Ultrasonic Evaluation of Early Atherosclerosis in Children and Adolescents with Type 1 Diabetes Mellitus

Taner Yavuz¹, Ahmet Akçay², Rukiye Eker Ömeroğlu³, Rüveyde Bundak⁴ and Mine Şükür⁴

¹Department of Pediatrics, Düzce School of Medicine, Abant Izzet Baysal University, Düzce,
²Department of Pediatrics, Pamukkale School of Medicine, Pamukkale University, Denizli,
³Division of Pediatric Cardiology and ⁴Division of Pediatric Endocrinology,
Department of Pediatrics, Istanbul School of Medicine, Istanbul, Turkey

ABSTRACT

Objective: To assess early atherosclerosis using B-mode imaging of the carotid artery in children and adolescents with type 1 diabetes mellitus (T1DM) and to evaluate the relationship between various risk factors and intimal plus medial thickness (IMT) in this population.

Methods: Fifty-two children and adolescents (aged 3-18 years) with uncomplicated T1DM and 43 age- and gender-matched healthy controls were examined. B-mode imaging was used to determine the intimal plus medial thickness (IMT) of the carotid artery in all subjects. Patients with T1DM and control subjects were divided into two groups according to age and gender. Furthermore, duration of DM was considered for comparison.

Results: Patients and control subjects showed no association between IMT and sex, systolic blood pressure (sBP), diastolic blood pressure (dBP), serum lipid levels or left ventricular ejection fraction (LVEF). However, statistical analysis indicated a good correlation between age and carotid arterial wall thickness in both diabetic and control groups. These findings were consistent with those in the literature. No correlation was found between IMT and the duration of DM.

Conclusions: This study indicates that there is no association between T1DM and IMT in children and adolescents with T1DM.

KEY WORDS

atherosclerosis, intimal plus medial thickness (IMT), macroangiopathy, type 1 diabetes mellitus, ultrasonography

INTRODUCTION

Type 1 diabetes mellitus (T1DM) is caused by autoimmune destruction of insulin-producing β-cells of the pancreatic islets of Langerhans. Absolute or relative insulin deficiency leads to metabolic alterations in carbohydrate, protein and fat metabolism, and water/electrolyte disturbances.

T1DM is one of the most common chronic diseases of childhood, with prevalence of approximately one in 300 children by the age of 18 years. As the disease progresses, chronic complications of T1DM start to appear. Diabetic complications related to micro- and macroangiopathy are the main causes of mortality and morbidity in patients with DM. Macrovascular complications, clinically evident as coronary, cerebrovascular, and peripheral arterial disease, are important causes of early death in DM.

Although the effects of atherosclerosis do not appear in most patients until middle age or later, the process begins much earlier. Identification of atherosclerosis can be made using high-resolution B-mode imaging of the carotid artery which enables direct in vivo monitoring of carotid arteries of living patients with T1DM. Combined thickness of the carotid intima and media is useful to examine early stages of atherosclerosis and to give information on the regression and progression of atherosclerotic lesions.
Intimal plus medial thickness (IMT) values for patients with T1DM have been shown to be significantly greater than those of age-matched non-diabetic subjects. Age and blood glucose control have an important effect on IMT in young patients with T1DM.

In the present study, we investigated early atherosclerosis using B-mode imaging of the carotid artery in children and adolescents with T1DM.

**METHODS**

Fifty-two subjects (24 males, 28 females; mean age 11.6 ± 3.8 years, range 3-18 years) with T1DM were recruited at the pediatric endocrinology outpatient clinic, Department of Pediatrics, Istanbul School of Medicine. All had a history of abrupt onset of DM and at least one episode of diabetic ketoacidosis. None had manifest macroangiopathy, such as coronary artery disease or ischemic arterial disease of the lower limbs. Patients with liver or renal function impairment were excluded. All patients with T1DM were under insulin therapy. Forty-three non-diabetic volunteers of comparable sex and age (19 males, 24 females; mean age 11.3 ± 3.3 years, range 3-16 years) were randomly selected as control subjects. This study was approved by the hospital’s ethics committee and written informed consent was obtained from parents.

Fasting blood was obtained for analysis of total and HDL cholesterol, serum triglycerides, glycosylated hemoglobin (HbA1c) and urine microalbumin. LDL cholesterol was calculated using the Friedewald formula, and determined by radioimmunoassay. Blood pressure was measured using a random-zero sphygmanometer after 5 min rest.

IMT defined by Pignoli et al. 
11 was measured as the distance from the leading edge of the first echogenic line to the leading edge of the second echogenic line. The first line represents the lumen-intimal interface, and the second line is produced by the collagen-containing upper layer of the tunica adventitia (Fig. 1). Ultrasonographic scanning of the carotid arteries was performed using an echotomographic system (Hewlett-Packard 1000) with an electrical linear transducer (midfrequency of 7.5 MHz). All studies were conducted by the same researcher (R.E.Ö.) who is a pediatrician with 11 years experience in vascular ultrasonography. The common carotid artery was chosen as it is known to be rather elastic and easily accessible to ultrasound. Subjects were examined in the supine position, with the head turned 45° away from the side being scanned. Three measurements of IMT were taken from the far wall of the right and left common carotid arteries at the maximum thickness and the average of the six measurements was used.

Patients and non-diabetic subjects were divided into two groups according to age and gender. IMT values were correlated with sex, body mass index (BMI), systolic blood pressure (sBP), diastolic blood pressure (dBP), serum lipid levels, HbA1c and left ventricular ejection fraction (LVEF). Furthermore, duration of DM was also considered. Differences between the patients and control subjects were analyzed by the Mann-Whitney U test and Student’s t-test as needed; p values less than 0.05 were considered to be significant. Linear regression analysis was also performed to correlate IMT with blood pressure, duration of DM, serum lipid levels and LVEF.

**RESULTS**

There was no significant correlation between IMT values and sex, BMI, sBP, dBP, serum lipid levels, HbA1c or LVEF (Table 1).

Patients with T1DM less than 10 years of age did not show a significant difference in IMT values from non-diabetic subjects of similar age (0.38 ± 0.05 vs 0.37 ± 0.03 mm, NS). Patients 10 years of age or older had greater IMT values than non-diabetic subjects of similar age (0.45 ± 0.06 vs 0.42 ± 0.04 mm); however, the difference was not statistically significant (Fig. 2).

The mean ± SD duration of DM was 4.1 ± 2.8 years. IMT values did not have a good correlation with the duration of DM (r = 0.30).

IMT values for children and adolescents with T1DM showed a good correlation with age (r = 0.71). (Fig. 3). There was no correlation between IMT and sex. BMI, sBP, dBP, serum lipid levels, HbA1c or LVEF.
Fig. 1: Typical B-scan pattern of common carotid artery.

**TABLE 1**

Comparison of the clinical characteristics of patients with type 1 diabetes mellitus (T1DM) and healthy controls

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>T1DM</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>43</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>19/24</td>
<td>24/28</td>
<td>NS</td>
</tr>
<tr>
<td>Age (years)</td>
<td>11.3 ± 3.3</td>
<td>11.6 ± 3.8</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>18.1 ± 3.4</td>
<td>17.9 ± 3.0</td>
<td>NS</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>153.6 ± 28.5</td>
<td>162.4 ± 33.9</td>
<td>NS</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>89.8 ± 31.6</td>
<td>90.9 ± 40.1</td>
<td>NS</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td>49.9 ± 12.9</td>
<td>54.3 ± 16.8</td>
<td>NS</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dl)</td>
<td>85.7 ± 25.7</td>
<td>91.3 ± 29.4</td>
<td>NS</td>
</tr>
<tr>
<td>sBP (mmHg)</td>
<td>106 ± 11.1</td>
<td>107.1 ± 9</td>
<td>NS</td>
</tr>
<tr>
<td>dBP (mmHg)</td>
<td>66.2 ± 9.5</td>
<td>68 ± 7.5</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>65.7 ± 7.2</td>
<td>66.4 ± 7.7</td>
<td>NS</td>
</tr>
<tr>
<td>IMT (mm)</td>
<td>0.40 ± 0.04</td>
<td>0.42 ± 0.06</td>
<td>NS</td>
</tr>
</tbody>
</table>

BMI = body mass index; TG = triglycerides; sBP = systolic blood pressure; dBP = diastolic blood pressure; LVEF = left ventricular ejection fraction; IMT = intimal plus medial thickness; NS = not significant.
Fig. 2: IMT values (average ± SEM) of controls and patients with type 1 diabetes mellitus (IDDM), grouped by age <10 and ≥10 years old.

Fig. 3: Relationship between IMT and age in children with type 1 diabetes mellitus.
DISCUSSION

Our results indicate that IMT values have a linear relationship with age, but no correlation with sex, BMI, sBP, dBP, serum lipid levels, HbA1c or LVEF.

Patients with DM tend to suffer unduly from premature and severe atherosclerosis. It was found that patients with DM in general show an increased morbidity and mortality from cardiovascular causes. DM, along with age, hyperlipidemia, smoking, and hypertension, aggravates carotid atherosclerosis.

B-mode imaging is a reliable method for measuring IMT of human arteries in vivo and evaluation of IMT can be carried out more precisely in the early stages of atherosclerotic disease. The extent of carotid artery atherosclerosis as measured by ultrasound B-mode imaging has been shown to have a strong correlation with the presence of coronary atherosclerotic disease. In the present study, we used this method to determine early atherosclerosis in children and adolescents with T1DM.

Only a few studies have been performed on IMT in patients with T1DM. Most of the studies on the IMT values of patients with T1DM were carried out in adolescents and young adults. Some of these studies concluded that patients with T1DM have significantly greater IMT values than non-diabetic subjects.

Yamasaki et al. examined 105 patients with T1DM ranging from 4 to 25 years of age. In their study, patients less than 10 years of age showed greater (but not significant) IMT values than non-diabetic subjects of similar age (0.454 ± 0.079, n = 23 vs 0.382 ± 0.056 mm, n = 5). In contrast to our study, IMT values of their patients with T1DM of 10 to 19 years of age (0.525 ± 0.124 mm, n = 68) were significantly greater than those of age-matched non-diabetic subjects (0.444 ± 0.057 mm, n = 12, p = 0.01169). This may be due to a shorter duration of the disease in our patients (5.5 ± 4.7 years vs 4.1 ± 2.8 years in our study). Gunczler et al. found no change in IMT in children and adolescents with T1DM of short duration (3.4 ± 3.3 years). Only a few studies have investigated the relationship between duration of DM and IMT in patients with T1DM. IMT was related to duration of DM in two studies, whereas this was not confirmed in four studies in addition to our study. IMT values for children and adolescents with T1DM showed a positive correlation with age (r = 0.71). This finding was consistent with those of the literature.

In conclusion, we showed that in young children with T1DM there was no association between the DM and early macrovascular lesions, such as IMT of the common carotid artery. IMT values may increase significantly after a certain age in patients with T1DM, which could only be revealed by further studies in children with T1DM.

REFERENCES


