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RESEARCH ARTICLE

Correlation of epicardial adipose tissue in metabolic syndrome with anthropometric and biochemical parameters.

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Abstract

Background: Epicardial fat, a true visceral adipose tissue, is highly insulin resistant and deposited around the heart.

Objectives: To compare the epicardial fat thickness of subjects with metabolic syndrome with normal individuals and to correlate epicardial fat thickness with various parameters of metabolic syndrome.

Methods and Results: A case control study involving 43 cases of metabolic syndrome and equal number of controls (age matched) was conducted at tertiary care hospital from October 2010 to July 2012. All the subjects underwent anthropometry (waist circumference, waist to hip ratio, BMI) and biochemical investigation consisting of fasting blood glucose and fasting lipid profile. Epicardial fat thickness was measured in all the subjects.

Results: There was increased epicardial fat thickness in cases (3.1±1.1mm) of metabolic syndrome as compared to controls (2.3±0.9mm). Epicardial fat thickness showed significant correlation with age ($p = 0.004$, $r= 0.43$), diabetes ($p=0.051$), Triglycerides ($p = 0.036$, $r =0.324$), LDL-C ($p=0.023$, $r =0.344$), BMI in males ($p=0.038$, $r=0.317$) and Waist-Hip ratio in females ($p=0.008$, $r=0.407$).

Conclusion: Patients with metabolic syndrome have higher amount of epicardial adipose tissue deposition. Hence, epicardial fat can be used as a tool for screening subjects with metabolic syndrome.

INTRODUCTION

Metabolic syndrome is a group of risk factors that can lead to atherosclerotic cardiovascular disease.[1] Widely recognized metabolic risk factors include hyperglycemia, obesity, elevated blood pressure, and dyslipidemia.1The components of metabolic syndrome occur with varying combinations in different individuals. Multiple components of metabolic syndrome grouped together in an individual are associated with higher risk of cardiovascular disease than each component independently.[2,3] Of all the components, abdominal obesity is considered as the central component of metabolic syndrome.[4]

Epicardial adipose tissue is a type of visceral fat which contributes to metabolic risk factors. It is a surrogate measure of visceral obesity. A positive relationship has been established between epicardial fat and several components of the metabolic syndrome.[5] So, this study, was aimed to evaluate the extent of epicardial fat deposition in individuals with metabolic syndrome and correlate various components of metabolic syndrome with epicardial fat.

Methods

A total of 86 subjects participated in this case control study. In-patients and patients attending the outpatient department were included. The study period extended from October 2010 to July 2012. The study was started after obtaining clearance from Institutional Ethics Committee (IEC No. 188/2010). After taking a written informed consent, the participants were included in the study. Cases comprised of subjects with metabolic syndrome as per International Diabetes Federation (IDF) cariteria.[6] Patients on lipid lowering agents, thiazolidinediones and those on any treatment for weight reduction were excluded from the study. Subjects with structural and ischaemic heart diseases and acutely ill patients were also excluded. The control group comprised of people who did not fit into the criteria of metabolic syndrome as per IDF criteria and had no features mentioned in the exclusion criteria of cases.

Anthropometric and biochemical assessment

Height was measured with the subject standing against an upright surface touching it with heels, buttocks and back on a level smooth surface. The measurement was taken when the subject held the breath in normal inspiration and the unit of measurement was meters. Subject wearing minimal clothing was made to stand in the centre of on an electronic weighing machine. Weight was recorded to the nearest tenth of kilogram. The same machine was used for calculating weight for all the subjects who underwent the study.

Body mass index(BMI) was calculated using the formula

$$BMI = \frac{\text{Weight (Kg)}}{[\text{Height (m)}]^2}$$

Hip circumference was taken as the widest diameter over the greater trochanters while the subjects were standing with their heels together.[7] Waist-Hip ratio(W-H ratio) was calculated using the formula-

$$\text{W-H ratio} = \frac{\text{waist circumference}}{\text{hip circumference.}}$$

Blood Pressure (BP) was recorded when the subject was seated quietly in a chair with feet on the floor with a comfortable room temperature. Two measurements were made and the average of two recordings was taken as the BP. Raised BP was defined as systolic pressure ≥ 130 mmHg, diastolic ≥ 85 mmHg, or antihypertensive treatment for previously diagnosed hypertension.

Clinical examination was supplemented by biochemical investigations, which included fasting blood sugar (FBS), and fasting lipid profile. Fasting blood glucose levels were assessed by hexokinase method. Total cholesterols were assessed using CHOD-POD and triglycerides by GPO-PAP method. High density lipoprotein (HDL-C) cholesterol levels were assessed using direct homogenous method. LDL cholesterol was calculated using the formula

Low density lipoprotein (LDL) cholesterol = Total cholesterol- (HDL-C + Triglycerides)

Echocardiographic assessment

All the 86 subjects underwent a conventional 2-D – m mode Echocardiography and tissue Doppler imaging. Vivid 7-echocardiography machine from G.E electronics, India was used during the study. Echocardiography was performed by standard techniques with subjects in left lateral decubitus position. Epicardial fat thickness was measured on the free wall of the right ventricle from both short and long axis views. Epicardial adipose tissue appears as an echo-free space (Fig.1).

Statistical analysis

SPSS 20 software was used for statistical analysis. Taking power of the study as 80%, a level of significance as 5% and 1.5mm as clinically significant difference between epicardial fat in cases and controls- the sample size obtained was 43

Results

The study population consisted of 86 subjects, 43 were cases and 43 were controls. The cases and controls were age matched. Out of the 43 cases 23(53.5%) were females and 20(46.5%) were males. Control group comprised of 22(51.1%) males and 21(48.9%) females. The anthropometric and biochemical variables of the study population are shown in Table 1. As waist circumference and HDL levels had different cut-off values in both the genders, they

have been tabulated separately (Table 1).Out of the 43 controls, 19 subjects did not have any component of metabolic syndrome and 15 had one component and 9 had two components of metabolic syndrome. However, in the cases 20 subjects had all the five traits of metabolic syndrome. The remaining 14 and 9 cases had four and three traits of metabolic syndrome respectively. Increased waist circumference was a common factor to all the cases. As the IDF definition of metabolic syndrome was used for defining the cases, all the males and females in the case group had waist circumference of $\geq$ 90cm and 80cm respectively.

The epicardial fat thickness in cases was 3.1±1.1 and in controls 2.3±0.9 (Table 2, Graph 1). There was a significant difference in epicardial fat between cases and controls. (p=0.001). The study population was divided into three groups- non-diabetic(n=37), subjects with impaired fasting glucose(n=25) and diabetic(n=24) and epicardial fat thickness was measured in all groups. It was found to be 2.4±0.9, 2.9±1.2 and 3±1.1mm in non-diabetics, subjects with impaird fasting glucose and diabetics respectively. On applying ANOVA, there was a significant difference in epicardial fat thickness between the three groups (p=0.050) with highest thickness in diabetics. There was a positive correlation between epicardial fat and various lipoprotein levels i.e triglyceride (p=0.036) and LDL (p=0.023) in control and cases group, but there was no significant difference between the two groups with respect to low HDL levels. The association betweeen epicardial fat thickness and waist circumference, waist-hip ratio, BMI and HDL-cholesterol was studied separately in male and female population. BMI showed a statistically significant correlation with epicardial fat(p=0.038; r=0.317) in males and in females there was significant correlation between epicardial fat and waist hip ratio (p=.008 and r=.407) Multiple regression analysis (Table 3) was performed to calculate the contribution of different covariates to the prediction of epicardial fat thickness. Age, Triglycerides and LDL-cholesterol were the strongest independent variables correlated to epicardial fat thickness.

Table 1: Descriptive statistics of the study population

	Cases	**Controls**
Age (years)	47.6 ±9.6	47.6±9.5
Weight (kg)	74.9± 14.1	53.7±9.3
BMI (kg/m^2)	29.1±6.1	20.5±2.8
SBP (mmHg)	138±16.3	115±10
DBP (mmHg)	86±11.9	77±7.7
FBS (mg/dl)	142±58	96.3±11.5
TC (mg/dl)	189±44	178±33
TG (mg/dl)	154±55.6	105±48.5
LDL (mg/dl)	117.9±39.1	123.6±36.9
Males		
Waist circumference(cm)	100 ±10.2	75.6±8.9
Waist Hip ratio	1.01± 0.05	0.9±0.05

HDL-C(mg/dl)	39±12.7	48.6±11
Females		
Waist circumference (cm)	105±13.3	72±5.2
Waist Hip ratio	1.01±0.07	0.8±0.05
HDL-C (mg/dl)	37±5.8	54.7±9.6

Table 2. Epicardial fat thickness (in cm) control and cases group.

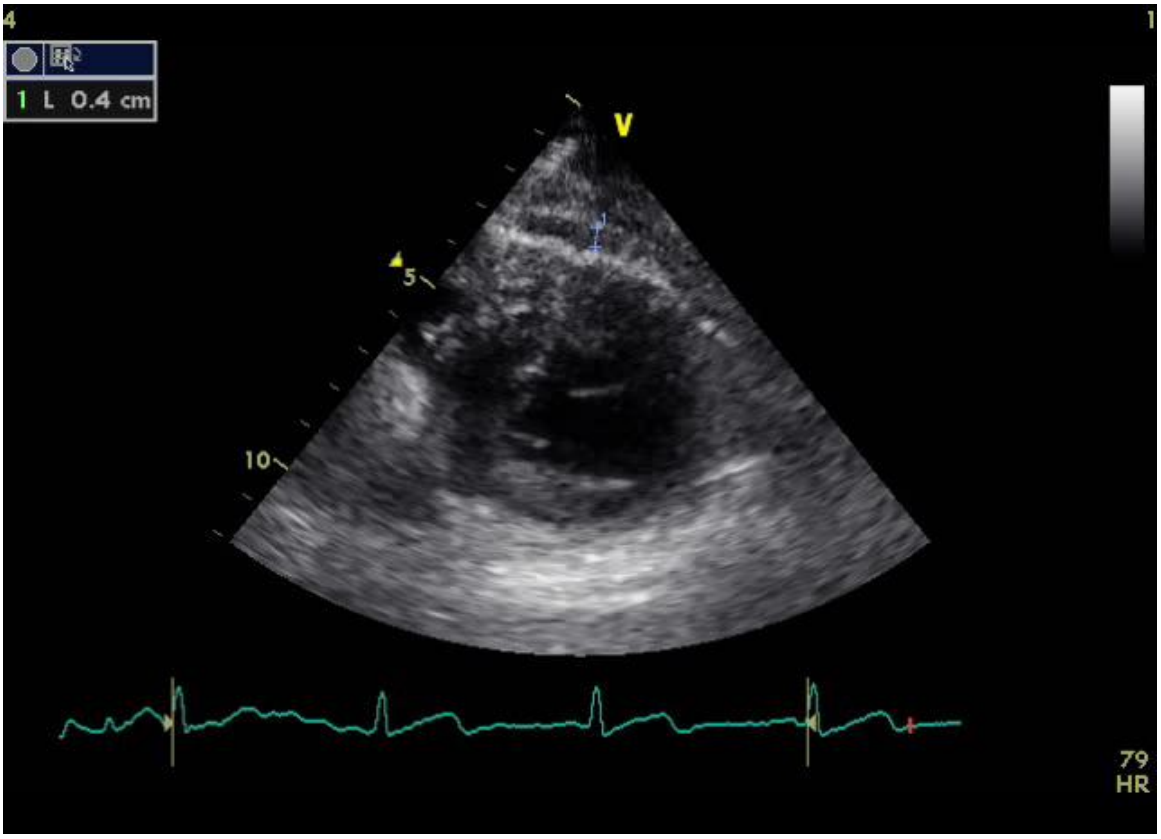
	Mean
Cases(n=43)	3.1±1.1*
Controls(n=43)	2.3±0.9

* p=0.001 vs control

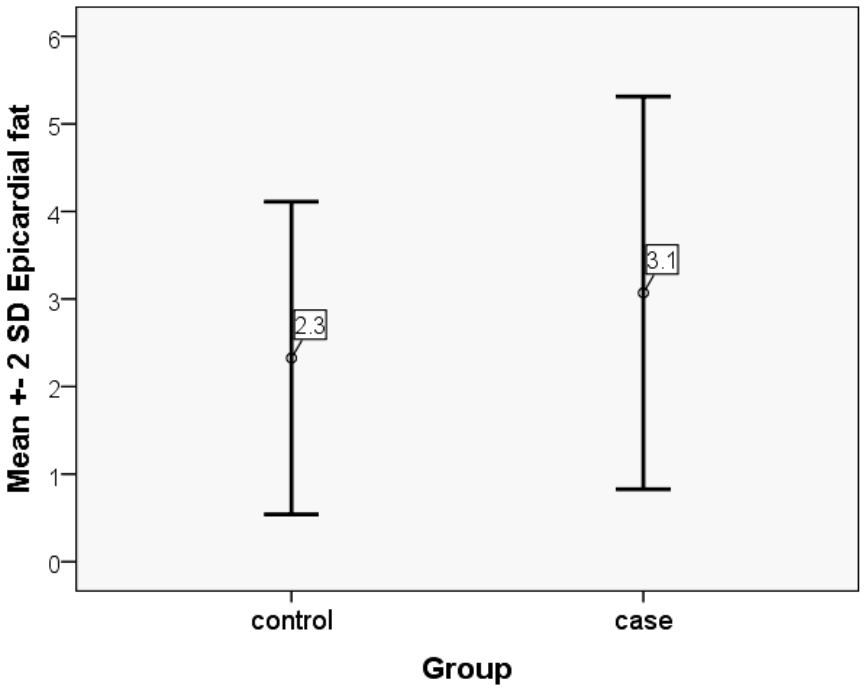
Table 3: Correlates of epicardial fat thickness with all the variables in metabolic syndrome patients: multiple regression analysis.

Model	**Unstandardized Coefficients**		**Standardized Coefficients**	**t**	**Sig.**	**95.0% Confidence Interval for B**	
	B	**S.E**	**Beta**			**Lower Bound**	**Upper Bound**
(Constant)	-5.951	2.988		-1.991	.056	-12.063	.161
Age	.056	.019	.455	3.034	.005	.018	.094
WC	.031	.023	.294	1.353	.187	-.016	.077
BMI	.009	.046	.043	.195	.847	-.086	.104
SBP	.003	.014	.041	.237	.814	-.025	.032
DBP	-.011	.019	-.104	-.578	.568	-.051	.028
HTN	.328	.832	.065	.395	.696	-1.374	2.030
FBS	-.002	.003	-.093	-.678	.503	-.008	.004
Raised blood sugar	.773	.565	.176	1.366	.182	-.384	1.929
TC	-.007	.009	-.227	-.734	.469	-.025	.012
TG	.010	.004	.413	2.688	.012	.002	.018
HDL-C	.002	.022	.016	.099	.922	-.043	.048
LDL	.019	.009	.580	2.042	.050	.000	.038

Fig.1 Electrocardiography showing epicardial adipose tissue



The arrow marked here shows deposition of epicardial fat on the free wall of the right ventricle



Graph 1: Difference of epicardial fat between cases and controls
p<0.001 compared to control.

Discussion

In the pathogenesis of metabolic syndrome, central obesity has been implicated in the causality as the most important component.[8]Abdominal obesity is determined by the accumulation of both subcutaneous adipose tissue and visceral adipose tissue. As it is difficult to obtain an accurate method for measurement of visceral obesity, several surrogate markers have been tried in the past for the same. Anthropometric parameters especially waist circumference has been used as a good predictor of intra-abdominal fat.[9,10] However imaging methods like MRI is considered the gold standard, for measurement of intra-abdominal fat.[11] But unfortunately MRI is not a cost-effective tool. Hence there have been studies for quantification of intra-abdominal fat using other cost-effective tools like abdominal ultrasonography.[12, 13]

Echocardiography, which is an ultrasound method commonly used in the clinical management of patients with metabolic syndrome, may be applied to indicate visceral adiposity by detection of epicardial adipose tissue. Hence we aimed to study the quantification of epicardial adipose tissue in patients with metabolic syndrome. We also aimed to study the relationship of epicardial adipose with anthropometric and biochemical parameters of metabolic syndrome.Epicardial fat thickness was measured on the free wall of the right ventricle from both short and long axis views. We found an epicardial fat thickness of 1-8mm in our study population. Iacobellis et al found a range of 1.8 to 16.5mm in normal healthy population in a study done in Rome, Italy.[14] Jeong et al studied a population of ischaemic heart disease patients and their study population had epicardial fat thickness varying from 1.1 to 16.5mm.[15]There have been no valid cut points to define normal range of epicardial fat thickness. Hence it was decided to evaluate the difference of epicardial fat thickness between people with metabolic syndrome and normal population. There was a definitive increase in epicardial adipose tissue with increasing age and age was an independent factor influencing epicardial fat thickness in our study population (p=0.004). Similar results were found by Jeong et al[15] and Mookadam et al,[16] epicardial adipose tissue correlated well with age. However Iacobellis et al showed that there was no significant correlation between epicardial fat thickness and age. Probably as the mean age of our study population was 47.6$\pm$9.6 years, where in the prevalence of diabetes and hypertension is more common, these factors could be influencing the outcome.

Epicardial fat thickness did not shown any significant difference between males and females in the current study. As our study population was age and sex matched, the confounding factor of age on epicardial fat thickness was

eliminated. Previous studies also support the fact that sex did not influence epicardial fat thickness.[14]Subjects with metabolic syndrome had higher amount of epicardial adipose tissue deposition compared to normal individuals (p=0.001). Mookadam et al found similar results, where in the group with epicardial fat thickness of >5mm consisted predominantly of people with metabolic syndrome.[16]The correlation of epicardial fat thickness with waist circumference in both males and females was done separately as the values for waist circumference differ in both the sexes. There was an increasing trend in epicardial adipose tissue with an increase in waist circumference in both the sexes (p=0.118 in females and 0.285 in males). However the association was not statistically significant. Studies have shown that waist circumference correlated well with epicardial adipose tissue and the correlation was statistically significant in their study group (p=0.01).[14,15]

The correlation between anthropometric parameters of metabolic syndrome with epicardial fat thickness such as waist hip ratio and BMI showed that there was a significant correlation between epicardial fat thickness and BMI in male population (p=0.038) and waist-hip ratio in females (p=0.008).
Association between epicardial fat thickness and hypertension in people with metabolic syndrome revealed non-significant difference (p=0.452). This can be explained by the fact that the group with metabolic syndrome included people with hypertension who were on antihypertensives. On the contrary some earlier studies have found a significant correlation between epicardial fat thickness with diastolic BP (P=0.001). [14]

Epicardial fat thickness was compared between people with normal blood sugar, impaired fasting glucose and diabetics, and it was found that there was an increase in epicardial fat thickness as the glycemic control of the group shifted from normal blood glucose to diabetes. A significant association between epicardial fat thickness between the three groups (p=0.051) was found. This has been already proven in earlier studies that fasting blood sugar (FBS) correlates significantly with epicardial fat thickness.[14]There was a positive correlation between raised triglycerides and epicardial fat thickness in people with metabolic syndrome in our study and the correlation was statistically significant (p=0.036). Hypertriglyceridaemia has been cited as an independent variable, which correlated well with epicardial fat thickness in previous studies.[14] Mookadam et al[16] and Iacobellis et al[14] have quoted a good correlation between epicardial fat and triglyceride levels (p=0.077 and p=0.06 respectively).

The correlation between epicardial fat thickness and HDL-cholesterol was assessed in both the sexes separately. We found that there was decreasing trend in epicardial fat thickness with increasing HDL levels in male population, however the same did not hold good in the female population. Moreover, the correlation between HDL-cholesterol and epicardial fat thickness was not statistically significant (p=0.658 in males and p=0.685 in females). The current study also demonstrated a positive correlation between LDL cholesterol and epicardial adipose tissue and it was statistically significant (p=0.023). Though LDL-cholesterol is not a component of metabolic syndrome, it is an independent cardiovascular risk factor. The association between LDL-cholesterol and epicardial fat tissue is significant and could correlate with cardiovascular risk profile.

There was an increasing trend in epicardial adipose tissue as the number of components of metabolic syndrome increased. This was quite evident when the increase in trend was quite drastic when the parameters of metabolic syndrome increased from two to three components. However there was no increase in mean epicardial adipose tissue between the cases with three, four and five components of metabolic syndrome. Probably clustering of three or more components of metabolic syndrome is essential to influence the epicardial fat thickness. As increased waist circumference was the only common variable in all the cases of metabolic syndrome, probably it might be playing a crucial deciding role, thereby suggesting a strong association with epicardial adipose tissue.Hence, we conclude that in resource poor countries, expensive tests like CT scan or MRI to assess visceral obesity may be difficult due to financial constraints; a simple test like echocardiographic assessment of epicardial fat will serve as a good surrogate. Such screening tests would identify the population at risk for cardiovascular disease and help in planning and executing early intervention.

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