

# Evaluation of cardiovascular disease risk in children with type 1 diabetes mellitus by oscillometric method and echocardiography

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## ABSTRACT

**Objective:** Type 1 diabetes mellitus (T1DM) patients have an increased risk of developing cardiovascular disease. Our study aimed to compare epicardial fat thickness (EFT), carotid intima-media thickness (cIMT), and arterial stiffness parameters such as pulse wave velocity (PWV), augmentation index (AI), which are well-known early markers of cardiovascular disease in adults, between children with T1DM and healthy individuals.

**Methods:** One hundred fifteen children with T1DM and 87 age, gender, and anthropometric measurements-matched healthy children were included. The inclusion criteria for patients were having T1DM for at least 2 years and ages 8–18 years. Epicardial fat thickness and cIMT were assessed by the same pediatric cardiologist. Noninvasively, the Mobil-O-Graph® was used to evaluate PWV, AI (normalized to a heart rate of 75 beats/sec: AI@75), and the hemodynamic parameters.

**Results:** Epicardial fat thickness and cIMT were higher ( $p<0.001$ ), stroke volume and cardiac index scores were found significantly lower ( $p<0.001$  and  $p=0.030$ , respectively) in the patient group compared with the control group. While the AI@75 was significantly higher in the patient group ( $p<0.01$ ), PWV did not differ between groups ( $p=0.782$ ). According to the glycated hemoglobin A1c (HbA1c) level, EFT ( $p=0.015$ ) was significantly higher, and cardiac index score ( $p=0.030$ ) was significantly lower in the HbA1c  $>9\%$  group. A strong positive correlation was detected between mean cIMT and microalbuminuria ( $Rho=,925$ ,  $p<0.01$ ).

**Conclusion:** These results support that children with T1DM present significant changes in important subclinical indicators for showing the development of cardiovascular disease. Cardiologic assessment of patients with T1DM can be beneficial for long-term care.

**Keywords:** arterial stiffness, carotid intima-media thickness, epicardial fat thickness, type 1 diabetes mellitus

## INTRODUCTION

Type 1 diabetes mellitus (T1DM), caused by an absolute or relative insulin deficiency due to the destruction of pancreatic beta cells, is a genetic autoimmune condition.<sup>1</sup> Although

there has been a decrease in complications as a result of tight glycemic control in recent decades; individuals with T1DM are at an increased risk of developing both acute and chronic complications. Chronic vascular complications are classified as microvascular and macrovascular. Macrovascular complications



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result in cardiovascular disease (CVD) and stroke.<sup>2</sup> Long duration of DM, poor metabolic control, and coexisting hypertension or dyslipidemia are other risk factors for the development of CVD in T1DM patients.<sup>3,4</sup> Studies have reported that atherosclerotic changes may start in the first two decades of life in patients with T1DM.<sup>5</sup> Even in children and young adults, manifestations of cardiovascular remodeling present early after initial diagnosis. This is found to be related to chronic hyperglycemia, endothelial dysfunction, and chronic inflammation.<sup>6,7</sup> Hyperglycemia leading to an increase in oxidative stress is considered the key pathophysiological factor of both complications.<sup>8</sup>

The main cause of morbidity and mortality in people with T1DM is CVD.<sup>2</sup> Although few data exist on the impact of CVD risk factors in pediatric patients with T1DM, epicardial fat thickness (EFT), carotid intima-media thickness (cIMT), and arterial stiffness (AS) may contribute to the assessment of CVD risk in patients with T1DM. In addition to being a visceral fat depot with protective functions for the heart under physiological conditions, EFT is also the source of several proinflammatory and proatherogenic cytokines that can biologically affect myocardial and epicardial coronary arteries.<sup>9</sup> Studies have shown that increased EFT is a potential indicator of cardiovascular risk factors and coronary calcification.<sup>10</sup> Epicardial fat thickness was found to be an indicator of endothelial dysfunction in T1DM by studies examining the relationship between EFT and endothelial dysfunction.<sup>11</sup> Carotid intima-media thickness is also a structural marker of early atherosclerosis and has been associated with both prevalent and incident CVD.<sup>12</sup>

Arterial stiffness, a biomarker of vascular health, reflects arterial elasticity and compliance and is an index of arterial wall rigidity. Pulse wave analysis (PWA) is used to measure AS. There are various indices to describe the AS. These include pulse wave velocity (PWV), which is accepted as the most simple, noninvasive, robust, and reproducible method to determine AS and augmentation index (AIx).<sup>13,14</sup> Despite the proposed contributions of increased EFT, cIMT, and AS to the atherosclerotic changes in adults with T1DM, studies in children with T1DM are limited.

Early detection of cardiovascular abnormalities in children with T1DM could significantly alter clinical management and improve long-term health outcomes. Given the advancements in T1DM management and the increasing lifespan of patients, understanding and mitigating long-term cardiovascular risks in this population has never been more crucial. Our study aimed to determine EFT, cIMT, and AS in T1DM patients in comparison to healthy control groups and determine the risk factors affecting these.

## MATERIAL AND METHODS

### Participants

Participants of this cross-sectional, single-center study were recruited from the pediatric endocrinology department of Ankara Bilkent City Hospital. 115 type T1DM patients with a body mass index (BMI) between the -2 and +2 standard deviation scores (SDS) according to age and gender, having this diagnosis for at least 2 years and ages 8–18 years, were consecutively included in the study. Diagnostic criteria for diabetes are based on the American Diabetes Association classification.<sup>15</sup> The T1DM patients were selected from those under an intensive insulin regimen (glargine and rapid insulin (lispro-aspart)) and whose routine clinical and laboratory evaluations were regularly monitored in the pediatric endocrinology clinic. Exclusion criteria for the patient were determined to be having any chronic diseases other than T1DM and the presence of a congenital and/or acquired heart disease, hypertension, etc. This exclusion was necessary to isolate the cardiovascular effects attributable solely to T1DM, though it may limit the applicability to children with comorbid conditions. Healthy adolescents were recruited from those who applied to the pediatric clinic for annual routine child health check-ups and were healthy. The control group consisted of 87 sex, age, Tanner stage, and anthropometric measurements-matched healthy children. Exclusion criteria for the control group were determined to be having any chronic diseases and the presence of a congenital and/or acquired heart disease, hypertension, etc. The study was approved by the clinical research ethics committee of Ankara Bilkent City Hospital with the decision no 23-3128 dated January 04, 2023. Informed consent was obtained from all guardians, and assent was sought from children where appropriate, following a child-friendly explanation of the study's purpose and procedures. Ethical principles were adhered to, and the research was conducted in accordance with the Declaration of Helsinki.

Medical history, as well as age at diagnosis and duration of being a diabetic, were recorded, and physical examinations were performed in all patients and controls. All physical examinations were performed by a single medical doctor. For each participant, weight and height measurements were done, and BMI and SDS were estimated. The BMI was assessed using the weight (kg) ratio to height squared (m<sup>2</sup>). We examined anthropometric measurements using an online calculation tool ([www.childmetrics.org](http://www.childmetrics.org)).<sup>16</sup> Fasting blood glucose (FBG), total cholesterol (TC), high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides (TG) were measured by enzymatic colorimetric assays (Atellica Solution CH90, Siemens, Germany). For patients, glycated hemoglobin A1c (HbA1c) plasma level, measured within 0 to 14 days from

the measurement of EFT, was determined using capillary electrophoresis on the Capillarys 3 Tera, Sebia (Lisses, France). The arithmetic average of the HbA1c levels in the last two years was taken. The blood pressure (BP) of the participants was categorized by percentiles.<sup>17</sup>

### Pulse wave analysis measurement

In our study, a cuff-based validated oscillometric Mobil-O-Graph device (I.E.M., GmbH, Aachen, Germany) was used to PWA. This device is a commercially available brachial oscillometric ambulatory blood pressure monitor approved by the European Society of Hypertension.<sup>18</sup> Measurements were taken from the left arm in a room after a minimum rest of 5 minutes. The cuff size was chosen based on the circumference of the middle upper arm. Data from the Mobil-O Graph device was exported and analyzed using Hypertension Management Software Client-Server version 5.2.3 (I.E.M.). In addition to PWV, other parameters such as Alx, and hemodynamic parameters such as stroke volume, cardiac output, and cardiac index were measured. The PWV is the speed of the pressure wave that passes through the vessels of an organism and is calculated by dividing the distance traveled by the time it takes to travel the distance. A higher PWV indicates increased AS.<sup>19</sup> Augmentation index, a surrogate measure of stiffness in the peripheral arterial resistance, is calculated as the difference between the second and the first systolic peak pressure and is expressed as a percentage of the central pulse pressure. The augmentation index was normalized to a heart rate of 75 beats/sec (Alx@75) for comparison with different heart rates.<sup>20</sup> A higher Alx suggests increased AS.<sup>21</sup> The stroke volume refers to the volume of blood pumped into the body from the left ventricle during a heartbeat. The cardiac index is a parameter for assessing cardiac output and is calculated as the quotient of the cardiac output and the body surface.

### Echocardiographic examination

Echocardiographic examinations were performed by using an ultrasound system (iE33, Philips, The Netherlands, Eindhoven) equipped with a broadband (1-5 MHz) X5-1 transducer. Echocardiographic examinations were obtained by a single experienced pediatric cardiologist blind to the diabetes status of participants. Epicardial fat was identified as the echo-free space between the myocardium's outer wall and the pericardium's visceral layer. Measurement of EFT was obtained with the participant in the left lateral decubitus position. The measurements were performed on each parasternal long-axis and short-axis view by directing the ultrasonic beam perpendicular to the right ventricular free wall from the reference point of aortic annulus on the parasternal long axis and from the

reference point of interventricular septum and papillary muscle tip on the parasternal short axis section. Epicardial fat thickness was measured from its thickest part in mm at the end of systole due to deformation and pressure on adipose tissue. The average value of three cardiac cycles from each echocardiographic view was considered.

Measurement of cIMT was performed by the same experienced pediatric cardiologist by using a Vivid E95 echocardiography machine (GE Vingmed, Horten, Norway) equipped with a 9L linear probe (2,4-10 Mhz). Carotid intima-media thickness is defined as the distance between the first echogenic line (lumen-intima interface) and the second echogenic line (media-adventitia interface) of the far wall. Measurements were obtained from the far wall of the common carotid artery on both sides at 10–20 mm proximal to the bifurcation at the end-diastole. On the images of the thickest cIMT, measurements were taken with calipers positioned on a zoomed image of the common carotid artery. The mean value of the three measurements on each side was calculated.

### Statistical analysis

All analyses were carried out using SPSS 25.0 (IBM, USA). The findings of the study are expressed as frequency and percentages. The normality test was conducted using the Kolmogorov-Smirnov test. Non-normally distributed variables were presented as the median and interquartile range (IQR) with 25<sup>th</sup>–75<sup>th</sup> percentiles, while variables with normal distribution are expressed as mean  $\pm$  standard deviation. Categorical variables were compared using the Chi-square test. Fischer's exact test was applied according to the percentage of expected counts. Numerical variables with and without normal distribution were compared using the independent samples t-test and Mann-Whitney U, respectively. The Kruskal-Wallis test was used to compare numerical variables without normal distribution between more than two groups. Spearman correlation analysis was performed to determine the variables associated with EFT, cIMT, Alx@75, and PWV scores, and  $p < 0.05$  was considered as a statistically significant value. Multivariable logistic regression analysis was performed to detect associated factors with PWV and Alx@75. Power analysis was conducted using G-power 3.1.9.4. According to the t-test for EFT between T1DM and the control group based on the study conducted by Chambers et al. it was determined that 38 patients should be included in each group for an effect size of 0.767, a margin of error of  $\alpha: 0.05$  and a power ratio of 95%.<sup>22</sup>

## RESULTS

The demographic, clinical, and laboratory parameters of the participants are presented in Table 1. There were no significant

Table 1. Demographic, clinical findings and laboratory results of the groups				
Variable		Type 1 DM group (n=115)	Control group (n=87)	P
Age (years)		14.0 (11.0-16.0)	14.0 (11.0-16.0)	0.374
Gender (n/%)	Female	57 (49.6)	46 (52.9)	0.672
	Male	58 (50.4)	41 (47.1)	
Weight (kg)		51.0 (38.0-61.0)	48.0 (35.0-57.0)	0.317
Height (cm)		158.00 (144.60-166.00)	155.00 (144.30-166.20)	0.636
BMI		20.16±3.10	19.41±2.8	0.077
BMI SDS		0.01 (-0.64-0.87)	-0.12 (-0.88-0.50)	0.173
Peripheral systolic blood pressure (percentile)		60.5 (36.75-74)	65 (45.5- 74.75)	0.234
Peripheral diastolic blood pressure (percentile)		57 (42-69)	60.5 (44-73.75)	0.198
Duration of tip 1 DM (year)		6.0 (4.0-9.0)	-	
Synchronous HbA1c (%)		8.6 (7.6-9.7)	-	
Average HbA1c in the last two years (%)		8.5 (7.7-9.6)	-	
TG (mg/dl)		84.0 (64.0-129.5)	72.0 (54.5-93.5)	<0.01
TC (mg/dl)		156.0 (144.0-180.0)	144.5 (132.3-155.5)	<0.001
LDL (mg/dl)		81.0 (69.0-94.5)	74.5 (59.8-85.3)	<0.01
HDL (mg/dl)		56.5 (46.8-64.0)	53.0 (44.8-63.3)	0.286
Microalbumiuria (n/%)	Yes	6 (5.2)	-	
Duration of microalbumiuria (mean±SD)		2.83±0.79	-	

BMI: Body mass index, BMI SDS: Body mass index standard deviation score, DM: Diabetes mellitus, HbA1c: Glycosylated hemoglobin, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, TC: Total cholesterol, TG: Tryglyseride.

differences in age, gender, and BMI SDS between the groups ( $p>0.05$ ). The median HbA1c of the patient group was 8.6%, and the median HbA1c of the last two years was 8.5%. Total cholesterol, TG, and LDL were higher in the patient group (for TG and LDL  $p<0.01$  and for TC  $p<0.001$ ); however, HDL levels were similar for both groups ( $p>0.05$ ). No significant differences were found in the peripheral systolic BP (SBP) percentile and diastolic BP (DBP) percentile ( $p>0.05$ ).

The PWA device scores, EFT, and cIMT values are shown in Table 2. The stroke volume and cardiac index scores were significantly lower in the patient group ( $p<0.001$  and  $p=0.036$ ). The Alx@75, EFT, and mean cIMT scores were higher in the patient group ( $p<0.01$  for the Alx@75 and  $p<0.001$  for other variables). There were no significant differences in other variables between the two groups ( $p>0.05$ ).

When the patient group was divided into three groups according to DM duration as 2-5 years ( $n=51$ ), 6-10 years ( $n=44$ ), and >10

years ( $n=20$ ), stroke volume ( $p=0.938$ ), cardiac output ( $p=0.92$ ), Alx@75 ( $p=0.823$ ), PWV ( $p=0.774$ ), EFT ( $p=0.432$ ), and mean cIMT ( $p=0.782$ ) were similar between groups. Therefore, the cardiac index score was significantly lower in the >10 years of DM group. ( $p=0.027$ ). According to the HbA1c level three groups were formed: HbA1c <7.5% ( $n=25$ ), 7.5-9% ( $n=50$ ), and >9% ( $n=40$ ). Stroke volume ( $p=0.882$ ), cardiac output ( $p=0.657$ ), Alx@75 ( $p=0.684$ ), PWV ( $p=0.417$ ), and mean cIMT ( $p=0.582$ ) were similar between groups. Therefore, EFT ( $p=0.015$ ) was significantly higher, and cardiac index score ( $p=0.026$ ) was significantly lower in the HbA1c >9% group. Epicardial fat thickness is weakly correlated with BMI and HbA1c in the last two years (respectively,  $Rho=,214$ ,  $p=0.022$ ;  $Rho=,201$ ,  $p=0.032$ ). There was a strong positive correlation between mean cIMT and microalbuminuria ( $Rho=,925$ ,  $p<0.01$ ), a weak positive correlation between mean cIMT and TG ( $Rho=,217$ ,  $p=0.021$ ), and a weak negative correlation between mean cIMT and HDL ( $Rho=-,292$ ,  $p<0.01$ ). No correlation was found between EFT, mean cIMT, and other variables ( $p>0.05$ ) (Table 3).

**Table 2. Comparison of the pulse wave analysis device scores and echocardiographic assessment of the patient and control groups**

	Type 1 DM group (n=115)	Control group (n=87)	p
<b>Hemodynamics</b>			
Stroke volume (ml)	46.30 (41.60-54.40)	49.1 (45.3-62.9)	<0.001
Cardiac output (l/min)	4.4 (4.1-4.8)	4.3 (4.0-4.9)	0.496
Cardiac index (l/min/m <sup>2</sup> )	2.9 (2.6-3.4)	3.3 (2.8-3.6)	0.036
<b>Arterial stiffness</b>			
Alx@75 (%)	33.2±11.5	28.1±11.6	<0.01
PWV (m/s)	4.5 (4.3-4.8)	4.6 (4.3-4.7)	0.782
<b>Echocardiographic assessment</b>			
EFT	4.9 (4.2-5.5)	3.10 (2.8-3.5)	<0.001
Right cIMT	0.43 (0.40-0.46)	0.40 (0.38-0.41)	<0.001
Left cIMT	0.43 (0.41-0.45)	0.40 (0.38-0.41)	<0.001
Mean cIMT	0.43 (0.41-0.46)	0.40 (0.39-0.42)	<0.001

Alx@75: Corrected augmentation index for heart rate of 75 beats/sec, cIMT: Carotis intima-media thickness, DM: Diabetes mellitus, EFT: Epicardial fat thickness, PWV: Pulse wave velocity. Data are represented as mean ± SD.

**Table 3. Correlation of epicardial fat thickness and mean cIMT with the duration of diabetes mellitus, body mass index, hemoglobin A1c, microalbuminuria, serum lipids, and carotid intima-media thickness**

EFT	Duration of DM	BMI	Average HbA1c*	Microalbuminuria	TG	TC	LDL	HDL	Mean cIMT
Rho	,081	,214	,201	-,016	,067	,025	,026	-,062	,158
P	0.393	0.022	0.032	0.865	0.486	0.790	0.783	0.517	0.093
<b>Mean cIMT</b>									
Rho	,128	,147	-,050	,925	,217	-,033	,132	-,292	-
P	0.171	0.117	0.595	<0.01	0.021	0.726	0.163	<0.01	

\*Average of previous 2 years. BMI: Body mass index, cIMT: Carotis intima-media thickness, DM: Diabetes mellitus, EFT: Epicardial fat thickness, HDL: High-density lipoprotein, HbA1c: Glycosylated hemoglobin, LDL: Low-density lipoprotein, TC: Total cholesterol, TG: Tryglyseride.

**Table 4. Correlation analysis of epicardial fat thickness, mean cIMT and pulse wave analysis device scores in the patient group**

		Stroke volume	Cardiac output	SBPp	DBPp	Cardiac index	Alx@75	PWV
<b>EFT</b>	Rho	,266	,224	,348	,248	-,148	-,057	,344
	P	0.009	0.028	<0.01	0.014	0.149	0.581	<0.01
<b>Mean cIMT</b>	Rho	,150	,059	-,035	-,025	-,099	-,088	-,018
	P	0.139	0.559	0.729	0.219	0.328	0.385	0.856

Alx@75: Corrected augmentation index for heart rate of 75 beats/sec, cIMT: Carotis intima-media thickness, EFT: Epicardial fat thickness, DBPp: Peripheral diastolic blood pressure; SBPp: Peripheral systolic blood pressure; PWV: Pulse wave velocity.

The patient group has a weak correlation between EFT-stroke volume, EFT-cardiac output, and EFT-PWV (p<0.05). The EFT is weakly correlated with SBP and DBP (respectively, Rho=,348, p<0.01; and Rho=,248 p=0.014). No correlation was found between median cIMT and pulse wave analysis device scores (p>0.05) (Table 4).

The correlation analysis of PWV and Alx@75 found no meaningful correlation of these parameters with each other, HbA1c, DM duration, and serum lipids in the patient group. However, a moderate positive correlation was found between PWV and BMI (Rho=,435 p<0.001).

## DISCUSSION

Our study demonstrated that EFT, cIMT, and Alx@75 are increased in children with T1DM compared to the healthy control group. In addition, stroke volume and cardiac index were significantly lower in patients with T1DM than the controls. These results support the idea that children with T1DM present significant changes in important subclinical indicators for the development of cardiovascular disease. We also determined the correlation between AS, EFT, cIMT and HbA1c, lipid profile, and diabetes duration in patients. To our knowledge, this is the first clinical study in the literature in which EFT, cIMT, and AS were evaluated together in the same patient group.

The risk of CVD begins in childhood with subclinical abnormalities in patients with T1DM. Epicardial fat thickness is an emerging method for detecting these early changes. In a recent systematic review and meta-analysis, Li et al. reported that EFT was higher in diabetic patients than controls.<sup>23</sup> The reason for the increase in EFT in patients with T1DM is not fully understood. Chambers et al. first showed that youth with T1DM (mean age 12.4 ± 2.9) exhibited significantly higher EFT compared to age, sex, and BMI-matched controls. They found that increased EFT was associated with age, adiposity, and BP but not disease duration, insulin dose, or glycemic control.<sup>22</sup> Another study including T1DM children with a diabetes duration of less than 5 years, with a diabetes duration of 5 years or more, and healthy controls reported that EFT was significantly higher in children with a diabetes duration of ≥5 years. They found a significant positive correlation between EFT and the age of children with diabetes, waist circumference, BMI, and duration of diabetes.<sup>24</sup> In the present study, we demonstrated similar results, with higher EFT in the patients compared to controls. A weak positive correlation of EFT with BMI and average HbA1c in the last two years was found. No significant correlation was observed between EFT and disease duration. Some studies found no relationship between EFT and DM duration when the literature was examined.<sup>22,25-28</sup> These suggest that structural alterations may begin in the early phases of T1DM. There is scarce data about this correlation in the T1DM group.

Recent results from a meta-analysis suggest that there is an association between ultrasonographic parameters of the carotid vessels and both complications of diabetes.<sup>29</sup> It was reported that cIMT is a sign of preclinical atherosclerosis.<sup>30</sup> Several cross-sectional studies have reported greater cIMT in children with T1DM compared to age-matched controls.<sup>31</sup> However, some studies have reported no differences in cIMT between children with T1DM and healthy controls.<sup>32</sup> While some studies reported an association between cIMT and age, blood pressure, lipid levels, HbA1c, or diabetes duration, some studies

found no association.<sup>31</sup> Glackin et al. found that children with T1DM who had ambulatory blood pressure monitoring (ABPM) abnormalities had greater cIMT compared to those with normal ABPM. This relationship was found to be positively influenced by BMI.<sup>33</sup> Another study also reported that the mean cIMT was greater in persons with diabetes. Especially they found that the mean cIMT was significantly higher in persons with a diabetic complication (including hypertension, retinopathy, or microalbuminuria). No correlation was detected between cIMT and age, Tanner stage, duration of diabetes, BMI, blood pressure, HbA1C, and lipids.<sup>34</sup> Strong positive correlation between mean cIMT and microalbuminuria, a weak positive correlation between mean cIMT and TG, and a weak negative correlation between mean cIMT and HDL were found in the present study. No correlation was found between mean cIMT and duration of diabetes and HbA1c. These findings suggest that the effects of glycemic control on atherosclerosis progression are a gradual process and may take years.

Arterial stiffness was measured by PWV (a marker of central aortic stiffness) and Alx@75 (a marker of peripheral stiffness) in children and adolescents with T1DM compared to healthy controls in systematic reviews and meta-analyses.<sup>35,36</sup> Results of studies are controversial. This may be due to a lack of data on clinical and biochemical parameters, different sample sizes, different racial populations, and different instruments and techniques used for measuring PWV and Alx@75 in studies. Duarte et al. have reported similar results to our study by using an oscillometric Mobil-O-Graph device. They evaluated 36 children and adolescents diagnosed with T1DM (mean age 12.4 ± 2.9) and 36 control group matched by sex and age. The Alx@75 was found significantly higher in the T1DM group. They did not find any difference between groups regarding PWV.<sup>37</sup> They showed that Alx@75 correlated negatively with age and height. This finding was interpreted as the first signs of vascular dysfunction are more likely to occur in intermediate-sized arteries rather than large arteries.<sup>38</sup> Also, a previous study suggested that Alx might be a more sensitive marker of arterial stiffening in younger individuals and aortic PWV more sensitive in those over 50 years of age.<sup>39</sup> From Turkey, Terlemez et al. evaluated 72 children with T1DM (mean age 12.8 ± 3.7 years). In this study, PWV and Alx@75 levels were significantly higher in T1DM patients than in the control group. They also showed a positive correlation between diabetes duration and HbA1c levels in patients with T1DM with respect to PWV and Alx@75 values.<sup>40</sup> Obermannova et al. found a positive association between PWV and HbA1c but not T1DM duration.<sup>38</sup> Another study indicated that AS was not associated with HbA1c. In this study, it was explained that the effects of hyperglycemia on the vascular system may not be seen with arterial stiffness measurements and that short diabetes durations do not measurably affect vascular structure



and function.<sup>41</sup> Similar to these studies, we also detected that the Alx@75 of the T1DM group was significantly higher than the control group. This finding is important because it indicates that AS increases in children with T1DM. In our study, the correlation analysis of PWV and Alx@75 showed no meaningful correlation of these parameters with each other: HbA1c, DM duration, and serum lipids. This may be related to the short duration of diabetes. These conflicting data highlight the need for comprehensive randomized controlled prospective studies.

Unlike other studies, the correlation between EFT and PWA device scores and between cIMT and PWA device scores was investigated in the present study. We found a weak correlation between EFT-PWV in the patient group. There was no correlation between cIMT and PWA device scores. We found that the stroke volume and the cardiac index of the T1DM group were significantly lower than the control group. These situations may be related to the increase in left ventricular afterload.

The strength of this study is that anthropometric measurements, including weight, height, BMI, and SDSs for all participants were consistent in the study groups. The limitations were as follows: The first was that our sampling method was taken only from a single center, and the second was related to vascular measurements. Pulse wave velocity and Alx were calculated indirectly by a cuff oscillometric method with an algorithm. The third is that the observational design of this study precludes the ability to establish causality between T1DM and cardiovascular risk factors.

## CONCLUSION

Significant increase in EFT, cIMT, and Alx@75 suggesting early CVD risk has been demonstrated in children with T1DM. Increased EFT and decreased cardiac index scores with increasing HbA1c levels and a strong positive correlation between mean cIMT and microalbuminuria highlight the importance of poor control in terms of CVD from childhood. Early detection and treatment of risk factors for CVD related to T1DM beginning in childhood are important. Assessment of EFT, cIMT, and Alx@75 can be of benefit to the long-term care of patients with T1DM. This helps to optimize the treatment of youth with T1DM to prevent future CVD.

## Ethical approval

This study has been approved by the Ankara Bilkent City Hospital Clinical Research Ethics Committee No. 2 (approval date 04.01.2023, number 23-3128). Written informed consent was obtained from the participants.

## Author contribution

Study conception and design:GB, YÖŞ, FG, MB, and USB; data collection: GB, YÖŞ, AKT, EÖ, NÖ, and Mİ; analysis and interpretation of results: GB, İİÇ, FG, and USB; draft manuscript preparation: GB, YÖŞ, İİÇ, and USB. All authors reviewed the results and approved the final version of the manuscript.

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## Conflict of interest

The authors declare that there is no conflict of interest.

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