Original Article

Epicardial fat thickness can predict severity and multivessel distribution in Egyptian patients with atherosclerotic coronary artery stenosis

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Abstract

Background: Epicardial fat, in addition to its secretory function, may have an important role in predicting and stratifying cardiovascular risk. There is a paucity of data regarding correlation between epicardial fat thickness and coronary artery disease in Egypt.

Aim of the study: To study the relationship between epicardial fat thickness (EFT) measured by trans-thoracic echocardiography (TTE) and severity of coronary artery disease (CAD) and its distribution in Egyptian population.

Methods: Our study was a prospective observational case control study that was conducted upon 150 patients with stable CAD presented to the cardiology departments in Ain Shams University hospitals and Al-Zaitoun Specialized hospital from March to October, 2015. EFT was measured by TTE for all patients at the same day of performing invasive coronary angiography (CA). We studied the statistical correlation between EFT and presence of CAD, also we tried to find if EFT is related to severity of CAD (according to Gensini score) or its distribution.

Results: The study population was divided according to CA results to 2 groups; patients’ group having atherosclerotic CAD consisting of 100 patients and control group consisting of 50 patients with normal coronaries. All the well-known risk factors of CAD (male sex, smoking, hypertension, diabetes, dyslipidemia, increased body mass index) were significantly more prevalent in the patients’ group. Patients had significantly lower systolic and diastolic functions. EFT was significantly correlated to presence of CAD (P < 0.001) with a cut-off value of 5.5 mm. EFT was significantly correlated to severity of CAD assessed by Gensini score (P < 0.001). Also we found a significant positive correlation between EFT and number of vessels affected (P < 0.001).

Conclusion: EFT is a good predictor of CAD severity and multivessel affection in Egyptian patients. It is also a potentially promising predictor for the presence of CAD.

1. Introduction

Atherosclerotic Coronary artery diseases (CAD) are the leading cause of death worldwide according to the latest data published by the world health organization (WHO).1 It is also the leading cause of death in Egypt.2 CAD worldwide is largely driven by modifiable risk factors, as The INTERHEART study showed that smoking, dyslipidemia, Diabetes, hypertension, obesity, physical inactivity, alcohol consumption, psychological factors and a high risk diet were responsible for over 90% of myocardial infarction (MI) risk.3 Primary prevention is paramount for the large number of people who are at high risk for acquiring CAD. In view of limited resources in developing countries, finding low-cost prevention strategies is a top priority.

The association between visceral obesity and cardiovascular risk has been well described.4 Visceral adipose tissue (VAT) which is distributed around the viscus or hollow muscular organs of the body is now well established as being associated with the development of metabolic syndrome and CAD.5

The mechanism of these effects of VAT are not entirely understood, but could be mediated by release of free fatty acids causing direct ‘lipotoxicity’.6 Adipose tissue, especially the VAT, also acts as an endocrine organ, releasing numerous proinflammatory and proatherogenic cytokines and hormones affecting endothelial function.4,6,7

Abbreviations: CAD, Coronary artery diseases; WHO, world health organization; MI, myocardial infarction; VAT, visceral adipose tissue; EAT, epicardial adipose tissue; EFT, epicardial fat thickness; BMI, body mass index; WC, waist circumference; CA, coronary angiography.

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Epicardial adipose tissue (EAT) fills the area between the pericardium and the myocardium, and has the same embryologic origin as intra-abdominal adipose tissue. The adipose tissue of the heart is divided into two layers: epicardial fat (the visceral layer) which lies between the myocardium and visceral layer of the pericardium (Fig. 1) and pericardial fat situated external to the parietal layer of the pericardium. Each layer has its own embryological origin and different blood supply. Epicardial fat is the visceral fat depot of the heart. Under physiological conditions, EAT acts as a buffer that protects the heart from lipotoxicity and provides the myocardium with the lipids needed to obtain energy through β-oxidation of fatty acids in addition to its mechanical protective effect. Under pathological conditions, as in metabolic syndrome, EAT dysfunction occurs, leading to the loss of its cardioprotective effect. Measuring the amount of EAT might represent a novel parameter that is inexpensive and easy to obtain and may be helpful in cardiovascular risk stratification. However, the relationship between epicardial fat and determinants of coronary artery disease is not well established.

In our study we tried to detect if there is a relationship between epicardial fat thickness (EFT) and severity of coronary artery disease in Egyptian population or not.

2. Methods

This study was a prospective observational case control study that was conducted upon 150 patients presented to the cardiology departments in Ain Shams University hospitals and Al-Zaitoun Specialized hospital in the time interval from March to October, 2015.

The study was approved by the local ethics committee and all patients signed an informed consent for participation in the study. All patients underwent coronary angiography at the same day of performing a full echocardiographic study. Patients were divided into two groups according to their coronary angiographic findings; group I (patients group), that included 100 patients who had documented CAD by coronary angiography (CA) and group II (control group), that included 50 patients who had normal coronaries confirmed by CA.

The study included all stable patients that were indicated for invasive CA according to the appropriateness criteria.

2.1. Exclusion criteria

Extremes of age (less than 18 or more than 70 years), patients with debilitating diseases, patients with poor acoustic windows, patients with normal coronaries despite having previously documented ischemic insult, patients with acute coronary syndromes, patients refusing to participate and patients with coronary ectasia were excluded from the study.

Clinical data, including the medical history, cardiovascular risk factors, and associate comorbidities, were collected by history taking from the patients followed by thorough clinical examination including calculation of body mass index (BMI) by the standard formula [weight (kg)/height (m)^2] and waist circumference (WC) measurement that is made at the approximate midpoint between the lower margin of the last palpable rib and the top of the iliac crest. 12 lead surface ECG was obtained from all study subjects in order to assess presence of new or old ischemic changes.

Trans-thoracic Echocardiography was performed using a high-performance cardiovascular ultrasound system Vivid S5 machine (GE healthcare Company, USA). Two independent investigators analyzed the recordings blinded to clinical data and the results of coronary angiography. Systolic functions were assessed by the Biplane disk summation volume method. Diastolic functions were assessed according to the 2009 American Society of Echocardiography guidelines 2009. Epicardial fat (which is defined echocardiographically as the echo-free space between the outer wall of the myocardium and the visceral layer of pericardium) was measured perpendicularly on the free wall of the right ventricle in the parasternal long-axis view at mid ventricle at end-diastole in 3 cardiac cycles at the point at which the ultrasound beam is oriented in a perpendicular manner, using the aortic annulus as an anatomic landmark. There is no consensus till now about whether EFT is to be measured at end-systole or end-diastole and data are conflicting regarding this issue.

All patients underwent CA according to our approved institutional protocol. Two independent operators analyzed the CA data blinded to clinical and echocardiographic data of all patients. The “Gensini” severity score which calculates severity of CAD by using both site and degree of stenoses was used to assess severity of CAD in the patients group (Fig. 2).

2.2. Statistical analysis

Data were analyzed using package for special science (SPSS) software version 20.0 (IBM, Armonk, NY, USA). T-test was used for comparison of quantitative variables. Chi-square test (or Fisher’s exact test when appropriate) was used for comparison of distribution of qualitative variables. The receiver operating characteristic (ROC curve) was used to find cutoff value. P value was used to determine the statistical significance. A value of 0.05 is arbitrary a cut off value: below it, the relation between variables is considered statistically significant, and above it the relation is considered statistically not significant.

3. Results

3.1. Demographic, anthropometric and clinical characteristics

Demographic, Anthropometric and clinical data of our study population are shown in (Table 1), there was a significant difference between both groups in most of these variables.

3.2. CA data of the patients group

39% of patients in the patients group were found to have single vessel affection, 33% had two vessels affection, while 28% had three vessels affection, we found that LAD affection contributes to 79% of reported coronary artery stenosis, while RCA affection to contribute to 63%. Severity score “Gensini” showed a mean value of 54.25 ± 49.29. CA data are shown in (Table 2).
3.3. Epicardial fat thickness measurements

A statistically significant difference between both groups was found regarding Epicardial fat thickness with mean thickness of 7.4 ± 1.3 mm for the patients group ranging from 4 mm to 9 mm and mean thickness of 4.12 ± 0.82 mm for the control group ranging from 3 mm to 5 mm (P < 0.001) (Table 1). Using Receiver Operating Characteristic Curve (ROC) we found a statistically significant cut-off point of 5.5 mm epicardial fat thickness that refers to presence of CAD with a significant area under the curve of 0.992%, 98% sensitivity, 100% specificity, 95% CI of 0.98–1.00 and P value <0.001 (Fig. 3).

3.4. Epicardial fat thickness in relation to different study variables

Epicardial fat thickness was found to have a statistically significant correlation to age (P < 0.001, r = 0.53), Smoking (P < 0.001), hypertension (P < 0.001), diabetes (P < 0.001), dyslipidemia (P < 0.001), BMI (P < 0.001, r = 0.68), systolic functions (P < 0.001, r = −0.62) and diastolic functions (P < 0.001) in the whole study population. Correlation between epicardial fat thickness and

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**Table 1**

Demographic, anthropometric and clinical characteristics.

| Demographic/clinical variable         | Patients (n = 100) | Controls (n = 50) | P value |
|--------------------------------------|-------------------|------------------|---------|
| Conventional risk factors           |                    |                  |         |
| Male                                 | 65 (65%)          | 21 (42%)         | 0.007   |
| 86 (57%)                             |                   |                  |         |
| Age                                  | 57.81 ± 8.18      | 44.82 ± 6.58     | <0.001  |
| Smoking                              | 37 (37%)          | 38 (76%)         | <0.001  |
| Non-smoker                           | 53 (53%)          | 9 (18%)          |         |
| Smoking                              | 10 (10%)          | 3 (6%)           | <0.001  |
| Ex-smoker                            | 88 (88%)          | 1 (2%)           | <0.001  |
| HTN                                  | 67 (67%)          | 0 (0%)           | <0.001  |
| DM                                   | 67 (67%)          | 0 (0%)           | <0.001  |
| Dyslipidemia                         | 56 (56%)          | 0 (0%)           | <0.001  |
| Body mass index                      | 35.98 ± 4.31      | 27.38 ± 2.03     | <0.001  |
| Waist circumference                  | 99.26 ± 10.08     | 81.8 ± 6.79      | <0.001  |
| Ejection fraction                    | 44.9 ± 8.59       | 64.4 ± 6.9       | <0.001  |
| Left ventricular mass index          | 84.4 ± 29.0       | 80.9 ± 28.8      | 0.494   |
| Ejection fraction                    |                    |                  |         |
| Normal diastolic function            | 3 (3%)            | 50 (100%)        | <0.001  |
| Grade I DD                           | 37 (37%)          | 0 (0%)           | <0.001  |
| Grade II DD                          | 36 (36%)          | 0 (0%)           | <0.001  |
| Grade III DD                         | 20 (20%)          | 0 (0%)           | <0.001  |
| Grade IV DD                          | 4 (4%)            | 0 (0%)           | <0.001  |
| Epicardial fat thickness             | 7.4 ± 1.3         | 4.12 ± 0.82      | <0.001  |

Bold values means either a variable or a significant P value.

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**Table 2**

CA data in patients group.

| CA data                              | Patients (n = 100) |
|--------------------------------------|-------------------|
| Gensini “Severity Score”             | 54.25 ± 49.29     |
| Number of affected coronary vessels  |                    |
| Single vessel                        | 39 (39%)          |
| Two vessel                           | 33 (33%)          |
| Three vessel                         | 28 (28%)          |
| Coronary Artery                      |                    |
| LM Disease                           | 10 (10%)          |
| LAD affection                        | 79 (79%)          |
| LCX affection                        | 42 (42%)          |
| RCA affection                        | 63 (63%)          |
| LAD + LCX                            | 30 (30%)          |
| LAD + RCA                            | 46 (46%)          |
| LCX + RCA                            | 33 (33%)          |
| LM + RCA                             | 8 (8%)            |

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3.3. Epicardial fat thickness measurements

A statistically significant difference between both groups was found regarding Epicardial fat thickness with mean thickness of...
Regarding echocardiographic assessment of the 2 groups; there was a significant difference between both groups as regards both systolic and diastolic functions. On the other hand there was no significant difference as regards LVMI. Systolic and diastolic functions can be highly affected by ischemic conditions while LV mass may be more affected by factors rather than ischemia as genetics, race and loading conditions that faces the ventricles in the course of chronic cardiovascular conditions.

4. Analysis of epicardial fat thickness

EFT showed a significant correlation with age, smoking, HTN, DM, Dyslipidemia, BMI and WC; all of which are settled predictors of CAD. These results agree with the results obtained from many of other similar studies. The causality relationship between HTN, DM, Dyslipidemia, BMI, WC and increased epicardial fat seems convincing given the strong evidence that epicardial adipose tissue has the same origin as visceral adipose tissue and that Epicardial fat thickness in subjects with metabolic syndrome is significantly higher than that observed in subjects without metabolic syndrome. Also, Epicardial fat thickness is inversely associated with insulin sensitivity.

Our study showed a significant difference between EFT in the patients group versus controls (7.4 ± 1.3 mm versus 4.12 ± 0.82 mm). A similar study done by Eroglu et al. found the same significant correlation 31. Despite epicardial fat may release factors that blunt the toxic effects of high fatty acid levels on the myocardium, it may also release factors that promote harmful coronary artery and myocardial changes. A body of evidence shows that epicardial fat is an extremely active organ that produces several bioactive adipokines. Some studies utilizing MSCT have shown similar significant correlation between epicardial fat and coronary artery disease. We found that EFT of 5.5 mm is the cut-off value at which we can expect presence of CAD with a high sensitivity and specificity. Finding such a value has been a concern for many similar studies done before. Faghihi et al., found an EFT cut-off value of 2.95 mm in their study with a sensitivity of 83% and specificity of 75%. Eroglu et al. found a cut-off point of 5.2 mm with 85% sensitivity and 81% specificity. Mustelier et al. postulated an EFT cut-off point of 5.2 mm with 65.4% sensitivity and 61.5% specificity. A point to be put in mind is that some of these investigators measured EFT at end-systole while others used end-diastolic frames and this may explain differences between them. Detection of such cut-off point is very appealing as it may be used after validation in other studies performed on larger number of patients and exclusion of the effect of other confounding factors as a simple, rapid and low cost method in screening patients for CAD; an idea similar to that of coronary calcium scoring done by multislice computed tomography but without exposing patients to hazards of radiation.

We found a significant correlation between EFT and severity of CAD in the patients’ group calculated by the “Gensini” score. Eroglu et al. and Meenakshi et al. showed similar significant correlations in their studies. Moreover, we found that there is a significant correlation between EFT and number of vessels affected and a significant correlation between LM disease and EFT. We thought that finding and confirming a relationship between EFT and severity of CAD in the Egyptian population would be of utmost importance given that the prevalence of abdominal obesity in men is 37.1% and in women 50.8% and based on available data from the Egyptian National Hypertension Project and since abdominal obesity is a cornerstone of the metabolic syndrome; the link between EFT (which seems to have a strong correlation with visceral obesity) and CAD can open the door for a new, simple and cheap method for detection of atherosclerosis even in its early phases to halt its progression and reduce any morbidity or mortality.
caused by it. Such approaches are extremely needed in developing countries to reduce healthcare expenses. Also, the role of EFT repeated assessments to evaluate results of life style modifications used for patients at risk of CAD is a possible field for future research.

From the above data we conclude that EFT measurement using 2D echocardiography is a good test for prediction of severity of CAD. EFT is also positively correlated to increased number of coronary vessels affected and it is a potentially good predictor for the presence of CAD. Our study limitations were that more accurate assessment of EFT using MSCT or cardiac magnetic resonance was not available, both allow more accurate 3D quantification; also our results needed larger number of patients with homogenous distribution of the other known risk factors for CAD between both study groups to detect the exact effect of EFT in prediction of CAD. Also future studies will be needed to correlate EFT with different scores that are commonly used for assessment of CAD severity (as the SYNTAX score for example) with possible use of intravascular ultrasound (IVUS) for detection of mild atherosclerosis that is not detectable by CA. Our study results were sometimes compared (in the discussion section) with other studies that were based on EFT measurement in end-systole, this difference in methodologies may have an effect on accuracy of comparison. Our study population was all from Caucasian race, future studies with multicultural population will be needed. Also, the effect of gender will need to be assessed in future studies. Again, future studies including patients presenting with acute coronary syndromes will be needed.

Conflicts of interest

No conflicts to declare.

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