Zagazig University Medical Journal
www.zumj.journals.ekb.eg

https://doi.org/10.21608/zumj.2024.234154.2873 Volume 30, Issue 1.6, September 2024, Supplement Issue
Manuscript ID ZUMJ-2303-2765 (R1) DOI 10.21608/ZUMJ.2023.199083.2765

ORIGINAL ARTICLE

Epicardial Adipose Tissue as a New Biomarker for Insulin Resistance and Predictive of Prediabetes

Fatma Said Amer Leaimesh[2*], Ayman A.M. Nsr-Allah[1], Islam Elsayed Shehata[3], Azza H. Abd-El Fatah[1]

[1]Department of Internal Medicine and Endocrinology, Faculty of Medicine, Zagazig University, Egypt
[2]Department of Internal Medicine and Endocrinology, Faculty of Medicine, Sirt University, Libya
[3]Department of Cardiology, Faculty of Medicine, Zagazig University, Egypt

Corresponding author*
Fatma Said Amer Leaimesh

E-mail address: Sirt0949@gmail.com

Submit Date: 09-03-2023
Revise Date : 20-03-2023
Accept Date: 23-03-2023

ABSTRACT

Background: Type 2 diabetes is predisposed by increased visceral obesity, insulin resistance, and B-cell dysfunction. Obesity, diabetes mellitus, and the metabolic syndrome are all risk factors for increased epicardial adipose tissue (EAT) thickness. Few published studies have examined the significance of EAT thickness in prediabetic patients and how it relates to insulin resistance, HbA1c levels, and the length of diabetes. The goal was to look at the relationship between EAT and the likelihood of developing Type 2 DM.

Methods: This study included 69 subjects. Subjects were split into the following three groups: Group I consists of 23 individuals who have good blood sugar levels, Group II consists of 23 patients with prediabetes, and Group III consists of 23 patients with type 2 diabetes. All patients underwent transthoracic echocardiography to estimate epicardial adipose tissue thickness.

Results: Our study reveals a statistically significant difference between the tested groups in terms of their thicker epicardial adipose tissue in diabetes than prediabetes group($p<0.05$). The median epicardial fat thickness (EFT) was considerably greater in the group of people with prediabetes than healthy control group ($p<0.05$). There is significant and direct relation between EAT thickness of studied groups as well as HOMA-IR, BMI, and waist size ($p<0.05$).

Conclusion: The EAT is simple, inexpensive, readily available, non-invasive, and a predictor of development of prediabetes and Type 2DM.

Keywords:Epicardial Adipose Tissue, Insulin Resistance, Prediabetes, type 2 Diabetes mellitus.

INTRODUCTION

Visceral obesity has been strongly linked to the onset and progression of both Type 2 Diabetes mellitus and cardiovascular disease, which are two of the major causes of death worldwide [1].

Type 2 diabetes mellitus (T2DM) is one of the most prevalent comorbidities in the world, and its incidence is rapidly rising. The most prevalent kind of diabetes is characterised by hyperglycemia, insulin resistance, and a relative lack of insulin [2].

The reversible early stage of type 2 diabetes is known as prediabetes. A blood glucose level that is both above and below the normal range and within the recommended diabetic range is referred to as prediabetes. Those with impaired glucose tolerance (IGT) and/or impaired fasting glucose (IFG) are now referred to as having prediabetes [3]. 90% of these people, however, were not aware of

their diagnosis. According to the World Diabetes Federation, there are 318 million adults worldwide who have impaired glucose tolerance (IGT), and by 2040, that number is projected to rise to 482 million [4]. So, it's crucial to look at whether obesity is a causal risk factor for developing T2DM early on (i.e. prediabetes). In addition, inflammation has been found to be the relationship between insulin resistance and obesity [5,6].

The prevalence of cardiometabolic illnesses, including Type 2 Diabetes, is rapidly increasing in tandem with the global obesity epidemic [7]. Obesity, prediabetes, and insulin resistance are all known to be closely related [8,9].

Insulin resistance is defined as a compromised physiologic response of target tissues, notably the liver, muscle, and adipose tissue, to insulin stimulation. Hyperinsulinemia and an increase in beta-cell insulin synthesis occur as a result of impaired glucose elimination brought on by insulin resistance. Type 2 diabetes mellitus, the metabolic syndrome, and nonalcoholic fatty liver disease (NAFLD) can all develop as a result of the progression of insulin resistance[10-12].

In order to lower the risk of developing diabetes and its complications, efficient approaches for identifying prediabetes will be needed [13].

The heart and the epicardial coronary arteries are encircled by epicardial fat, which is situated on the surface of the heart between the myocardial and visceral layer of the epicardium. The aetiology of atherothrombotic heart disease is actively influenced by the thickness of epicardial adipose tissue [14]. Through the action of cytokines, adipokines, and paracrine and autocrine processes, adipocytes affect the myocardium and coronary arteries [15].This study aimed to look at the relationship between EAT and the likelihood of developing Type 2 DM.

METHODS

An informed written consent was taken from all patients. The study protocol was approved by the Institutional Review Board of Zagazig University (IRB number: 9680/28-7-2022) and was conducted according to the principles of the Declaration of Helsinki. Our case control study was conducted at Departments of Internal Medicine, Endocrinology Department, and Department of Cardiology, Faculty of Medicine at Zagazig University Hospitals during the period from 8/2022 to 3/2023 and included 69 aged from 40 to 70 years who were placed into the following three groups: I group: diabetic group HbA1C ≥6.5%), group II: prediabetic group HbA1C: 5.7-6.5%, group III: healthy control group HbA1C≤ 5.7% the patients included in our study were older than 18 years.the diagnosis of Type 2DM was confirmed by American Diabetic Association criteria: In addition to random plasma glucose levels of 200 mg/dl or higher, uncontrolled DM with HbA1C levels of more than or equal to 7%, and fasting plasma glucose levels of greater than or equal to 126 mg/dl or 2 h postprandial plasma glucose levels of greater than or equal to 200 mg/dl.

The study's participants ranged in age from 18 to 70 and included prediabetic, T2DM, and prediabetic patients as an experimental group and non-DM persons as a control group. Diabetes type 1 and/or gestational diabetes, ischemic heart disease, people with overt

cardiovascular disease (CVD), clinical signs of peripheral arterial diseases such as claudication, absent peripheral pulses, or ischemic leg ulcers, renal or hepatic impairment, cerebrovascular disease, peripheral vascular disease, congestive heart failure and valvular heart disease, or chronic kidney disease are all risk factors were also excluded.

All patients underwent thorough history taking, physical examinations, blood pressure checks, clinical examinations, and laboratory tests like FBG, PPG, HbA1C, lipid profiles, among others fasting insulin, HOMA-IR

Measurement of epicardial adipose tissue (EAT) thickness:

Each individual had complete transthoracic echocardiography by an experienced cardiologist blinded to the clinical data, utilising an HD11XE ultrasound device with 3.6 MHz transducers. According to the recommendations of the American Society of Echocardiography, exams were performed in the left lateral decubitus position. Epicardial fat (EF) was characterised as an echo-free region between the outer wall of the myocardium and the visceral layer of the pericardium. The maximum diameter of EF found on the right ventricular free wall was determined. Epicardial adipose tissue (EAT) was quantified in the parasternal long-axis view during end-systole in three cardiac cycles. The average of three cardiac cycles was used for statistical analysis. There is yet no definite value considered normal for EAT thickness. There are inconsistencies regarding EAT thickness. The EAT thickness >5 mm during end-diastole is associated with cardiac abnormalities (left atrial dilatation, lower ejection fraction, increased left ventricular mass, and diastolic dysfunction) that have been detected by echocardiography according to **Mookadam et al.,**[16].

Statistical Analysis

Data management using SPSS IBM Corp. Printed in 2015. Version 23.0 of IBM SPSS Statistics for Windows. IBM Corp., Armonk, New York. Anova test, Kruskall wallius, and spearman's correlation coefficient were computed. Quantitative data were expressed as the mean, standard deviation (SD), and median (range), and qualitative data were expressed as absolute frequencies (number) and relative frequencies (%). Receiver Operating Characteristic (ROC) curve was used. AUC ranges from (0 to 1), very good (0.9 -1), good (0.8-0.9), fair (0.7 -0.8), fail (0.6 -0.7) and poor (0.5-0.6).

RESULTS

Table (1)display the fundamental traits of the studied groups: mean age of diabetic group was 57.2±12.2 ranged from 42 to 85 years, 91.3% of them were female. The prediabetic group's average age was 49.9±11.5 ranged from 40 to 70 years, 69.6% of them were women. The healthy control group's average age was 53.2±14.2 ranged from 28 to 77 years, 78.3% of them were female. There was higher significant systolic and diastolic blood pressure in diabetic group with mean ± SD 122.6± 6.9 ,82.6± 4.5 respectively compared to prediabetic with mean± SD 115.2± 6.6, 77.4± 4.5 respectively and healthy control group with mean± SD 115.3± 8.4, 76.9± 4.7 however there was no discernible difference in the other baseline data.

Table (2) demonstrates that there is a statistically significant difference in the blood glucose profile of the tested groups ($p<0.05$). HbA1C value and fasting blood sugar levels

were considerably higher in the diabetes patient group with mean ± SD 7.9± 1.7 than pre diabetic group with mean ± SD 5.8± 0.46 and healthy control group with mean ± SD 5.07± 0.38($p<0.05$). Fasting insulin significantly higher in pre diabetic group with mean ± SD 16.9 ± 9.7 than diabetic group with mean ± SD 9.5± 6.1 and healthy control group with mean ± SD 7.6 ±3.04($p<0.05$). In addition; fasting blood glucose, post prandial blood glucose, HbA1C is significantly higher in pre diabetic group than healthy control group. Between the studied groups, there was a statistically significant difference in LDL, TC and TG that was higher in diabetes with mean ± SD 184.5± 59.3 and pre diabetes with mean ± SD 141.1 ±73.7 than control with mean ± SD 111.1± 53 and regarding HDL that was lower in diabetes and pre diabetes than control($p<0.05$). There are statistically significant differences between the groups under study regarding their epicardial adipose tissue thickness($p<0.05$).

Table (1): Baseline characteristics of the studied groups

Variables	Diabetic group N 23	Prediabetes group N 23	Healthy control Group N23	f/ χ^2	p
Age (in years) Mean ± SD Median (range)	57.2±12.2 55(42-85)	49.9±11.5 45(40-70)	53.2±14.2 57(28-77)	1.88	0.16
Sex n.(%) Females Males	21(91.3) 2(8.7)	16(69.6) 7(30.4)	18(78.3) 5(21.7)	3.4	0.18
Disease duration /years Mean ±SD Median(range)	9.7±6.9 10(0.17-20)	-	-		
Medication (n%)	Oral hypoglycemic 23(100.0)	Glucophage 23(100.0)	No 23(100.0)	-	-
Weight(kg) Mean ±SD Median(range)	81.9±14 83(55-101)	78.04±8.3 81(55-86)	79.2±11.2 85(65-101)	0.71	0.49
High (cm) Mean ±SD Median(range)	164.2±2.9 164(160-172)	167.1±5.5 165(160-177)	165.5±9.8 162(150-192)	1.09	0.32
Body mass index (kg/m$^{2)}$ Mean ±SD Median(range)	30.4±5.3 31 (21.48-38.1)	28.1±4.3 30.1(20.2-33.2)	29.1±3.4 28.9(23.7-34.4)	1.52	0.22
Waist circumference(cm) Mean ±SD Median(range)	99.5±11.1 101(81-115)	94.9±11.7 100(77-108)	94.4±9 97(78-110)	1.63	0.204
Systolic blood pressure (mmHg) Mean ±SD Median(range)	122.6±6.9 120(110-130)	115.2±6.6 120(100-120)	115.3±8.4 120(100-130)	7.7	.001
Diastolic blood pressure (mmHg) Mean ±SD Median(range)	82.6±4.5 80(80-90)	77.4±4.5 80(70-80)	76.9±4.7 80(70-80)	10.9	.0001

Table (3) shows there is significant and direct relation between epicardiac adipose tissue thickness of diabetic patients and BMI, waist circumference, HbA1C, fasting blood glucose, fasting insulin and HOMA-IR. There is significant and direct relation between epicardiac adipose tissue thickness of prediabetic group and BMI, waist circumference, HbA1C, fasting blood glucose and fasting insulin and HOMA-IR $p<0.05$. There is significant and direct relation between epicardiac adipose tissue thickness of control group HOMA-IR with mean ± SD 1.7± 0.69 and BMI, waist circumference. Otherwise there is no relation between epicardiac adipose tissue thickness and other parameters $p>0.05$.

Table (4) reveals the ROC curve analysis was performed to analyze epicardiac adipose tissue thickness as a biomarker for detecting prediabetic cases. epicardiac adipose tissue thickness at a cut-off value of ≥3.6 established a sensitivity of 82.61%, a specificity of 47.83%, a PPV of 61.29%and NPV of 73.33%, and an accuracy of 65.22% area under the curve (AUC) is 0.711 with (95%CI :0.559-0.862) (p-value0.014). This meaning epicardiac adipose tissue thickness a fair biomarker for detecting prediabetic cases. ROC curve analysis was performed to analyze fasting insulin as a biomarker for detecting prediabetic persons. insulin at a cut-off value of ≥8.5 established a sensitivity of 78.26%,a specificity of 69.57%,a PPV of 72%and NPV of 76.19% and an accuracy of 73.91% area under the curve (AUC) is 0.8 with (95%CI :0 .654-0.945) (p-value0.0001). This meaning insulin resistance a good biomarker for detecting prediabetic persons.

Table (5) reveals the ROC curve analysis was performed to analyze epicardiac adipose tissue as a biomarker for detecting prediabetic persons acorrding HOMA level. Epicardial adipose tissue at a cut-off value of ≥4.2 established a sensitivity of 70.8%.a specificity of 63.6%,a PPV of 68%and NPV of 66.7% and an accuracy of 64.4% area under the curve (AUC) is 0.69 with (95%CI :0.54-0.85) (p-value0.026)**.** This meaning epicardiac adipose tissue fail for detecting prediabetic persons. ROC curve analysis was performed to analyze epicardiac adipose tissue as a biomarker for detecting diabetic persons according HOMA level. epicardiac adipose tissue at a cut-off value of ≥5.6 established a sensitivity of 22.6%.a specificity of 40%,a PPV of 43.8%and NPV of 20% and an accuracy of 28.3% area under the curve (AUC) is 0.62 with (95%CI :0.43-0.8) (p-value 0.21). This meaning epicardiac adipose tissue fail for detecting diabetic cases versus prediabetic persons.

In **table (6)**, multivariate logistic regression for prediction of prediabetic patients from normal persons showed that significant predictor of presence of prediabetes was increase insulin level.

Table (2): Metabolic features of the studied groups

Variables	Diabetic group N 23	Pre diabetic group N 23	Healthy control group N23	f/KW	P value	LSD
Fasting blood glucose (mg/dl) Mean ±SD Median(range)	155.9±54.9 150(95-312)	131±14.2 125(101-157)	89.3±7.1 90(73-99)	23.9	.0001	P1=.03 P2=.0001 P3=.0001
Post prandial blood glucose(mg/dl) Mean ±SD Median(range)	202±76.8 200(112-400)	157.9±22.8 150(120-188)	118.9±13.8 115(93-144)	18.07	.0001	P1=.002 P2=.006 P3=.0001
Fasting insulin (µU/L) Mean ±SD Median(range)	9.5±6.1 9.1(0.98-20.96)	16.9±9.7 15.1(0.44-32.4)	7.6±3.04 7.9(3.42-15.1)	12.4	KW 0.002	P1=.019 P2=.0001 P3=.36

HOMA-IR Mean ±SD Median(range)	4.1±3.8 3.3(0.23-16.15)	5.6±3.7 4.7(0.11-12.54)	1.7±0.69 1.8(0.72-3.17)	18.2	KW 0.0001	P1=.063 P2=.0001 P3=.014
HbA1C (%) Mean ±SD Median(range)	7.9±1.7 8(5.4-12)	5.8±0.46 5.8(5.1-6.5)	5.07±0.38 5.1(4.4-5.6)	45.4	0.0001	P1=.0001 P2=.028 P3=.0001
HDL(mg/l) Mean ±SD Median(range)	35.5±10.03 37 (30-45)	42.8±5.3 40 (36-55)	60.3±4.04 61 (56-69)	**F** 77.3	**P value** 0.0001	
LDL(mg/dl) Mean ±SD Median(range)	167.6±30.02 155 (123-180)	136.4±20.2 137(105-167)	111.3±14.1 116(81-178)	36.3	0.0001	
Total cholesterol(mg/dl) Mean ±SD Median(range)	292±33.2 297(191-310)	210.8±46.7 207(180-220)	187.3±23.3 190(150-192)	56.2	0.0001	
TG(mg/dl) Mean ±SD Median(range)	184.5±59.3 180(98-350)	141.1±73.7 130(100-300)	111.1±53 115(74- 150)	KW 7.99	0.0008	
Epicardial adipose tissue(mm) **Mean ±SD** **Median(range)**	6.1304±1.06 6.4(4.4-8.3)	4.387±0.96 4.5(2.3-5.8)	3.5829±1.1 3.7(2.2-5.3)	34.67	0.0001	

HOMA-IR: Homeostatic Model Assessment for Insulin Resistance, HbA1C: hemoglobin A1C, HDL: high-density lipoprotein, LDL: low-density lipoprotein, TG: triglycerides.

Table (3): Correlation between epicardiac adipose tissue thickness and clinical data, laboratory finding in study group:

Epicardiac adipose tissue thickness(mm)	**Diabetic group**		**Prediabetic group**		**Control group**	
	R	**p**	**R**	**P**	**r**	**p**
Age per years	-0.028	0.899	0.064	0.77	0.079	0.718
BMI (kg/m^2)	0.445*	0.033	.539**	0.008	.582**	0.004
Waist circumference (cm)	0.537**	0.008	.601**	0.002	.493*	0.017
Systolic blood pressure (mm Hg)	-0.061	0.782	-0.121	0.581	0.073	0.741
Diastolic blood pressure(mm Hg)	0.116	0.599	-.0127	0.562	0.309	0.151
HbA1C (%)	0.582**	0.004	0.532**	0.0001	0.268	0.216
Fasting blood glucose(mg/DL)	0.668**	0.0001	0.566**	0.005	0.274	0.206
Fasting insulin (µ U/l)	0.443*	0.034	0.452*	0.03	0.164	0.453
HOMA-IR	0.492*	0.017	0.497*	0.016	0.118	0.591
PPBG (mg/dl)	0.068	0.759	0-.158	0.473	0.006	0.979
TG (mg/dL)	0.016	0.943	0.153	0.485	.459*	0.028
HDL (mg/dL)	-.094-	0.669	-0.098	0.657	0.185	0.399
LDL (mg/dL)	0.053	0.812	0.029	0.895	0.188	0.389
Total cholesterol (mg/dL)	-0.085	0.7	0.138	0.53	.414	0.051
Duration of diabetes per years	0-.058	0.793				

BMI: body mass index, HbA1C: hemoglobin A1C, PPBG: post prandial blood glucose, HOMA-IR: Homeostatic Model Assessment for Insulin Resistance, TG: triglycerides, HDL: high-density lipoprotein, LDL: low-density lipoprotein.

Table (4): Performance of epicardiac adipose tissue thickness: in comparison with fasting insulin

	Prediabetic person n.23	Healthy control n.23
Epicardiac adipose tissue thickness Cut off level ≥3.6 <3.6	 19 4	 12 11
Sensitivity	82.61%	
Specificity	47.83%	
Positive Predictive Value	61.29%	
Negative Predictive Value	73.33%	
Accuracy	65.22%	
Fasting insulin Cut off level ≥8.5 <8.5	 18 5	 7 16
Sensitivity	78.26%	
Specificity	69.57%	
Positive Predictive Value	72.00%	
Negative Predictive Value	76.19%	
Accuracy	73.91%	

Table (5): Performance of epicardiac adipose tissue for detecting prediabetic and diabetic according to HOMA-IR

	Prediabetic			Diabetic	
	Epicardiac adipose tissue Cut off level	**HOMA-IR(abnormal) n.24**	**HOMA-IR Normal n.22**	**Epicardiac adipose tissue Cut off level**	**HOMA-IR(abnormal) n. 31**	**HOMA-IR Normal n.16**
	≥4.2 <4.2	17 7	8 14	≥5.6 <5.6	7 24	9 6
Sensitivity	70.8%			22.6%		
Specificity	63.6%			40.0%		
Positive Predictive Value	68%			43.8%		
Negative Predictive Value	66.7%			20.0%		
Accuracy	64.4%			28.3%		

HOMA-IR: Homeostatic Model Assessment for Insulin Resistance.

Table (6): Multivariate Logistic regression for predictors for prediabetic patients

	B	S.E.	Wald	Sig.	Exp(B)	95% C.I.for EXP(B)	
						Lower	Upper
Insulin	.155	.068	5.2	.023	1.2	1.022	1.3
Epicardiac adipose tissue	.682	.38	3.25	.072	1.98	.942	4.2
Waist circumference	.021	.043	.241	.623	1.021	.94	1.1

DISCUSSION

We used epicardial adipose tissue in our cross-sectional investigation as a novel biomarker for insulin resistance and as a predictor of prediabetes where there are statistically significant differences between the groups regarding their epicardial adipose tissue thickness ($p<0.05$). We found that EAT thickness and insulin resistance a good biomarker for detecting prediabetic persons.

Our study showed that there were no statistically significant differences in the demographic information across the groups we analysed, ($P>0.05$). We demonstrated that Higher significant systolic in comparison to the prediabetic and healthy control groups, and diastolic blood pressure in the diabetic group, ($P<0.05$). There is no difference in systolic and diastolic blood pressure between the pre-diabetic group and the healthy control group $p>0.05$.

This came in agreement withAltin et al. [17]who showed that Age, sex distribution, and medication use of the patients within the examined groups did not differ significantly. Then again,Sugita et al. [18]demonstrated that there was no significant difference in the three groups' BMI, age, or sex. Furthermore**,** Baloglu et al. [19]found that there were no differences between patients and control participants in terms of the following factors: gender and BMI. Also, We demonstrated that there is a statistically significant difference in the blood glucose profile between the tested groups ($P<0.05$). Significantly higher fasting blood sugar, postprandial blood sugar, and HA1C values in the diabetes patients group than in the nondiabetic and healthy control groups $P<0.05$. Pre diabetics had fasting insulin levels that were considerably greater than those in diabetics and the healthy control group (p 0.05). Also, the pre-diabetic group had significantly higher fasting, postprandial, and HbA1C levels than the healthy control group. $P<0.05$. Regarding their lipid profiles, there were statistically significant differences between the tested groups. In agreement with our study,Schofield et al. [20]who found that diabetic patients had higher TG and TC than non-diabetic. Araki et al. [21]found that triglyceride levels was higher in type 2 diabetes. Su et al. [22]revealed that there is a higher correlation between diabetes and hypertriglyceridemia than there is in the general population. High triglyceride levels are a hallmark of type 2 diabetes dyslipidemia, alterations that were noted many years before the onset of clinically significant hyperglycemia. Baloglu et al. [19]demonstrated that the serum levels of triglyceride, TC, and LDL-C were not significantly different.

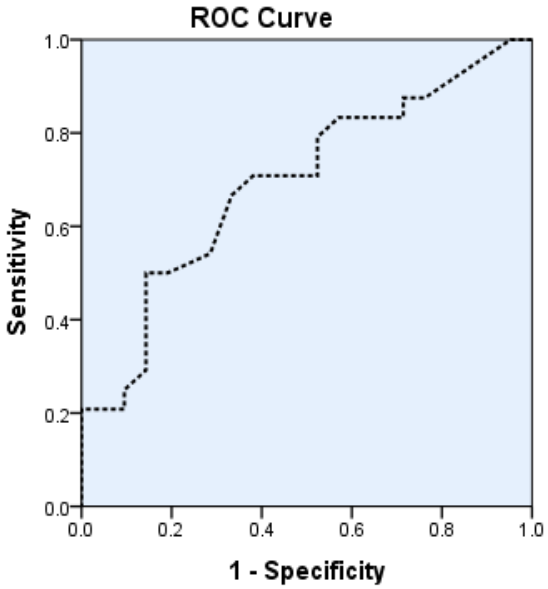

Figure (1): Receiver operating characteristic (ROC) curves of pericardiac adipose tissue for detecting prediabetic according HOMA. Illustrated area under the curve (AUC) is 0.69 with (95%CI : (0.54-0.85) (p-value0.026).

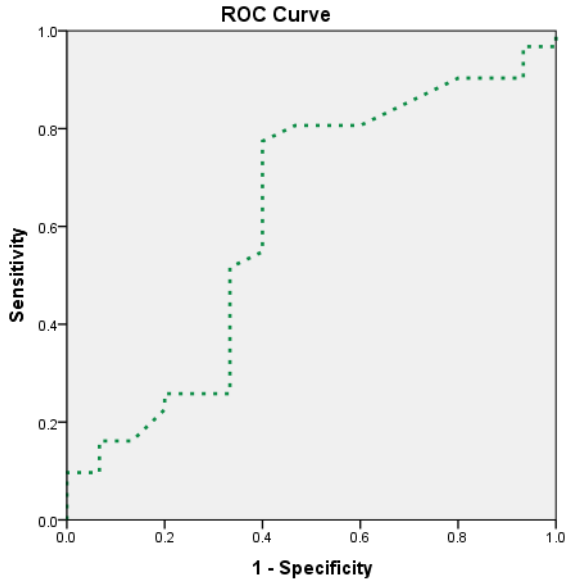

Figure (2): Receiver operating characteristic (ROC) curves of epicardiac adipose tissue for detecting diabetic patients according HOMA. Illustrated area under the curve (AUC) is 0.62 with (95%CI: 0.43-0.8) (p-value 0.21).

According to the current study, there is a statistically significant difference between the analysed groups in terms of the thickness of their epicardial adipose tissue (P<0.05). The thickness of the epicardial adipose tissue (EFT) in the diabetic groupwas found to be substantially larger than that in the prediabetic group (p<0.05). When compared to the healthy control group, the median EFT in the prediabetic group was significantly higher, (p<0.05). There is significant and direct relation between epicardiac adipose tissue thickness of diabetic patients and HOMA-IR, BMI, waist circumference, p<0.05. There is significant and direct relation between epicardiac adipose tissue thickness of prediabetic patients and HOMA-IR, BMI, waist circumference, p<0.05. BMI and waist circumference had a substantial and direct relationship with the thickness of the epicardial adipose tissue in the control group p<0.05.

In agreement with our study,Baloglu et al. [19] indicated that when compared to healthy

controls, EAT was found to be considerably greater in diabetes patients. Furthermore,Lima-Martínez et al. [23]showed that EAT thickness was higher ($p < 0.0001$) compared to participants in the low-moderate risk group for DM. in the high-risk group for DM.Ozcicek et al. [24]demonstrated that EAT was closely associated diabetes. Akbas et al. [25] demonstrated that Compared to control subjects, EAT measures were higher in diabetic patients.

We demonstrated a substantial and direct correlation between diabetic patients' epicardiac adipose tissue thickness and HbA1C, fasting blood glucose, and fasting insulin $p<0.05$. There is significant and direct relation between epicardiac adipose tissue thickness of prediabetic group and HbA1C, fasting blood glucose and fasting insulin $p<0.05$. Otherwise there is no relation between epicardiac adipose tissue thickness and other parameters $p>0.05$.

In agreement with our study,Altin et al. [17]showed that the EFT was significantly and positively correlated with plasma concentrations of fasting glucose, insulin and HOMA index.

Epicardiac adipose tissue thickness was examined using ROC curve analysis as a biomarker for identifying cases of prediabetes. a cut-off value for the thickness of the epicardial adipose tissue of ≥3.6 established a sensitivity of 82.61%, a specificity of 47.83%, a PPV of 61.29%and NPV of 73.33%, and an accuracy of 65.22% area under the curve (AUC) is 0.711 with (95%CI :0.559- 0.862) (p-value0.014).This meaning epicardiac adipose tissue thickness a fair biomarker for detecting prediabetic cases. ROC curve analysis was performed to analyze fasting insulin as a biomarker for detecting prediabetic persons. insulin at a cut-off value of ≥8.5 established a sensitivity of 78.26%, a specificity of 69.57%, a PPV of 72%and NPV of 76.19% and an accuracy of 73.91% area under the curve (AUC) is 0.8 with (95%CI :0 .654-0.945) (p-value0.0001).This meaning insulin resistance a good biomarker for detecting prediabetic persons.

In agreement with our study**,** Lima-Martínez et al. [23]demonstrated how the ROC curve was built to determine the EAT thickness cut-off point for predicting high T2DM risk. The ROC curve analysis revealed an AUC of 0.931 (CI 95%: 0.866-0.996), which is an indication of the very high precision of the test. The cut-off value of 6.65 mm obtained the highest Youden index (YI: 0.743), with 92.9% sensitivity and 99.8% specificity for predicting high T2DM risk.

ROC curve analysis was performed to analyze epicardiac adipose tissue as a biomarker for detecting prediabetic persons according to HOMA level. Pericardiac adipose tissue at a cut-off value of ≥4.2 established a sensitivity of 70.8%. A specificity of 63.6%,a PPV of 68%and NPV of 66.7% and an accuracy of 64.4% area under the curve (AUC) is 0.69 with (95%CI :0.54-0.85) (p-value0.026). This meaning epicardiac adipose tissue fail for detecting prediabetic persons.

Epicardiac adipose tissue was examined using ROC curve analysis as a biomarker for identifying diabetic individuals based on HOMA level. Epicardial adipose tissue at a threshold level of ≥5.6 established a sensitivity of 22.6%. A specificity of 40%, a PPV of 43.8%and NPV of 20% and an accuracy of 28.3% area under the curve (AUC) is 0.62 with (95% CI :0.43-0.8) (p-value 0.21)**.** This meaning epicardiac adipose tissue fail for detecting diabetic cases versus prediabetic persons.

Multivariate Logistic regression for predictors for prediabetic patients from normal persons showed that significant predictor of present of prediabetes was increase insulin level.Multivariate Logistic regression for predictors for diabetic patients from

prediabetic showed that significant predictor of present of diabetes was epicardiac adipose tissue.

In agreement with our study,Lima-Martínez et al. [23]showed that the multivariate regression analysis showed that EAT thickness (p = 0.007) persisted independently associated with high T2DM risk (odds ratios of 6.61 for EAT thickness. In addition, Iacobellis et al. [26]assess relationship between EAT thickness, T2DM, Also, it has been demonstrated that subjects with impaired fasting glucose had bigger epicardial fat deposits than their normoglycemic counterparts. This connection may be explained by the relationship between EAT thickness and indicators of insulin resistance like HOMA-IR. Independent of Obesity and age, type 1 diabetic patients also have larger EAT thickness than people without diabetes mellitus [27].

EAT thickness is a sign of accumulating visceral fat in the pericardial sac. It has been demonstrated that epicardial fat has endocrine and paracrine effects that may increase the risk of developing diabetes [28]. This association between EAT thickness and metabolic syndrome elements may be the cause of this link [23].Indeed, a previous study on Venezuelan population showed that an EAT thickness ≥5 mm has a sensitivity of 84.62% and a specificity of 71.11% to predict metabolic syndrome presence; however, this study has for the first time revealed that a 6.65 mm EAT thickness predicts high risk for T2DM, with a sensitivity of 92.9 and a specificity of 99.8%, this threshold being higher than that found to predict metabolic syndrome [23].

The current study showed many limitations.We have a relatively small number of patients. Measurement of EAT was an operator-dependent system. All of the patients enrolled in the study were Egyptian. One should consider that our results cannot therefore be applied to all patients because of the differences between nationalities. The lack of data on inflammatory markers. Due to financial constraints we were unable to analyze the possible effects of inflammation on the results.

We recommended that in order to prove this hypothesis, long-term prospective studies with greater numbers of patients are required. Further studies in multi centers are needed to support these findings. Longitudinal and an interventional studies are needed to clarify the relationship between EAT, LV structure and function, and exercise capacity in diabetic and pre-diabetic patients. Further studies, especially prospective ones comprising more randomly selected patients, are necessary to corroborate these findings and evaluate if in fact, subjects having higher EAT thickness have a greater incidence of T2DM and also cardiovascular disease. Further randomized and controlled studies evaluating the relationship between VAI and EAT in patients with diabetes are needed. Larger-scale and more detailed studies should be designed to clarify the exact mechanisms underlying the favorable effects of diabetic drugs on EAT thick- ness and BMI.

CONCLUSION

For the assessment of diabetes and prediabetes, the EFT is a straightforward, affordable, easily available, noninvasive, and objective approach. Compared to control persons, the EFT is higher in patients with diabetes and prediabetes. Our research demonstrates that EFT may serve as a marker for both the increase of visceral adiposity in the heart and glucose abnormalities.

Conflict of interest: None.

REFERENCE

1. **Neeland, I.J., Ross, R., Després, J.P., Matsuzawa, Y., Yamashita, S., Shai, I. et al.** Visceral and ectopic fat, atherosclerosis, and

cardiometabolic disease: a position statement. Lancet Diabetes Endocrinol, 2019,7(9), 715-25.

2. **Mastebhakti, B., Garg, S., Gupta, N., Singh, S., Aggarwal, S.& Singh R.** Epicardial Adipose Tissue Thickness as a Reliable Marker of Increased Cardiovascular Risk in Patients with Type 2 Diabetes Mellitus. J Endocrinol &Metab, 2020,10, (6),173-81.
3. **Benjamin, E.J., Muntner, P., Alonso, A., Bittencourt, M.S., Callaway, C.W.& Carson, A.P.** American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics-2019 update: a report from the American Heart Association. Circulation, 2019, 139(10), e56-e528.
4. **Atlas D. International diabetes federation**. IDF Diabetes Atlas, 7th edn. Brussels, **Belgium**: Inter Diabetes Fed.2015, 33: 2.
5. **Pedersen, D.J., Guilherme, A., Danai, L.V., Heyda, L., Matevossian, A., Cohen, J., et al.** A major role of insulin in promoting obesity-associated **adipose** tissue inflammation. Mol Metab,2015, 4(7),507–18.
6. **Adabimohazab, R., Garfinkel, A., Milam, E.C., Frosch, O., Mangone, A., Convit, A. et al.** Does Inflammation Mediate the Association Between Obesity and Insulin Resistance? Inflammation. 2016,39(3),994–1003.
7. **Zamora-Mendoza, R., Rosas-Vargas, H., Ramos-Cervantes, M.T., Garcia-Zuniga, P., Perez-Lorenzana, H., Mendoza-Lorenzo, P. ,et al. Dysregulation** of mitochondrial function and biogenesis modulators in adipose tissue of obese children. Int J Obes. 42(4), 618–24.
8. **Meah, F.A., DiMeglio, L.A., Greenbaum, C.J., Blum, J.S., Sosenko, J.M., Pugliese, A., et al.**The relationship between BMI and insulin resistance and progression from single to **multiple** autoantibody positivity and type 1 diabetes among TrialNet Pathway to Prevention participants. Diabetologia. 2016,59(6),1186–95.
9. **Cheng, Y.H., Tsao, Y.C., Tzeng, I.S., Chuang, H.H., Li, W.C., Tung, T.H., et al.** Body mass index and waist circumference are better **predictors** of insulin resistance than total body fat percentage in middle-aged and elderly Taiwanese. Med (United States). 2017,96(39),1–6.
10. **Seong, J., Kang, J.Y., Sun, J.S., Kim, K.W.** Hypothalamic inflammation and obesity: a **mechanistic** review. Arch Pharm Res. 2019, 42, 383-92.
11. **Brown, T.J., Brainard, J., Song, F., Wang, X., Abdelhamid, A.& Hooper, L.** Omega-3, **omega-**6, and total dietary polyunsaturated fat for prevention and treatment of type 2 diabetes mellitus: systematic review and meta-analysis of randomised controlled trials. Bmj,2019,366.
12. **Deacon, C.F.** Physiology and pharmacology of DPP-4 in glucose homeostasis and the treatment of type 2 diabetes. Front Endocrinol, 2019, 10:80.
13. **Dorcely, B., Katz, K., Jagannathan, R., Chiang, S.S., Oluwadare, B., Goldberg, I.J., et al.** Novel biomarkers for prediabetes, diabetes, and associated complications. Diabetes Metab Syndr Obes, 2017,10, 345- 61.
14. **Aykan, A.Ç., Gül, I., Gökdeniz, T., Hatem, E., Arslan, A.O., Kalaycıoğlu, E., et al.** Ankle brachial **index** intensifies the diagnostic accuracy of epicardial fat thickness for the prediction of coronary artery disease complexity. Heart Lung Circ, 2014,23, 764-771.
15. **Christensen, R.H., von Scholten, B.J., Lehrskov, L.L., Rossing, P., Jørgensen& P.G.** Epicardial adipose tissue: an emerging biomarker of **cardiovascular** complications in type 2 diabetes? Ther Adv Endocrinol Metab, 2020,11, 1–16.
16. **Mookadam, F., Goel, R., Alharthi, M.S., Jiamsripong, P.& Cha, S.** Epicardial fat and its association with cardiovascular risk: a cross-**sectional** observational study. Heart Views 2010, 11, 103-8.
17. **Altin, C., Sade, L.E., Gezmis, E., Ozen, N., Duzceker, O., Bozbas, H., et al.**Assessment of subclinical atherosclerosis by carotid intima–media thickness and epicardial adipose tissue thickness in prediabetes. Angiology, 2016, 67(10), 961-9.

18. **Sugita, Y., Ito, K., Sakurai, S., Sakai, S.& Kuno, S.** Epicardial adipose tissue is tightly associated with exercise intolerance in patients with type 2 diabetes mellitus with **asymptomatic** left ventricular structural and functional abnormalities. J Diabetes Complications, 2020, 34(5), 107552.
19. **Baloglu, I., Turkmen, K., Selcuk, N.Y., Tonbul, H.Z., Ozcicek, A., Hamur, H., et al.** The **relationship** between visceral adiposity index and epicardial adipose tissue in patients with type 2 diabetes mellitus. Exp Clin Endocrinol Diabetes, 2021,129(05), 390-5.
20. **Schofield, J.D., Liu, Y., Rao-Balakrishna, P., Malik, R.A.& Soran, H.** Diabetes **dyslipidemia**. Diabetes therapy, 2016, 7, 203-19.
21. **Araki, E., Yamashita, S., Arai, H., Yokote, K., Satoh, J., Inoguchi, T., et al.**Efficacy and safety of pemafibrate in people with type 2 diabetes and elevated triglyceride levels: 52week data from the PROVIDE study. Diabetes Obes Metab, 2019, 21(7), 1737-44.
22. **Su, L., Hong, Z., Zhou, T., Jian, Y., Xu, M., Zhang, X., et al.**Health improvements of type 2 **diabetic** patients through diet and diet plus fecal microbiota transplantation. Sci Rep, 2022, 12(1), 1152.
23. **Lima-Martínez, M.M., Colmenares, L., Campanelli, Y., Paoli, M., Rodney, M., Santos, R.D., et al.**Epicardial adipose tissue thickness and type 2 diabetes risk according to the FINDRISC modified for Latin America. Clin Investig Arterioscler. (English Edition), 2019, 31(1), 15-22.
24. **Ozcicek, A., Ozcicek, F., Yildiz, G., Timuroglu, A., Demirtas, L., Buyuklu, M., et al.**Neutrophil-to-lymphocyte ratio as a possible indicator of epicardial adipose tissue in patients undergoing **hemodialysis**. Arch Med Sci., 2017, 13 (1), 118–23.
25. **Akbas, E.M., Demirtas, L., Ozcicek, A., Timuroglu, A., Bakirci, E.M., Hamur, H., et al.**Association of **epicardial** adipose tissue, neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio with diabetic nephropathy. Int J Clin Exp Med. 2014, 15, 7 1794–801
26. **Iacobellis, G., Barbaro, G.& GersteinH.C.** Relationship of epicardial fat thickness and fasting glucose. Int J Cardiol. 2008,128, 424-6.
27. **Iacobellis, G., Diaz, S., Mendez, A.& Goldberg, R.** Increased epicardial fat and **plasma** leptin in type 1 diabetes independently of obesity. Nutr Metab Cardiovasc Dis, 2014,24:725-9.
28. **Iacobellis G.** Local and systemic effects of the multifaceted epicardial adipose tissue depot. Nat Rev Endocrinol, 2015, 5,11,363-71.
29. **Riccio, P.& Rossano, R.** Nutrition facts in multiple sclerosis: ASN Neuro,2015,7(1),**1759091414568185**.
30. **Cree, B. A.** Diagnosis and differential diagnosis of multiple sclerosis: CONTINUUM: Lifelong Learning. Neurol,2010,16(5):19–36.
31. **Ascherio, A.& Munger, K.L.** Environmental risk factors for multiple sclerosis. Part I: the role of infection: Ann Neurol, 2007,61(4),288–299.
32. **Van der Mei, I.A., Simpson, S., Stankovich, J.& Taylor, B.V.** Individual and joint action of **environmental** factors and risk of MS: Neurol Clin, 2011,29(2),233–255.
33. **Crabtree-Hartman, E.** Sex differences in multiple **sclerosis**. CONTINUUM: Lifelong Learning: Neurol, 2010,16(5),193–210.
34. **Leray, E., Moreau, T., Fromont, A.& Edan, G. Epidemiology** of multiple sclerosis; Rev Neurol,2016,172(1),3–13.
35. **Hashem, S., El-Tamawy, M. S., Hamdy, S.& Elmasry, T.** Epidemiology of multiple sclerosis in Egypt: The Egyptian Journal of Neurology Psychiatry and Neurosurgery, 2010,47(4),625-632.
36. **El-Sawy, H. Abdel Hay, M.& Badawy, A.** Gender differences in risks and patterns of drug abuse in Egypt: Egypt J Neurol Psychiat Neurosurg, 2010,47(1),413–418.
37. **El-Tallawy, H., Farghaly, W.& Metwally, N.** Prevalence of neurological disorders in Al Quseir, Egypt: methodological aspects: Neuropsychiatr Dis Treat,2013, 9,1295–1300.
38. **Afifi, Z. E., Shehata, R.I.& Salem, M.R. Nutritional** status of multiple sclerosis (MS) patients attending Kasr Alainy MS unit: an

exploratory cross-sectional study: Journal of the Egyptian Public Health Association, 2021,96, (20),13.

39. **Filippi, M., Rocca, M.A., Barkhof, F., et al.**Association between pathological and MRI **findings** in multiple sclerosis: Lancet Neurol, 2012,11(4),349-360.
40. **Jarius S. K., Ruprecht, J. P., Stellmann, A., Huss I. et al.** MOG-IgG in primary and secondary chronic progressive multiple sclerosis: a multi-center study of 200 patients and review of the literature article information: J Neuroinflammation,2018, 15: 88.
41. **Stenager, E.** A global perspective on the burden of multiple sclerosis: Lancet Neurol,2019, 18(3),227-228.
42. **Galal, S.** Total population of Egypt 2021, by governorate: Statista, 2021,20.
43. **Zakaria M, Zamzam DA, Abdel Hafeez MA, et al.**Clinical characteristics of patients with multiple sclerosis enrolled in a new registry in Egypt: Mult Scler Relat Disord, 2016, 10,30-35.
44. **Adnan A & Mohammed AI.** Multiple sclerosis in Iraq: does it have the same features **encountered** in Western countries?:J Neurol Sci,2005,15;234 (1-2),6771.
45. **Deleu, D., Mir, A., Al Tabouki, A. & Mesraoua, R.**Prevalence, demographics and clinical **characteristics** of multiple sclerosis in Qatar: Multiple Sclerosis, 2012, 19(6),10.
46. **Hamdy, S.M., Abdel-Naseer, M. & Shehata, H.S.** Neuropsychiatric disease and treatment characteristics and predictors of progression in an Egyptian multiple sclerosis cohort: a multicenter registry study: Neuropsychiatr Dis Treat, 2017, 13: 1895–1903.
47. **Inshasi, J.& Thakre, M.** Prevalence of multiple sclerosis in Dubai, United Arab **Emirates**: Ternational Journal of Neuroscience, 2011,121, 393–398.
48. **Alroughani, R.A. & Lamdhade, A.S.** Clinical Characteristics of Multiple Sclerosis in **Kuwait**: data from the new MS registry of Amiri Hospital: International Journal of Neuroscience,2012,122,(2),230-238.
49. **Ojeda,E. , Díaz-Cortes, D., Rosales, D., Quartet-Rey, C., et al.**Prevalence and clinical features of multiple sclerosis in Latin America: Clinical neurology and neurosurgery, 2012,115(4),381-387.
50. **Goldman, M. D., Motl, R.W., Rudick, R.A.** Only possible clinical outcome measures for clinical trials in patients with multiple sclerosis: **Therapeutic** advances in neurological disorders,2010, 3(4), 229-239.
51. **Florian, D., Zetterberg, H., Fitzner, B., Zettl, U.K.** The Cerebrospinal Fluid in Multiple **Sclerosis**: Front. Immunol, 2019,12.(5),258–264.
52. **AlJumah, M., Bunyan, R., Al Otaibi, H., et al.**Rising prevalence of multiple sclerosis in Saudi Arabia: a descriptive study BMC Neurol, 2020, 20, 49.

Citation:

Amer Leaimesh, F., Nsr-Allah, A., Shehata, I., Abd-El Fatah, A. Epicardial Adipose Tissue as a New Biomarker for Insulin Resistance and Predictive of Prediabetes. *Zagazig University Medical Journal*, 2024; (2818-2831): -. doi: 10.21608/zumj.2023.199083.2765