

Original Research Article

A correlative study of Epicardial fat thickness with other cardiovascular risk factors in patients with prediabetes

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Abstract: Prediabetes is a condition between a normal glucose tolerance and diabetes mellitus. It includes impaired glucose tolerance (IGT), impaired fasting glucose (IFG), or both. Prediabetes is related with undesirable cardiovascular outcomes. Epicardial fat thickness (EFT) has been correlated with cardiovascular risk factors. We herein aimed to assess EFT in prediabetic patients. We evaluated 100 patients with prediabetes and 100 age- and gender-matched healthy subjects. Demographic and anthropometric characteristics [age, sex, height, weight, body mass index (BMI), and waist circumference (WC)] and laboratory findings [fasting plasma glucose (FPG), postprandial plasma glucose (PPG), hemoglobin A1c (HbA1c), low density lipoprotein (LDL), high density lipoprotein (HDL), and triglycerides (TG)] were assessed. Transthoracic echocardiography was used to evaluate EFT. All the study subjects were also subjected for assessment of hepatic steatosis. There were no significant differences between the case and control groups in terms of age, gender, and BMI. Waist circumference, systolic and diastolic blood pressure were found to be significantly higher in the case group than control group ($p < 0.05$). When compared with the control group, the mean EFT was significantly higher in all prediabetic subgroups (IGT or IFG, $p < 0.001$) than controls. The presence of hepatic steatosis had significant positive correlation with EFT. We concluded that EFT levels to be increased in all prediabetic patients regardless of FPG and HbA1c. Furthermore, EFT significantly correlated with the patients' WC and hepatic steatosis.

Keywords: Epicardial fat thickness, prediabetes, cardiovascular risk

INTRODUCTION

Worldwide, the number of individuals with diabetes mellitus (DM) is expected to double in the next 25 years and to affect more than 350 million individuals by 2030 [1]. Hence, there is an increasing interest in identifying individuals in stages preceding overt DM in order to potentially prevent the occurrence of DM and associated complications. The majority of complications of DM are related to cardiovascular disease. Therefore it is important to assess whether prediabetes stages are also associated with detrimental vascular outcomes [2]. Prediabetes includes impaired glucose tolerance (IGT), impaired fasting glucose (IFG), or both.

According to ADA criteria [3], prediabetes is defined as two hour plasma glucose of 140-199 mg/dL during an oral glucose tolerance test (OGTT) and IFG is defined as fasting plasma glucose (FPG) between 100-125 mg/dL and HbA1c between 5.7-6.4%. It remains a state of high risk for developing diabetes with yearly conversion rate of 5%-10%. Observational evidence

suggests an association between prediabetes and complications of diabetes such as early nephropathy, small fiber neuropathy, early retinopathy and risk of macrovascular disease [4, 5].

Increased levels of abdominal visceral adipose tissue (VAT) are associated with the metabolic syndrome (MS), type 2 diabetes mellitus (T2DM), cardiovascular disease [6] and NAFLD [7] the common basic mechanism in all seems to be insulin resistance.

Transthoracic echocardiography has been validated as an easy and reliable method to quantify the presence of VAT by measuring epicardial fat thickness (EFT) also called as epicardial adipose tissue thickness, which correlates very well with the presence of general VAT [8-10]. The epicardial adipose tissue thickness has been suggested as a new cardiometabolic risk factor. It has been related to insulin resistance, hypertension, and dyslipidemia [11].

In the present study, we aimed to evaluate EFT and presence of hepatic steatosis in patients with prediabetes compared with age, gender and BMI matched healthy control subjects. We also sought to determine if EFT correlated with other cardio metabolic risk factors.

MATERIAL AND METHODS

We evaluated 100 patients with prediabetes and 100 age- and gender-matched healthy subjects. The patients in prediabetes were enrolled from relatives of patients with type 2 diabetes and Glucose tolerance and metabolism were evaluated using a75 g OGTT. After an overnight fast of 12 hours, all subjects underwent an OGTT. Glucose tolerance categories were defined according to the ADA criteria [3].

The exclusion criteria were a previously known diabetes, ischemic heart disease, cerebrovascular disease, peripheral vascular disease, congestive heart failure, valvular heart disease, malignancy or chronic kidney disease.

In all study subjects, demographic and anthropometric characteristics [age, sex, height, weight, body mass index (BMI), and waist circumference (WC)] and laboratory findings [fasting plasma glucose (FPG), postprandial plasma glucose (PPG), hemoglobin A1c (HbA1c), low density lipoprotein (LDL), high density lipoprotein (HDL), and triglycerides (TG)] were assessed.

Measurement of epicardial adipose tissue thickness-Each subject underwent transthoracic two-dimensional guided M-mode echocardiography using commercially available equipment (General Electric Company, CT, USA). Standard parasternal and apical views were obtained in the left lateral decubitus position. Epicardial fat was identified as echocardiographic free space between the outer wall of the myocardium and the visceral layer of the pericardium. Epicardial fat thickness was measured perpendicularly on the free wall of the right ventricle at end diastole in 3 cardiac cycles. The average value of 3 cardiac cycles from each echocardiographic view was considered [12].

Five point ultrasonographic criteria of diagnosis of fatty liver disease recommended by Dasharty [13] was used to diagnose NAFLD: (1) Increased hepatic brightness” or hyperechogenicity (2) posterior attenuation of the right lobe (3) increased contrast between the right kidney and liver (4) loss of visualization of right diaphragm and (5) diminished visibility of the intrahepatic vessels.

STATISTICAL ANALYSIS

Data analyses were performed using SPSS for Windows,version 13.0 (SPSS, Chicago, USA). The normal distribution of continuous variables was assessed using the Kolmogorov Smirnov test. Variables were presented as means ± standard deviation (SD). The differences between the means of the case and control groups were compared using Student’s *t*-tests. Nominal data were analyzed using Pearson’s chi-squared tests. Correlation of numerical variables was examined by Pearson correlation. The degrees of association between continuous variables were evaluated using Spearman correlation tests.

RESULTS

In this study, we evaluated 100 subjects in the prediabetes group and 100 age and gender matched subjects in the control group. Patient demographics, anthropometric characteristics, and clinical features are shown in Table 1. No significant differences were detected between the case and control groups with regards age, gender and BMI though waist circumference, systolic and diastolic blood pressures, were significantly higher in the prediabetes group compared with the control group.

TG, fasting plasma glucose level, glycosylated hemoglobin and EFT were also significantly higher in the case group compared with the control group, respectively; Table 2. Mean EFT in prediabetes patients was 7.8± 2.2mm and in controls 4.6± 1.8mm, P=0.01 Presence of hepatic steatosis was more common in patients with prediabetes than controls.

The data revealed that EFT had significant positive correlations with waist circumference and presence of hepatic steatosis. However, no other significant correlation was found between EFT and the other cardiovascular risk factors (Table 3)

Table-1: Base line Characteristics of the case and control group

Variable	Patients with prediabetes(n=100)	Controls(n=100)	P value
Age(years)	47.24± 8.56	46.32± 10.67	0.12
Male sex	46%	48%	0.56
BMI (kg/m ²)	26.87± 3.64	26.15± 3.92	0.47
Waist circumference(cm)	96±7	88± 4.2	0.04

Data is expressed in mean±SD or (%)

Table-2: Metabolic parameters in cases and controls

Variables	Patients with prediabetes(n=100)	Controls(n=100)	P value
Hypertension(blood pressure>130/85mmHg)	47	12	0.001
Hypertriglyceridemia(>150mg/dl)	36	10	0.002
Low HDL(<50mg/dl)	19	6	0.06
Fasting glucose(>100mg/dl)	30	0	0.001
IGT	56	0	0.001
HbA1c(5.7-6.4%)	14	0	0.02
EFT(mm)	7.8 ±2.2	4.6± 1.8	0.01

Table-3. Correlations of epicardial fat thickness with cardiovascular risk factors

Variables	Epicardial fat Correlation coefficient	P value
Waist circumference	0.35	0.001
Hypertension	0.12	0.06
Hypertriglyceridemia	0.18	0.42
Impaired glucose tolerance	0.16	0.20
Low HDL	0.18	0.12
Hepatic steatosis	0.34	0.01

DISCUSSION

Prediabetes is a clinical condition that is between a normal metabolic state and diabetes, and prediabetes is also reported to be associated with other major risk factors (e.g., hypertension and dyslipidemia) of atherosclerosis [14]. According to population-based studies, the development of macrovascular complications and mortality are increased in prediabetic populations [15,16].

Microvascular complications, especially autonomic neuropathy, are also seen in prediabetics and results in increased mortality [17]. Subclinical atherosclerosis develops several years before the occurrence of cardiovascular events. If the patients are diagnosed at subclinical stages, preventive measures can be initiated.

EFT, which is the adipose tissue accumulated between the visceral pericardium and the myocardium measured by echocardiography, has been proposed as a novel cardio-metabolic imaging marker. In previous studies, EFT was shown to correlate well with the degree of atherosclerosis in patients with coronary heart disease, hypertension, and metabolic syndrome and was suggested to be a predictive marker for early atherosclerotic changes [18,19].

The role of EFT in the pathogenesis of vascular disease is not well understood, but it is suggested that vasoactive peptides and cytokines

produced by epicardial fat tissue increases cardiovascular risk [20].

In previous reports, EFT was determined to significantly correlate with FPG, insulin resistance, hypertension, obesity, MS, diabetes, and coronary artery disease [21]. EFT is an independent risk factor for future cardiac events [22] and EFT also correlated with peripheral vascular thickening and arterial stiffness [23]. In a previous report, EFT was suggested as a tool to assess cardiac risk in the screening of asymptomatic individuals [24].

Akyol *et al.* suggested that EFT correlated with insulin resistance and the homeostasis model assessment of insulin resistance (HOMA-IR) index. Furthermore, they suggested that EFT may be a better indicator of visceral obesity and could replace WC as criteria in the diagnosis of MS [25]. In another study, on patients with type 1 diabetes Momesso *et al.* found that EFT was higher in patients than controls and epicardial fat was related to central obesity and MS [26].

Our study showed that EFT is higher in prediabetes patients than in the controls. In the present study, EFT positively correlated with WC and hepatic steatosis. Similar to our results, EFT showed independent positive correlation with metabolic parameters including postprandial glucose, HbA1c level and insulin resistance in other studies too [27, 28] and it had, unfavorable and adaptive effects on progression of cardiovascular diseases [29]. In a meta-analysis of 38

studies, the relationship between EFT and generalized obesity, central or visceral adipose tissue, and components of MS linked to coronary artery disease [30].

The limitations of this study are the small number of patients enrolled in the case and control groups and cross sectional design of the study. Further studies using larger sample size and follow up are necessary to elucidate the correlation of different metabolic parameters with EFT in glucose metabolism disorders.

CONCLUSION

EFT was found to be higher in all pre diabetic patients regardless of FPG and HbA1c. Furthermore, EFT had significant positive correlation with the waist circumference and hepatic steatosis.

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