Research Article

Adipose Tissue of Atrial Septum and Coronary Artery Disease

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Abstract
Background: Adipose tissue seems to play a key role in cardiovascular physiology through paracrine and endocrine mechanisms. Aim is to evaluate the relationship between adipose tissue of atrial septum to presence and severity of coronary artery disease (CAD). **Methods:** A total of ٤١٤ patients (Pts) underwent coronary angiography between January and September ٢٠١١, Eighty were studied. According to angiographic data, Pts were classified into group١ with CAD and group ٢ which included ٢٠ pts with normal angiography as a control group. Group ١ was further subdivided according to modified Gensini's score (each of eight vessel segments was graded from ١-٤ according to the severity of occlusion. The score in each of the eight segments was added to give a total score out of theoretical maximum of ٣٢). Group ١a included ٣٤ pts with coronary stenosis score < ٥. Group ١b included ٢٦ pts with coronary stenosis score ≥ ٥. All pts underwent a detailed clinical evaluation beside laboratory investigations and echocardiography for measurement of atrial septum and epicardial fat thickness. **Results**: There was statistically significant increase in atrial septum and epicardial fat thickness in group ١b compared to group ١a and group II (P = ٠.٠٠). Pts with predominant visceral fat accumulation showed higher epicardial fat and atrial septum thickness than pts with average body weight (P= ٠.٠١٢ & ٠.٠) respectively. **Conclusion:** Cardiac adipose tissue, represented by atrial septum thickness is a new marker of CAD.
Keywords: Adipose tissue, Coronary artery disease, Echocardiography.

Introduction
Visceral obesity seems to play a key role in the development of all features of metabolic syndrome.(١) Hence, the detection of visceral adipose tissue, fat deposited around the internal organs, might be important for the risk stratification of metabolic syndrome. Several methods are applied as surrogates for estimation of visceral adipose tissue. Epicardial adipose tissue is a visceral fat deposited around the heart, particularly around subepicardial coronary vessels.

It may act as an endocrine organ given the production of a comparable pattern of adipocytokines(٢) and has been implycated in the development of coronary atherosclerosis.(٣) Possible association between a thick atrial septum and obesity, advanced age, atrial arrhythmias, obstructive symptoms, and sudden death have been reported. An autopsy study showed more atherosclerotic CAD in patients with fatty deposition in the atrial septum.(٤)

The aim of this study is to evaluate the relationship between the adipose tissue of atrial septum to presence and severity of coronary artery disease as a new marker of CAD.

Subjects and Methods
Out of ٤١٤ pts who underwent coronary angiography at the cardiology department, Al-Minia University Hospital, during the period between January to September ٢٠١١, ٨٠ pts were included in our study. Exclusion criteria included patients with acute myocardial infarction, total occlusion of any epicardial vessels as well as congenital, pericardial and valvular heart diseases. Incomplete clinical data and inadequate echocardiographic images were also within the exclusion criteria .

Patients were subjected to:

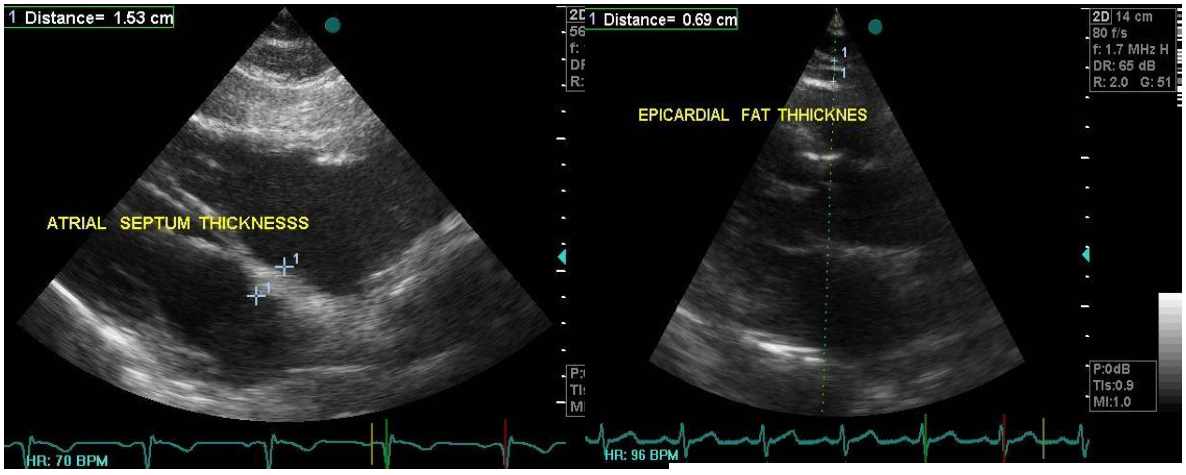
- History taking including reviewing the previous investigations, risk factors of CAD.
- General examination including vital signs. Height (in square meters) and weight (in kilograms) were used to calculate body mass index. Obesity was defined as patients with a body mass index ≥ ٣٠ kg/m², Minimum waist circumference and maximum hip circumference (in centimeters) were measured. Obese subjects were sub-divided, according to waist circumference value, into subjects with predominant visceral fat accumulation and with predominant peripheral fat accumulation[٥]

- Cardiac examination.

- **Laboratory investigations** including total lipid profile, fasting and two hours post-prandial blood sugar

- **Echocardiography**: Examinations were performed by using general electric vivid ٣ ultrasound with simultaneous ECG tracing. The measurements represent a mean of at least three consecutive cardiac cycles. Visual assessment of regional wall motion was performed. left ventricular end systolic and diastolic volumes by manual tracing of endocardial borders and left ventricular ejection fraction was calculated using Simpson's rule. We measured epicardial fat thickness on the free wall of the right ventricle from parasternal long axis views. Epicardial fat thickness appears as an echo-free space. The measurement was performed at a point on the free wall of the right ventricle along the midline of the ultrasound beam, perpendicular to the aortic annulus. The atrial septum was identified using subcostal view, and its thickness representing the adipose tissue of the atrial septum was measured perpendicular at the thickest part at end-diastole. (figure١)

Figure ١: Example of measurement of epicardial fat, atrial septum thickness by the two dimensional echocardiography



Coronary angiography: Coronary angiography was performed by the femoral approach and included at least ٤ views of the left coronary artery and ٢ views of the right coronary artery.

Stenosis Score used was a modified Gensini's score[٦]. Stenosis score provides information related to the bulk of the atherosclerotic lesion. Each of eight vessel segments was graded according to severity of occlusion; grade ١ for ١٪ to ٤٩٪ occlusion in lumen diameter, ٢ for ٥٠٪ to ٧٤٪, ٣ for ٧٥٪ to ٩٩٪, and ٤ for total occlusion. The score in each of the eight segments was added to give a total score out of theoretical maximum of ٣٢. This score therefore, places emphasis on the severity of stenosis.

According to angiographic data, pts were classified into two groups. Group ١ with coronary artery disease (CAD) with further classification into two subgroups according to modified Gensini's score. Group ١a: included ٣٤ pts (age ٤٨- ٦٣ years) with coronary stenosis score < ٥ and Group ١b: included ٢٦ pts (age ٥٠- ٦٨ years) with coronary score ≥ ٥

while group ٢ included ٢٠ pts with normal coronary angiography (age ٣٣-٦٠ years) as a control group .

Statistical analysis

The data were coded and verified prior to data entry. The Statistical Package of SPSS version ١٦ for windows was used for data entry and analysis. All values were given as mean ± SD. To determine the statistical significance of the difference between study groups, we used t-test to compare two groups and one way ANOVA to compare more than two groups. P value less than ٠.٠٥ was considered significant.

Results

Eighty patients fulfilled our inclusion criteria during the study period; their Clinical data including risk factors of CAD and medical regimen and also laboratory findings in studied groups were reported in table ١.

Table ١: Baseline characteristics, heart rate , blood pressure and laboratory findings in the overall populations.

	Group ١a N (٣٤)	Group ١b N (٢٦)	Group II N (٢٠)
Sex			
Male: N (%)	٢٤ (٧٠.٥٪)	١٩ (٧٣.١٪)	١١ (٥٥٪)
Female: N (%)	١٠ (٢٩.٥٪)	٧ (٢٦.٩٪)	٩ (٣٥٪)
Age (years)	٥٥	٥٨	٤٨
Range	(٤٨-٦٣)	(٥٠-٦٨)	(٣٣-٦٠)
Positive family history of CAD			
N (%)	٦ (١٧.٦ %)	٧ (٢٩.١ %)	١(٥٪)
Smoking			
N (%)	١٣ (٣٨.٢ %)	١٤ (٤٦.١٥ %)	٤ (٢٠ %)
Hypertension			
N (%)	١٤ (٤١.١٧٪)	١٣ (٥٠ %)	٤ (٢٠٪)
Dyslipidemia +			
N (%)	٢٨ (٨٢.٣٪)	٢٢ (٨٤.٦٪)	١١ (٥٥٪)
Diabetes Mellitus:			
N (%)	١٢ (٣٥.٢٩٪)	١٢ (٤٦.١٪)	٣ (١٥٪)
Obesity.			
Central type N (%)	٧ (٢٠.٥٪)	٩ (٣٤.٦٪)	٢ (١٠٪)
Peripheral type N (%)	٦ (١٧.٦٪)	٣ (١١.٥٪)	٣ (١٥٪)
Medications			
-beta blockers N (%)	٣٠ (٨٨٪)	٢٤ (٩٢.٣٪)	١٨ (٩٠٪)
- ACEI N (%)	١٥ (٤٤.١٪)	١٤ (٥٣.٨٪)	٣ (١٥٪)
- ARBS N (%)	٥ (١٤.٧ %)	٥ (١٩.٢٪)	١ (٥٪)
- CCBS N (%)	٥ (٥.٨٪)	٥ (١٩.٢٪)	---
- Statins N (%)	٢٤ (٧٠٪)	٢٠ (٧٦.٩٪)	١١(٥٥٪)
- Fibrates N (%)	٣ (٨.٨٪)	٤ (١٥.٣٪)	١ (٥٪)
-Oral hypoglycemic agents N (%)	١٠ (٢٩.٤٪)	٨ (٣٠.٧٪)	٣(١٥٪)
-Insulin therapy N (%)	٢ (٥.٨٪)	٤ (١٥.٣٪)	--
Heart rate (beats/minute)			
Mean± SD	٧١± ١.٨	٦١ .٨± ٢.٠	٦٥.٦± ١.٩
Systolic BP (mmHg)			
Mean± SD	١٢٣.٩± ٧.٤	١٠٩.٦ ± ٧.٣	١١٨.٣ ± ١٠.٧
Diastolic BP(mmHg)			
Mean± SD	٨٠± ٩.١	٧٥± ٦.١	٧٥± ٧.٧
FBS (mg/dl)			
Mean ± SD	١١٨.٢± ٦.٨	٣٧ ±٣.٨١	٩٨±٣.٣
٢hPP (mg/dl)			
Mean ± SD	١٦٧± ٣.٦	١٩٠± ٥.٧	١٤٥ ± ٤.٢
LDL (mg/dl)			
Mean ± SD	١٠٨± ٣.٩	١١٥± ٣.٤	١١٠± ٥.٣
HDL (mg/dl)			
Mean ± SD	٤١± ٣.٩	٣٧± ٤.٣	٤٨± ٦.٠٥

ACEI= angiotensin converting enzymes inhibitors ARBS = angiotensin receptors blockers CCBS = calcium channel blockers FBS = fasting blood sugar ٢hPP = two hours postprandial LDL = low density lipoprotein HDL = high density lipoprotein

Group Ib showed a high coronary stenosis score compared to group Ia according to modified Gensini's score (each of eight vessel segments was graded from ١-٤ according to the severity of occlusion. The score in each of the eight segments was added to give a total score out of theoretical maximum of ٣٢) (Table ٢). There was statistically significant increase in atrial septum and epicardial fat thickness in group Ia and Ib compared to group II (P= ٠.٠٠ & ٠.٠٤) respectively. At the same time, Group ١b showed statistically significant increase in atrial septum and epicardial fat thickness compared to group ١a (P= ٠.٠٠) (Table ٢) .

- Obese pts with central obesity (BMI ≥ ٣٠ kg/m² and the waist-hip ratio > ٠.٩ for men and >٠.٨٥ for women) showed statistically significant increase in the severity of coronary artery disease according to modified Gensini's score when compared to pts with average body weight and peripheral obesity (p value ٠.٠٠١, ٠.٠٦) respectively (table ٣). Also obese pts with central obesity showed statistically significant increase in atrial septum thickness compared to obese pts with peripheral obesity and pts with average body weight (P = ٠.٠٠ & ٠.٠٦) respectively while epicardial fat thickness showed statistically significant increase in pts with central obesity compared to pts with average body weight (P = ٠.٠١٢) (tables ٣)

Table ٢: Comparison between different groups as regarding modified Gensini' s score. atrial septum and epicardial fat thickness

	Group Ia	Group Ib	Group II	P	P١	P٢
Mean score ± St deviation	٢.٨±١.٠٥	٦.٥± ١.٧	---------	----	٠.٠٠٢	----
Atrial septum thickness (cm)	١.٣ ± ٠.٣	١.٧± ٠.١٤	١.١± .١٧	٠.٠٠	٠.٠٠	٠.٠٤
Epicardial fat thickness (mm)	٦.٥ ± ٠.٢	٨.٤± ٠.١٦	٤.٠٧±٠.٢٢	٠.٠٠	٠.٠٠	٠.٠٤

P = between group Ib and II
P١= between group Ib and Ia
P٢= between group Ia and II

Table ٣: Comparison between obese pts (different types) and pts with average body weight as regarding modified Gensini's score, atrial septum and epicardial fat thickness

	Pts with average body weight	Pts with peripheral obesity	Pts with central obesity	P value	P١	P٢
Mean score± St deviation	٢.٧± ١.٥	٣.٣ ± ١.٠٥	٥.١٨± ٢.٦	٠.٠٠١	٠.٠٦	٠.٤٦
Atrial septum thickness (Cm) mean ±SD	١.٢ ± ٠.٣٤	١.٣ ± ٠. ٣٧	١.٦± ٠.٣٧	٠.٠٠	٠.٠٦	٠.١٠
Epicardial fat thickness (mm) mean ±SD	٦.٢ ± ١.٦	٦.٤ ± ١.٧	٧.٤± ١.٢	٠.٠١	٠.١١٦	٠.٧

P = between pts with central obesity and average body weight P١= between pts with central and peripheral obesity P٢ = between pts with peripheral obesity and average body weight

Discussion

Adipose tissue distribution has significant impact on disease risk with central abdominal fat increasing both cardiovascular diseases and type ٢ diabetes mellitus risk compared with gluteo-femoral fat[٧]. Such differences in risk may be attributable to the depot specific differences in the expression and secretion of adipocytokines[٨]. The clinical significance of a thick atrial septum has been increasingly recognized since the initial description of lipomatous hypertrophy of the atrial septum in ١٩٦٤. Since then, a possible association between a thick atrial septum and obesity, advanced age, atrial arrhythmias, obstructive symp-toms, and sudden death have been reported[٩].

In the current study, obese Pts with central obesity showed significant increase in atrial septum and epicardial fat thickness compared to pts with average body weight. These results were similar to the results obtained by Iacobellis et al, who reported that quantity of epicardial fat, as measured by echocardiography, has been well correlated with the mass of visceral adipose tissue measured by magnatic resonance imaging and Epicardial adipose tissue, a true visceral fat tissue, is deposited around the heart, parti-cularly on the free wall of right ventricle and on the left ventricular apex, but also around the atria[١٠]. Subepicardial fat is also the main determinant of atrial septum thickness and Postmortem studies have sugge-sted that the posterior portion of the atrial septum is essentially an extra-cardiac structure, produced by the infolding of the atrial roof and containing subepicardial adipose tissue[١١]. An experimental study showed that epicardial adipose tissue should be considered an important cardio-vascular and metabolic risk indicator[١٢]. In fact, Iacobellis et al., observed that epicardial adipose tissue is related to body mass index and fat mass. Nevertheless, their data suggest that body fat distribution, particularly abdominal fat tissue, is more strongly correlated to epicardial fat. This finding could have an embriogenetic reason. Epicardial fat and intra-abdominal fat seem to be both originally in the brown adipose tissue of infancy[١٠]. In the current study, high coronary stenosis score pts showed significant increase in atrial septum and epicardial fat thickness when compared to pts with normal coronary angiography and also pts with low stenosis score. Chaowalit et al., showed that atrial septum thickness correlated with the presence of CAD, but not with traditional CAD risk factors, suggesting that the association between atrial septum thickness and CAD is not mediated by traditional CAD risk factors. Furthermore, body mass index was not associated with atrial septum thickness, making it unlikely that atrial septum thickness is simply a reflection of body adiposity. However, atrial septum thickness may be an indirect measure of total visceral fat. This study suggests that the adipose tissue of the atrial septum, measured by transtho-racic echocardiography, is associated with the presence of angiographic CAD. They used a simple and reproducible measurement, namely, echocardiographic assessment of the atrial septal thickness, as a surrogate for the amount of subepicardial adiposity. In agreement with previous studies showing the significance of visceral adiposity rather than generalized obesity as a marker of cardio-vascular risk, their findings further confirm the significance of visceral adiposity, in the association with the presence of angiographic CAD[١٣]. Also, our results were in agreement with results of Jeong et al. This study was the first clinical study indicating that echocardiographic fat thickness is associated with the severity of coronary artery stenosis in patients with known coronary artery disease[١٤].

The biochemical properties of epicardial fat tissue suggest its possible role as a cardiovascular risk that studies using epicardial fat obtained during coronary artery bypass surgery revealed that a significantly higher expression of interleukin-١, interleukin-٦, tumor necrosis factor and mRNA was shown in epicardial fat than those in leg subcutaneous adipose tissue[١٥]. Jeong et al., revealed that epicardial and omental fat exhibit a comparable pathogenic inflammatory mRNA. Therefore, epicardial fat plays a role as a local inflam-matory burden and store in patients with coronary artery disease[١٤]. Baker et al., casted light on the role of human epicardial adipose tissue as a potential paracrine and/or endocrine tissue, specifically within the context of cardiovascular risk. Epicardial adipose tissue shows a similar pattern of expression for a number of key adipocytokines to that of omental adipose tissue. They have also confirmed a high level of macrophage infiltration in this depot

which may contribute to the pathogenic gene expression profile in this tissue[١٦]. Taguchi et al., found a significant association between pericardial fat volume and the prevalence of coronary artery disease in non-obese Japanese subjects[١٧].

In a study of ٢٠٣ participants from Korea, a close association between epicardial fat thickness and the severity of coronary artery disease was found[١٨]. Overall, results of Mahabadi et al., are consistent with the hypothesis that perivascular fat may be associated with local vascular injury[١٩]. The specific composition and meta-bolic activity of visceral fat tissues such as pericardial fat and visceral adipose tissue are widely recognized as differing from subcutaneous fat. Visceral fat tissues have smaller adipocyte size[٢٠] higher protein content, high rate of fatty acid incorporation, and fast insulin-induced fatty acid breakdown[٢١] and secrete several pro- and anti-inflammatory mediators and cytokines such as adiponectin, tumor necrosis factor (TNF-α) and interleukin-٦.[٢٢] The amount of adipon-ectin, a stabilizer of the inhibitor of NF-κB released from pericardial fat,[٢٣] decreases with an increased amount of fat[٢٤] and leads to a local increase of inflammation[٢٣]. The hypo-thesis of an impact on local inflammation of pericardial fat and its role in the pathogenesis of atherosclerosis of the coronary arteries are supported by findings of Mahabadi et al.,[١٩].

Study limitations

The major limitation of the present study is the selection bias because all patients underwent coro-nary angiography as clinically indi-cated. This method of patients selection creates a group with a very high prevalence of advanced coronary disease and a very small proportion of subjects without any angiographic evidence of coronary disease. However, random coronary angiography in the absence of clinical indica-tions, would not be ethically or logistically feasible. Two dimensional echocardiography does not asses the total amount of epicardial adioposity as epicardial fat has a ٣-dimensional distribution .

Conclusion

Despite local adipose tissue (atrial setum and epicardial fat thickness) calculation by echocar-diography requires very little time and can be easily applied during echocar-diographic examination but represents a novel indicator of cardiovascular risk and has the potential of a reliable and easy diagnostic tool for cardio-vascular risk stratification..

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