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Epicardial Adipose Tissue Thickness is Related with Systolic Blood Pressure, But not with Atherogenic Indicators in Patients with Type 2 Diabetes

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Abstract

Background: Epicardial adipose tissue (EAT) has been proposed as a marker of cardiovascular risk, however there are few studies regarding its relationship with atherogenic risk, particularly in the population with diabetes.

Objective: to assess the impact of EAT on different atherogenic index in diabetic patients from a population from Mexico City.

Material and method: Case-control study. Patients of both genders with or without type 2 Diabetes Mellitus (DM), without previously known cardiac, thyroid, renal or malignant abnormalities were included. Sociodemographic, clinical, and biochemical data were collected, including anthropometry, blood pressure, blood glucose, HbA1c levels, serum lipids, and the calculation of various atherogenic indicators such the Castelli, Kannel, and Tg/HDL ratios. The echocardiogram was used to calculate the EAT. T-tests were used to compare the epicardial fat means. Using Pearson's analysis and association risk, the correlation and connection of epicardial fat thickness with atherogenic index was assessed.

Results: There were 71 individuals in total, 35 of them had type 2 diabetes and 36 had not. Their average age was 49.1 9.4 years. Groups of people who share similar traits in terms of height, age, sex, BMI, and waist size. In the group with DM2, the EAT were higher (5.1 0.8 vs 3.3 0.9 mm, p 0.001). When the study population was separated into groups based on the median EAT (> 4.2 1.2 mm), it was found that those groups had higher systolic blood pressure (SBP) values (p 0.001). The Castelli, Kannel, and Tg/HDL means in DM2 are the same as those in non-DM2, with no differences. But in the multivariate linear regression analysis, BMI and SBP showed a positive connection (r = 0.33, odds ratio 2; 95% confidence interval [CI], 0.45 to 8.72); It served as an independent EAT predictor for the rise in SBP.

Conclusions: The study indicates a substantial association between EAT and SBP, especially in patients with DM2. However, there was no evidence of a connection with atherogenic markers.

Keywords: Epicardial Fat Thickness, Atherogenic Index, Diabetes Mellitus

Background

Dyslipidemia is a strong risk factor for the development of cardiovascular events (CV) such as stroke, CHD, AMI, PAD, as demonstrated in the GloboRisk study, with Mexico being one of the countries with the highest proportion of people with high CVR, with a prevalence of 16% for men and 11% for women in Mexico [1, 2, 3, 7]. The prevalence of previous diagnosis of diabetes mellitus (DM) increased from 7 to 10.3%, dyslipidemia increased from 26.5 to 30.4%, and the prevalence of overweight/obesity increased from 69.3 to 75.2%, according to the results of Ensanut 2006 and 2018 [2, 3]. These figures underscore the importance of these diseases and their avoidance as the key therapeutic measure. The Framingham table 5, 6 and indexes to measure the risk of atherosclerosis, which are composed of the ratio or mathematical proportion between the levels of total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), or low-density lipoprotein (LDL), are two of the most popular tools used to evaluate CVR [7].

The Castelli Risk Index I (CRI-I) assessed as TC/HDL and II (CRI-II estimated as LDL/HDL, also known as the Kannel index) are more reliable predictors of CVR than the standard lipid parameters, according to recent data [8, 9, 10, 11]. Since EAT has a close relationship with the myocardium and coronary arteries, as demonstrated by numerous studies, it adds value to other parameters that are currently used to predict future CVR in the general population [13, 14]. Although the link between EAT thickness and CV disorders is well documented, there is still no proof that elevated EAT is related to alterations in atherogenic indices.

This study's goal was to determine whether EAT is linked to variations in atherogenic indices, especially in the setting of people with diabetes.

Methods

Study carried out from June 2019 to February 2020 in which patients from the Internal Medicine outpatient clinic of the Ticomán General Hospital from Mexico City, DM2 and Non-DM2 groups were included in the study, who were at least 18 years old, free of vascular events, neoplastic disorders, or chronic degenerative diseases were chosen for participation in the study. They also provided their consent voluntarily. Anthropometric measurements were taken, including height, weight, and BMI calculations. The waist circumference was measured, with values below 88 cm for women and over 102 cm for males being deemed normal. After a 12-hour fast, blood samples were drawn by venipuncture. The serum from the centrifuged samples was used to analyze the blood's TC, TG, LDL, and HDL levels. The Castell I index (TC/HDL cholesterol) was found to have three atherogenic indices; a value of 4.5 was deemed low risk, a value between 4.5 and 7 was considered moderate risk, and a value >7 was considered high risk. The Kannel index (LDL/HDL) with low-risk findings of <3 and high-risk results of >3, was constructed. The TG/HDL index was obtained; results <3 and high risk ≥3 were considered low risk, the average of three measurements in three cardiac cycles, as described by Iacobellis [22], was taken into consideration to make the correlations. EAT was measured in the free wall of the right ventricle at the end of systole from a long parasternal axis in three cardiac cycles by two echocardiographers who were unaware of the patient's clinical data.

The SPSS 25.0 statistical package was used for the analysis. A p value of 0.05 was judged significant. The Kolmogorov-Smirnov test was used to determine whether the variables had a normal distribution, and the continuous variables were presented as mean and standard deviation or median and interquartile range depending on whether they had a normal distribution, and they were compared with the t-student test or the non-parametric Mann-Whitney test as appropriate. The Pearson parametric test was used for the correlation study, and a link with the Odds Ratio (OR) was also investigated. Finally, a multiple linear regression was used to identify variables that were not affected by the increase in EAT.

Results

A total of 71 patients were studied, with a mean age of 51.05 9.3 years, 50.7% of which were men, and subdivided based on the EAT (cutoff to median = 4.2 mm). Table 1 displays the clinical-demographic characteristics. Subjects with EAT greater than 4.2 mm had a higher frequency of DM2 and higher SBP values (p0.001).

Table 1: Comparison of clinical and biochemical characteristics between patients with epicardial adipose tissue below and above the median

	Epicardial Adipose Tissue < 4.2 cm (34)	Epicardial Adipose Tissue > 4.2 cm (37)	Total (71)	p value
T2DM %(n)	5.6% (4)	43.6% (31)	49.2% (35)	0.001
No T2DM %(n)	42.2% (30)	8.4% (6)	50.8% (36)	0.001
Age (years)	48.5±9.3	53.6±9.3	51.05±9.3	0.001
Male	19.7%(14)	30.9%(22)	(36)	0.026
Weight (Kg)	72.6±14.1	70.0±16.9	71.3 ±15.5	0.638
Height (m)	1.62±0.08	1.57±0.06	1.59±0.07	0.126
BMI (Kg/m^2)	27.4±3.9	28.1±5.9	27.7±4.9	0.659
waist circumference (cm)	101.0±17.4	104.0±29.4	102.5±23.4	0.677
SBP (mmHg)	118.3±13.1	138.0±11.4	128.15±12.2	<0.001
Glucose (mg/dL)	130.6±69.0	132.6±50.6	131.6±59.8	0.938
HbA1c (%)	7.2±2.3	8.9±3.2	8.0±2.7	0.075
Cholesterol (mg/dL)	190.7±47.1	204.2±31.9	197.4±39.5	0.433
Triglycerides (mg/dL)	182.3±108.8	192.2±107.6	187.2±108.2	0.809
HDL-c(mg/dL)	47.1±21.4	52.1±23.4	49.6±22.4	0.540
LDL-c (mg/dL)	108.4±40.5	129.4±41.6	118.9±41.0	0.174
SBP: Systemic blood pressure, BMI: Body Mass Index, HbA1c: Glycosylated hemoglobin, HDL: High-density cholesterol, LDL: low-density cholesterol; T for student				

Following that, the degree of association between EAT and the various atherogenic indexes (Castelli, Kannel, TG/HDL) was examined, and given the preliminary results, the correlation with SBP was included. Only a significant positive connection (r=0.33, p=0.04) was found between EAT and SBP, which was shown to be more specific in the DM2 subgroup (r=0.41, p=0.01) (Fig 1). An association study with an OR of 2 ([95% CI], 0.45 to 8.72; p < 0.05) (Table 2).

Table 2: Correlation between epicardial adipose tissue and atherogenic indices

	Castelli	Kannel	TG/HDL	SBP
All (p)	0.50 (0.68)	0.06 (0.62)	0.14 (0.22)	0.33 (0.04)
No DM (p)	-0.12 (0.45)	-0.13 (0.44)	-0.031 (0.85)	-0.006 (0.97)
DM (p)	0.14 (0.39)	0.28 (0.09)	0.26 (0.88)	0.41 (0.013)
TG/HDL: Triglycerides/High-density cholesterol index, DM: Diabetes mellitus, SBP: Systolic blood pressure. Pearson.				

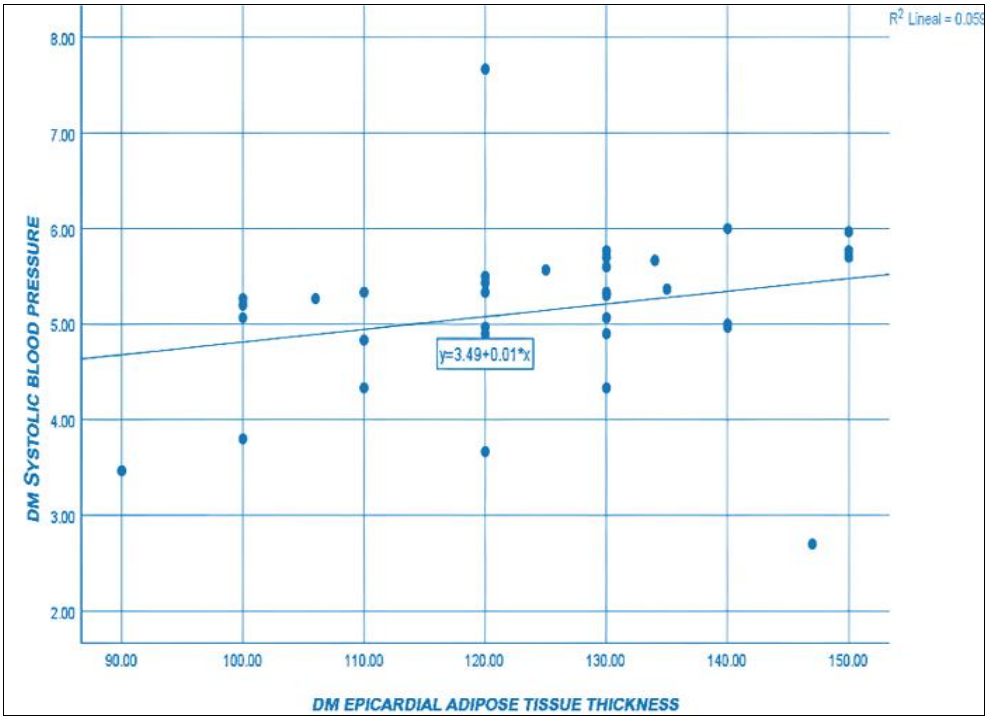

Fig 1: Positive correlation between epicardical adipose tissue thickness and increased systolic blood pressure in patients with DM. Pearson

Table 3: Association between epicardial adipose tissue > 4.2 mm and atherogenic indices

	Castelli > 4.5	Kannel > 3	TG/HDL >3	SBP >140
All	13 (18.3 %)	14 (19.7 %)	26 (36.6%)	6 (8.4 %)
No DM	2 (2.8%)	3 (4.2%)	2 (2.8%)	0 (0%)
DM	11 (15.4%)	11 (15.4%)	24 (33.8%)	6 (8.4%
OR (95% CI)				
All	1.50 (0.54 – 4.16)	1.11 (0.42 – 2.93)	1.46 (0.54 – 3.92)	2 (0.45 – 8.72)*
No DM	1.16 (0.18 – 7.55)	1.72 (0.29 – 10.08)	0.28 (0.04 – 1.84)	N.A.
DM	N.A.	1.65 (0.15 – 17.82)	3.42 (0.40 – 28.94)	0.72 (0.06 – 8.19)*
OR: Odds ratio, DM: Diabetes mellitus, SBP: Systolic blood pressure, CI: Confidence interval, TG/HDL: (*) Statistically significant.				

There was no clinically significant association between EAT > 4.2mm and the atherogenic indexes studied, nor with SBP (cut-off 140 mmHg) (Table 3).

Discussion

This study is an extension of that previously published by Prestegui *et al*. 2022, who investigated the effect of increasing EAT on several atherogenic indicators in DM2 and non-DM2 individuals. Evidence indicates patients with DM2 had an increase in EAT, since a cutoff >4.1 mm has previously been demonstrated to raise CVR [13].

In this study the correlation between EAT and atherogenic indices was sought, unlike what was mentioned by Caliskan *et al*. Those who discovered a positive correlation between EAT and atherogenic indices found no significant correlation in our current analysis, though it should be noted that the Caliskan study was conducted in celiac disease patients, who have a different pathophysiological process for the increase in CVR [15]. Like our study, no relationship was detected between EAT and atherogenic markers in the study by Koshelskaya *et al*. They also revealed a mean EAT 4.94.2±3.9mm, which was close to the 4.24.2±1.24 in our study [16].

Although it was not the purpose of the study, the pertinent analyses were carried out to determine other variables that could increase SBP, which may be related to what was described by Ng e cols, who found that increased EAT is associated with myocardial systolic dysfunction in patients with DM, preserved LVEF, and no atherosclerotic disease [17], likewise Gastalde found that increased EAT is associated with myocardial systolic dysfunction in patients with DM They, like Sironi *et al*., found a connection between EAT, hypertension, atherosclerosis, and CHD [18].

An increase in accumulated fat in abdominal and epicardial visceral regions was observed in men with CVR and essential hypertension [19], all of which is likely associated with increased vascular dysfunction, which leads to activation of the renin-angiotensin axis, leading to greater arterial hypertension, as demonstrated by Cheung *et al* [20, 21].

The increase in BMI was found to be an independent factor for the increase in SBP in the multivariate analysis, as

previously demonstrated by the Framingham Offspring Study [21], but the endocrine factor of epicardial fat must be recognized because it is in direct contact with the coronary arteries. Because it is brown adipose tissue, it produces more heat and undergoes more coronary remodeling; however, as EAT increases, this brown tissue becomes hypoxic and secretes more inflammatory cytokines and Vasoactive peptides, including increased free fatty acids, IL6, TNF alpha, and angiotensin II; all of these factors are involved in the pathophysiology of systemic arterial hypertension [22, 23, 24] Paolisso *et al*. They indicated that a rise in EAT raises the concentration of catecholamines, which is caused by the release of fatty acids, and that this is likely connected with endothelial dysfunction [25].

Conclusion

In patients with DM2, there is no association between the increase in EAT and the increase in CVR measured by atherogenic indices, but they did have higher SBP as well as higher EAT; However, the increase in SBP is related to an increase in BMI rather than an increase in EAT.

Study Limitations

The number of patients included in the study was limited. The study was a cross-sectional study. EAT evaluation was performed by two-dimensional echocardiography instead of CT or MR.

Table 4: Abbreviations

EAT	Epicardial adipose tissue
DM2	Diabetes Mellitus type 2
HbA1c	Hemoglobin A1c
BMI	Body Mass Index
SBP	Systolic blood pressure
CV	Cardiovascular
CHD	Coronary heart disease
AMI	Acute myocardial infarction
PAD	Peripheral arterial disease
CVR	Cardiovascular risk
TC	Cholesterol
TG	Triglycerides
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
Ensanut	National Health and Nutrition Surveys
LVEF	Fracción de eyección del ventriculo izquierdo
OR	Odds ratio
CI	Confidence Interval

Ethics Approval: The study was approved by the research and ethics committee of Ticoman General Hospital, it was carried out in accordance with the Declaration of Helsinki, the patients gave their informed consent prior to their inclusion in the study.

Availability of Data and Materials: Data will be provided by contacting David Prestegui.

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