5	0/0	156/49.5	≤ 0.0001
DM	43/13.7	116/36.8	159/50.5	97/30.8	59/18.7	156/49.5	≤ 0.0001
CKD	0/0	159/50.5	159/50.5	30/9.5	126/40.0	156/49.5	≤ 0.0001
HTN	41/13.0	118/37.5	159/50.5	137/43.5	19/6.0	156/49.5	≤ 0.0001
Smoking	61/19.4	98/31.1	159/50.5	25/7.9	131/41.6	156/49.5	≤ 0.0001

The mean waist circumference of the control group was 98.19±13.91 cm, while in cases it was 102.15±16.30 cm (Fig. 3). We found a significant difference (P=0.025) of EAT with waist circumference in control and CAD groups (p=0.002) (Fig. 4 and Table 3). There is weak positive association (r=0.032) of EAT with waist circumference in controls and CAD patients (r=0.063) (Figs. 3, 4 and Table 3). Studies done by Rabkin SW [17] in Canada, Ranjan Shetty [16] in India, and Lai YH [18] in Taiwan showed strong association of waist circumference with EAT thickness. Waist circumference is widely accepted as a marker for subjects with adverse metabolic profile and high cardiovascular risk. It has been positively correlated with abdominal fat content not VAT (visceral adipose tissue). VAT has strong association with EAT in previous studies as suggested by Janssen I [20], Iacobellis G [29], Vicennati V [21]. Therefore, this may be the reason for weak association between EAT thickness and waist circumference in our study. After applying multivariate regression model we found weak association of EAT thickness with BMI, waist circumference and age (Table 5).

5. LIMITATIONS

EAT has an obvious distribution around the heart and 2D echocardiographic assessment may not give accurate estimate of the total amount of fat.

6. FUTURE CLINICAL IMPLICATIONS

Although there is few data available on epicardial adipose tissue, therefore the evidences suggested that it has anatomical and clinical relation to cardiac morphology and function. Epicardial adipose tissue has bioactive power and it affects cardiac functions. This fat depot reflects intra-abdominal visceral fat; therefore its assessment by echocardiography might serve as a reliable marker of visceral adiposity. Further studies of this neglected tissue and its relationship with cardiac function, as well as of its use as a marker of metabolic and cardiovascular risk, should be encouraged.

7. CONCLUSSION

The mean EAT thickness is significantly higher in CAD group as compared to control group in Karachi population. EAT thickness has weak positive association with BMI and waist circumference. Therefore, we can conclude that BMI and Waist Circumference are the indicators of generalized obesity while EAT thickness may be considered as a true indicator of visceral obesity.

COMPETING INTERESTS

Authors have declared that no competing interests exist

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Peer-review history:
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