INTRODUCTION

The incidence of type 2 diabetes mellitus tends to grow steadily worldwide and associated with higher risk of cardiovascular disease which is the leading cause of death now-a-days in diabetics. It has been already proved that the insulin resistance, obesity and diabetes mellitus are the proinflammatory states associated with increased adiposity. Epicardial adipose tissue is the visceral fat depot of the heart located on the surface of the ventricles and apex along the major coronary arteries and embryologically similar to the intra-abdominal visceral adipose tissue. The epicardial adipose tissue is not only an anatomic depot of fat but also serve as a local source of proinflammatory cytokines related to coronary artery disease. Therefore, EAT thickness has been considered to be a possible cardiovascular risk indicator. Transthoracic echocardiography (TTE), MRI and multislice CT scanning have been used as conventional methods for quantifying EAT. Assessment of EAT by TTE could be a simple and practical tool for cardiovascular risk prediction.
risk stratification in clinical practice.2 Carotid intima-media thickness (CIMT) is a simple and inexpensive tool to assess the cumulative effect of atherosclerotic risk factors and is an independent predictor of future cardiovascular risk.3 The ultrasound-based measurement of CIMT has become a standard for assessing arteriosclerosis and is recommended by the American Heart Association for the non-invasive assessment of cardiovascular risk.4,5 Previous studies have reported that increased EAT is associated with CAD, metabolic syndrome (MetS) and obesity.6–8 In the present study, we evaluated type 2 diabetic patients to investigate epicardial fat thickness by TTE and investigate its relationship with CIMT.

MATERIALS AND METHODS

In this hospital based cross sectional observational study a total of 64 patients with type 2 diabetes mellitus, having this diagnosis for at least 1 year, were consecutively included in the study and compared with 76 age and sex-matched non-diabetic control. T2DM was diagnosed according to the American Diabetes Association criteria.9 The study protocol was approved by our local ethics committee, and all patients gave their written informed consent to participate in the study. Exclusion criteria of the study were subjects with known ischemic heart disease, cerebrovascular disease, peripheral vascular disease, congestive heart failure, valvular heart disease, and chronic kidney disease. Medical history was obtained and physical examination was performed in all patients and controls. Blood samples for fasting blood glucose level were withdrawn by venepuncture following 12 h of fasting and were determined using standard laboratory methods.

Measurements of Epicardial Adipose Tissue Thickness:
Each patient underwent a complete transthoracic echocardiography using the American Society of Echocardiography guidelines of measurement.10 Echocardiogram was performed using a Vivid 7 (General Electronic, Waukesha, Wisconsin, USA) with a 2.5–3.5 MHz transducer, placed on the III–IV left intercostal space along the parasternal line, with patients being supine in left lateral decubitus and the head of the bed kept at 30°. All examinations were performed by an experienced cardiologist, blind to the patient’s clinical information. Epicardial fat was identified as the space or layer anterior to the right ventricle with decreased echo-reflectivity compared with thymic myocardium and pericardium. Epicardial fat thickness (EFT) was measured in end diastole on the free wall of the right ventricle from the parasternal long-and short-axis views, as previously described.11–13 The maximum values at any site were measured, and the average value was considered. Imaging constraints were used to ensure that the epicardial fat thickness was not measured obliquely. Parasternal long- and short-axis views allow the most accurate measurement of EAT on the right ventricle, with optimal cursor beam orientation in each view.

Carotid Ultrasonography
Carotid arteries were evaluated using a Logiq 7 (General Electronic, Waukesha, Wisconsin, USA) with a 7.5 MHz transducer. All examinations were performed by an experienced radiologist, blind to the patient’s clinical information. Measurements involved a primary transverse and longitudinal scanning of the common carotid artery, bifurcation, and internal carotid. The CIMT was measured on the far wall at 1 cm from bifurcation of the common carotid artery as the distance between the lumen intima interface and the media-adventitia interface. At least three measurements were performed on both sides, and the average measurement was taken as the CIMT. All measurements were made at a plaque-free site.

SPSS statistical software version 20 for Windows was used for all statistical analysis. Categorical variables were expressed as number and proportions, while continuous variables were expressed as mean and standard deviation. Chi-square (χ²) test was used to compare groups regarding categorical variables. Continuous variables were compared with Student t-test while comparing parametric variables between diabetic patients and controls. Correlation analysis was performed using Pearson or Spearman tests. Linear regression analysis was used to explore the independent determinants of EFT. Levels of statistical significance were set at a P value <0.05.

RESULT

In this cross-sectional hospital based observational study we evaluated a total of 140 patients of whom 64 were diabetic and 76 were non-diabetic control.

The mean age and gender distribution in between diabetic patients and non-diabetic control had no significant difference (p value >0.05), i.e., the study groups were age and sex matched. In diabetic patients, the mean duration of diabetes was 7.23±1.61 years. The numbers of smoker, hypertensive and dyslipidemic patient were more associated with diabetes compared to non-diabetic control. The family history of coronary artery disease was also higher in diabetics (Table 1).

The Epicardial fat thickness and Carotid intima-media thickness both were significantly higher in diabetic group of patients. The mean BMI and fasting blood glucose level were also high in diabetic patients compared to non-diabetic.
Table 1: Baseline characteristics of the patients with diabetic and non-diabetic controls

<table>
<thead>
<tr>
<th>Parameters</th>
<th>DM</th>
<th>Control</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54.51±6.60</td>
<td>54.97±6.11</td>
<td>0.673</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>75</td>
<td>71.1</td>
<td>0.601</td>
</tr>
<tr>
<td>Duration of DM (years)</td>
<td>7.23±1.61</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Hypertensive (%)</td>
<td>56.2</td>
<td>34.2</td>
<td>0.009</td>
</tr>
<tr>
<td>Smoker (%)</td>
<td>31.2</td>
<td>25</td>
<td>0.411</td>
</tr>
<tr>
<td>Dyslipidemia (%)</td>
<td>64.1</td>
<td>40.8</td>
<td>0.006</td>
</tr>
<tr>
<td>Family history of CAD (%)</td>
<td>28.1</td>
<td>14.5</td>
<td>0.047</td>
</tr>
<tr>
<td>Epicardial fat thickness</td>
<td>6.15±0.99</td>
<td>4.39±0.61</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Carotid intima-media thickness (mm)</td>
<td>0.77±0.09</td>
<td>0.51±0.05</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>26.5±2.24</td>
<td>25.66±2.30</td>
<td>0.025</td>
</tr>
<tr>
<td>Fasting glucose (mg/dL)</td>
<td>141.85±22.99</td>
<td>114.75±21.93</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 2: The bivariate correlations of the epicardial fat thickness

<table>
<thead>
<tr>
<th>Variable</th>
<th>r</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid artery intima-media thickness</td>
<td>0.724</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of DM (years)</td>
<td>0.723</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fasting glucose (mg/dL)</td>
<td>0.542</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 3: Independent predictors for epicardial fat thickness by linear regression analysis

<table>
<thead>
<tr>
<th>Dependent variable: epicardial fat thickness</th>
<th>Standardized coefficients</th>
<th>t</th>
<th>Sig.</th>
<th>95.0% Confidence Interval for B</th>
<th>Beta</th>
<th>Lower bound</th>
<th>Upper bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DM duration</td>
<td>0.324</td>
<td>3.658</td>
<td>0.000</td>
<td>1.336</td>
<td>3.481</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CIMT</td>
<td>0.358</td>
<td>3.668</td>
<td>0.000</td>
<td>1.336</td>
<td>4.481</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FBS</td>
<td>0.210</td>
<td>3.302</td>
<td>0.000</td>
<td>0.004</td>
<td>0.015</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The epicardial fat thickness is significantly correlated with carotid artery intima-media thickness, duration of diabetes and fasting plasma glucose level (Table 2).

From simple linear regression analysis taking epicardial fat thickness as dependent variable, we found that the carotid artery intima-media thickness, duration of diabetes and fasting plasma glucose level as the independent predictor or risk factor of epicardial fat deposition (Table 3).

**DISCUSSION**

In this study, we observed that, (1) the patients with diabetes had increased epicardial fat and carotid intima media thickness compared to age and sex matched non-diabetic controls; (2) the epicardial fat thickness was correlated with CIMT, duration of diabetes and fasting plasma glucose level; and (3) the CIMT, duration of diabetes and fasting plasma glucose level were found to be the independent predictors of EFT.

Epicardial, mesenteric, and omental fats are originated from the same splanchno-pleuric mesoderm. The EAT produces inflammatory mediators such as interleukin (IL)-6, IL-1b, TNF alpha, and monocyte chemotactic protein (MCP-1) in patients with coronary artery disease and expresses mRNAs of adiponectin, resistin, leptin, IL-6, TNF-a, and CD-45. EAT play a role in the development and aggravation of CAD. In addition, EFT has been shown to be related to MetS, abdominal visceral adiposity, subclinical atherosclerosis, non-alcoholic fatty liver disease, type 1 DM, impaired fasting glucose, and hypertension. There is very limited study investigating the relationship between T2DM and EFT. Recently, in a study performed by Kim et al., increased EAT thickness assessed by cardiovascular magnetic resonance (CMR) was an independent risk factor for significant coronary artery stenosis in asymptomatic type 2 diabetes. Mustafa Cetin et al., observed in their study that the echocardiographic EFT was significantly higher in patients with T2DM and also showed that EFT was strongly correlated with waist circumference and CIMT as being independent of sex. In another study reported by Wang et al., EAT volume assessed by cardiac multislice computed tomography was shown to be increased and was associated with unfavourable components of MetS and coronary atherosclerosis in type 2 diabetic patients.

In our study, we found that EFT and CIMT were increased in patients with T2DM compared to non-diabetic controls. It is also important that a positive linear and significant relationship between EFT with CIMT, duration of diabetes and fasting plasma glucose level were found in our study. CIMT is now increasingly used as a surrogate marker for atherosclerosis. According to these results, EFT may be used as a marker of subclinical atherosclerosis and disease progression in patients with T2DM. Further and large scale studies are required to support this hypothesis.

Although epicardial fat is readily visualized on high-speed CT and MRI, widespread use of these methods for its assessment is not practical. Echocardiographic EFT measurement in the current practice appears to be feasible, as well as reliable due to good reproducibility.

**CONCLUSION**

In conclusion, we found that the echocardiographic EFT was significantly higher in patients with T2DM; and it...
was well correlated with CIMT, duration of diabetes and fasting plasma glucose level as being the independent predictors of EFT. From our study we may suggest that the echocardiographic assessment of EFT is a reliable marker of atherosclerosis and increased cardio-vascular risk in patients with T2DM. Further and large scale studies are needed to confirm these findings.

REFERENCES


Authors Contribution:
PKM, SP, KM, SKD, AKD - Concept, Design, Manuscript writing, Review of Literature; SD, PS, AP - Data Collection, Literature Search, Review of Literature.

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