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Retinal vascular caliber in turkish adolescents with type 1 diabetes mellitus

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Abstract

Diabetic retinopathy (DR) is a common result of diabetes mellitus (DM). Alterations in retinal vascular caliber may be early finding of diabetic retinopathy. The aim of this study is to demonstrate retinal vascular caliber changes in Turkish adolescents with type 1 diabetes mellitus (T1D). This prospective and cross-sectional study included 108 eyes of the T1D adolescents and 75 eyes of the age-sex matched control group. Fundus images of the both groups were taken with fundus camera system (FA; Visucam500; Carl Zeiss Meditec, Jena, Germany) and were analyzed with IVAN which is a semi-automated system used to measure the width of retinal vessels using a digital retinal image (Nicole J. Ferrier, College of Engineering, Fundus Photography Reading Center, University of Wisconsin, Madison, WI, USA). Central retinal artery equivalent (CRAE), central retinal vein equivalent (CRVE) and artery-vein ratio (AVR) were compared between groups. Both groups were comparable in baseline characteristics ($p>0.05$). The mean CRAE value was higher in T1D group ($179.03\pm 29.58 \mu$ in T1D group and $166.64\pm 15.76 \mu$ in control group, $p<0.001$). The mean AVR value was higher in T1D group, too (0.97 ± 0.46 in T1D and 0.84 ± 0.19 in control group, $p=0.01$). There was no statistically significant difference in CRVE value between groups. CRAE was found to be higher in T1D patients. This arteriolar dilation may be the early finding of diabetic retinopathy.

Keywords: Retinal vascular caliber, arteriolar dilation, type 1 diabetes mellitus, diabetic retinopathy

Introduction

Diabetes mellitus (DM) is a common disease which effects 366 million people around world, while 20 million to 40 million of these patients is type 1 diabetes mellitus (T1D) [1]. The prevalence of T1D in Turkey is 0.75/1 000 (95% CI 0.74–0.76) [2]. T1D is of the most common chronic disease in adolescents and it can affect both anterior and posterior segment of eyes [3-5]. The diabetic retinopathy (DR) is the most common complication and main reason of vision loss in T1DM [6]. In current literature, some studies showed that measurement of retinal vascular caliber may provide useful information regarding risk of DR in adulthood [7-10]. Vasodilatation which is accepted as a sign of retinal arterial dysfunction were demonstrated in these studies. Most of these studies were in elderly population with type 2 DM which have coexisting disease such as hypertension, hyperlipidemia which can affect retinal vascular

caliber. Some studies also showed vasodilatation in children and adults with T1D [11-13]. But there is not any study regarding Turkish adolescents with T1D.

The aim of the current study is to investigate retinal vascular caliber in Turkish adolescents with T1D.

Material and Methods

This prospective and cross-sectional study was conducted in Department of Ophthalmology, - Okmeydanı Research and Training Hospital, University of Health Sciences, İstanbul, Turkey. Protocol of the study was approved by Ethics Committee of Marmara University (protocol number 09.2018.120). The study was performed in accordance with Declaration of Helsinki. Written informed consent was obtained from all the parents of the children.

The adolescents with T1D were selected among the patients which were referred us for DR screening. The control groups selected among the patients which came to hospital for normal ophthalmic examination. Inclusion criteria was T1DM adolescents (age between 12-20), no systemic disorder than T1DM, normal body-mass index (BMI), no ocular disease, spherical or cylindrical refractive

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errors < 1.00 D, no diabetic retinopathy, best-corrected visual acuity (BCVA) \geq 20/20 at snellen charts. Control group had healthy subjects without any systemic or ocular disease. HbA1c levels, age, gender, duration of DM were noted.

All the patients underwent a complete ophthalmic examination. BCVA, slit-lamb bio-microscopy, intraocular pressure (IOP) values with Goldman applanation tonometry, posterior segments examination with dilated pupillary were performed. Fundus images of the both groups were taken with fundus camera system (FA; Visucam500; Carl Zeiss Meditec, Jena, Germany). Before and after fundus images examination blood pressure of the participants were measured. Only right eyes of the subjects were taken. Retinal vascular caliber was analyzed with IVAN which is a semi-automated

system used to measure the width of retinal vessels using a digital retinal image (with permission of Dr. Nicola Ferrier of the University of Wisconsin - Madison School of Engineering and the Department of Ophthalmology and Visual Sciences, University of Wisconsin – Madison) [14-16].

Three concentric rings were placed in images of fundus to determine the vascular measurement field. After ring implantation two zones were formed. The area from the disc margin to half-disc diameter was defined as Zone A, while the area from half-disc diameter to 1 disc diameter was defined as Zone B. Central retinal artery equivalent (CRAE) and central retinal vessel equivalent (CRVE) measurements were performed using the formula created by Hubbard15 and later revised by Knudtson16 (Figure 1).

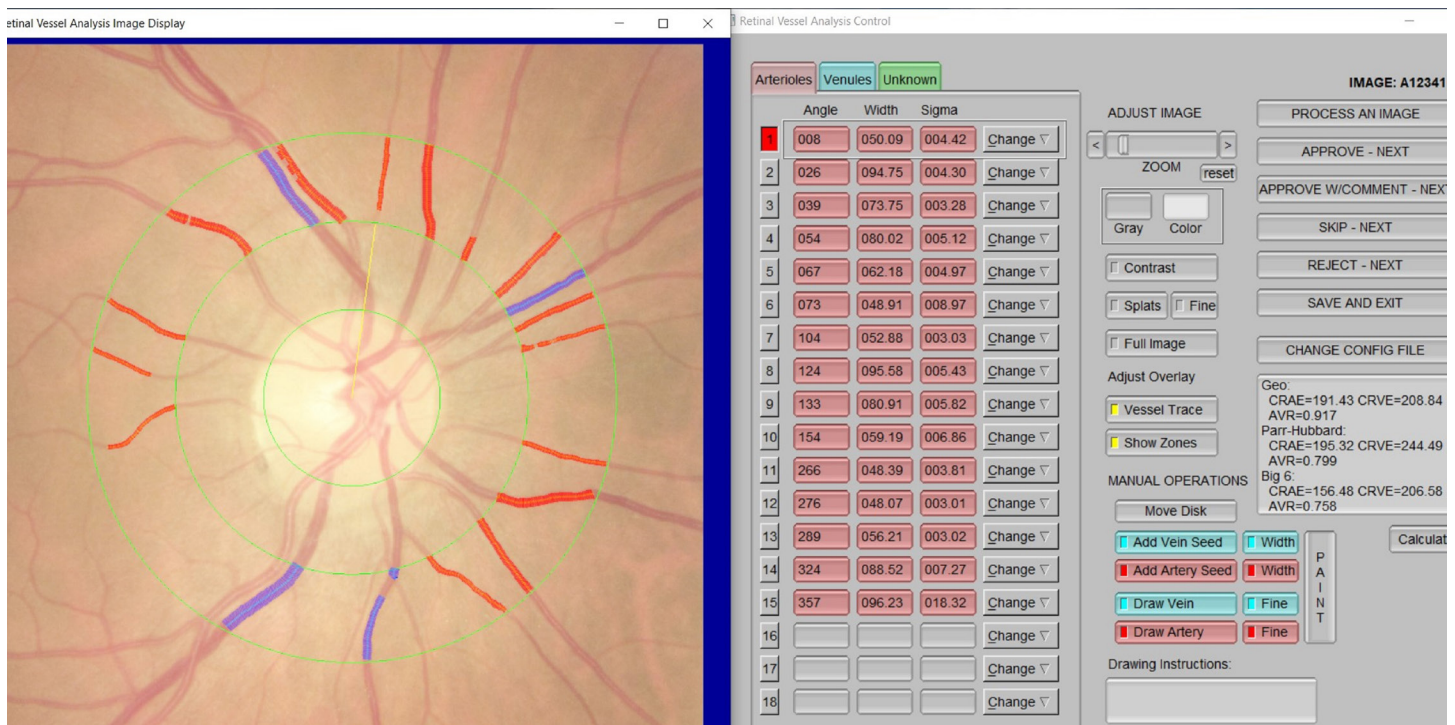


Figure 1. Measurement of retinal vascular caliber in IVAN

Statistical analyses were performed using the SPSS software version 25. Descriptive analyses were presented using means and standard deviations for normally distributed variables. An assessment of normality was done using the Kolmogorov-Smirnov test. The independent-t, Man-Whitney-U, Chi-squared tests were used for analyses. A p-value of less than 0.05 was considered to show a statistically significant result.

Results

One hundred eight eyes of 108 patients were in T1D group, while 75 eyes of healthy subjects were in control groups. The groups were comparable in baseline characteristics. The baseline characteristics of the patients were summarized in table 1.

Table 1. Demographic and clinical characteristics of the patients

	T1D group	Control group	p value
Age, y, mean±SD	14.78±1.96	15.16±2.42	0.261
Gender			
Female (n)	66	42	
Male (n)	42	33	0.489
The duration of DM, y	4.75±1.99		
The mean value of HbA1c, %, mean±SD	7.76±2.17		

SD: Standard deviation, y: years, DM: Diabetes Mellitus, HbA1c: glycated hemoglobin

The mean CRAE value was $179.03 \pm 29.58 \mu$ in T1D group, while it was $166.64 \pm 15.76 \mu$ in control group ($p < 0.001$) (Figure-2). The mean CRVE value was 206.19 ± 55.57 in T1D group, 205.04 ± 38.45 in control group ($p = 0.869$). AVR was 0.97 ± 0.46 in T1D group and 0.84 ± 0.19 in control group ($p = 0.01$) (Figure-3).

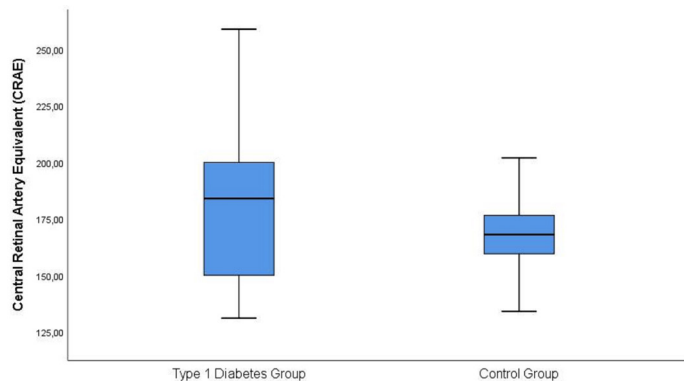


Figure 2. The mean central retinal artery equivalent (CRAE) value in groups

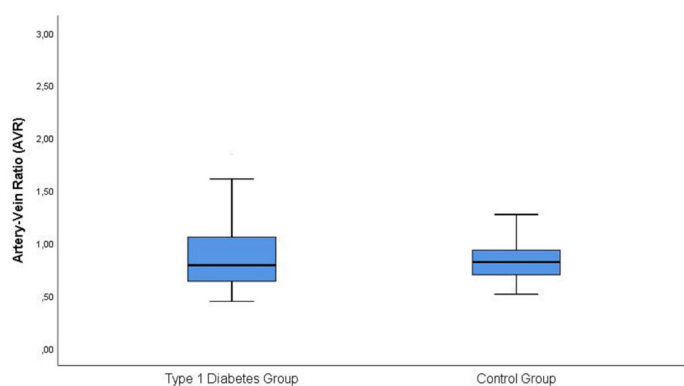


Figure 3. The mean artery-vein ratio (AVR) value in groups

The mean value of CRAE and AVR did not have correlation with age, gender, duration of DM and HbA1c value ($p > 0.05$).

Discussion

Adolescents with T1D have an increasing for vision loss through their lives. The risk of developing DR is associated with duration of DM [17]. It is common knowledge that if DR can be detected in early stages, the risk for vision lose can be reduced with early treatment [18]. Hence, health-care professionals want to develop a noninvasive method to detect complications of DM, especially for children. IVAN is semi-automated system used to measure the width of retinal vessels using digital retinal images. So we used IVAN as a noninvasive method to detect early changes of retinal vessel caliber before developing DR in Turkish adolescent with T1D.

Our study shows that the adolescent with T1D have larger retinal arteriolar caliber and larger arterio/venous ratio. Previous studies have shown that retinal arteriolar dilatation is an indicator of diabetes micro vascular complications [12,19]. In an experimental study, researchers showed that arteriolar vasodilatation and an increase in retinal blood flow are commonly found in eyes of diabetic patients [20]. It is reported that retinal vasodilatation and retinal hyper perfusion which is to cause release of nitric oxide, can be key factors in diabetic retinopathy development [21-23]. Retinal

hyper perfusion has been related with micro aneurysm development because it can cause epithelial damage and vascular permeability [21]. With all this information, it is too important to detect early vascular changes in diabetic patients. We aimed to show retinal caliber changes in Turkish adolescent with T1D.

Several studies showed retinal arteriolar dilatation in T1D children. Cheung et al [12] showed that diabetic children have larger retinal vascular caliber than healthy subjects. They also show that the children with larger retinal vascular caliber have higher risk of DR development. Their study demonstrated that each standard deviation increase in retinal vascular caliber was associated with a 46% increase in retinopathy risk [12]. In the Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR), researchers evaluated that an association of larger retinal vascular caliber with 10 year incident retinopathy risk in type 2 diabetes and 4 year progression of DR risk in type 1 diabetes [8]. While the WESDR show larger retinal arteriolar and venular dilatation in adults with T1D [8]. In our study we did not find any difference in retinal venular caliber. This is probably related to mean age of study population. The Atherosclerosis Risk in Communities study showed that vasodilatation in retinal venular caliber was related to metabolic syndrome components in the middle age person [24].

Conclusion

In conclusion, our study shows that the Turkish adolescent with T1D have larger retinal caliber than healthy people. These patients may have high risk of diabetic retinopathy development. Retinal vascular caliber might be a sensitive biomarker to define early diabetic retinopathy risk. Larger cohort studies in Turkish population are needed to describe early detection of diabetic retinopathy in adolescents and children.

Conflict of interests

The authors declare that they have no competing interests.

Financial Disclosure

The financial support no have.

Ethical approval

Protocol of the study was approved by Ethics Committee of Marmara University (protocol number 09.2018.120).

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