ORIGINAL ARTICLE

Neurodegeneration of the retina in type 1 diabetic patients

Aleksandra Araszkiewicz[1], Dorota Zozulińska-Ziółkiewicz[1], Mikołaj Meller[2], Jadwiga Bernardczyk-Meller[2], Stanisław Piłaciński[1], Anita Rogowicz-Frontczak[1], Dariusz Naskręt[1], Bogna Wierusz-Wysocka[1]

1 Department of Internal Medicine and Diabetology, Poznan University of Medical Sciences, Poznań, Poland
2 OCU SERVICE Private Ophthalmology Unit, Poznań, Poland

KEY WORDS

diabetic retinopathy, neurodegeneration, optical coherence tomography, retinal thickness, type 1 diabetes

ABSTRACT

INTRODUCTION The degeneration of retinal neurons and glial cells has recently been postulated in the pathogenesis of diabetic retinopathy. Optical coherence tomography (OCT) allows to perform qualitative and quantitative measurements of retinal thickness (RT) with identification of individual retinal layers.

OBJECTIVES We compared RT, retinal nerve fiber layer (RNFL) thickness, and ganglion cell layer (GCL) thickness obtained by OCT in type 1 diabetic patients with and without clinically diagnosed retinopathy.

PATIENTS AND METHODS The study included 77 consecutive patients with type 1 diabetes (39 men, 38 women; median age, 35 years [interquartile range (IQR), 29–42]; median disease duration, 10 years [IQR, 9–14]) and 31 age- and sex-matched controls. We measured RT in the fovea, parafovea, and perifovea, as well as RNFL and GCL thickness. We divided diabetic patients into 2 subgroups, i.e., those with diabetic retinopathy and without retinopathy.

RESULTS We observed thicker perifoveal retina ($P = 0.05$), mean RNFL ($P = 0.002$), inferior RNFL ($P < 0.0001$), and superior and inferior GCL ($P = 0.05$ and $P = 0.04$, respectively) in diabetic subjects compared with the control group. We detected retinopathy in 23 diabetic patients (29%). Compared with patients without retinopathy, subjects with retinopathy had thinner parafoveal retina ($P = 0.05$), mean RNFL ($P = 0.002$), inferior and nasal RNFL ($P = 0.002$, $P = 0.03$), superior ($P = 0.05$) and inferior GCL ($P = 0.006$). Significant correlations were found between duration of diabetes and nasal RNFL thickness ($r = –0.32$, $P = 0.004$) and parafoveal RT ($r = –0.47$, $P < 0.001$).

CONCLUSIONS The results might suggest the loss of intraretinal neural tissue in type 1 diabetic patients with retinopathy. Neurodegeneration in diabetic retinopathy is closly associated with disease duration.

Correspondence to:
Aleksandra Araszkiewicz, MD, PhD, Katedra i Klinika Chorób Wewnętrznych i Diabetologii, Uniwersytet Medyczny im. K. Marcinkowskiego w Poznaniu, ul. Mickiewicza 2, 60-834 Poznań, Poland, phone/fax: +48-61-847-45-79, e-mail: olaaraszkiewicz@interia.pl
Received: July 20, 2012.
Revision accepted: August 22, 2012.
Published online: August 22, 2012.
Conflict of interest: none declared.
Pol Arch Med Wewn. 2012; 122 (10): 464-470

INTRODUCTION Diabetic retinopathy is still the leading cause of blindness in the working-age population of the Western countries.[1] Early recognition of changes in the retina in diabetic subjects is essential in the prevention of vision loss.[2] Degeneration of retinal neurons and glial cells has been postulated recently in the pathogenesis of diabetic retinopathy.[3-5] These abnormalities were described even before the development of microaneurysms.[6] However, for years apoptosis of the neural tissue could be assessed only by fundus photography.[5] Recently, optical coherence tomography (OCT) has been introduced into clinical practice as the most sensitive and objective method to visualize the retina.[7,8] First, OCT was applied to detect macular edema in diabetic patients.[9] Then, it allowed to perform quantitative and qualitative measurements of retinal thickness (RT) and volume with the identification of individual retinal layers. This method provided significant clinical and pathological data in several studies of different retinal conditions.[10,11] However, the information concerning the clinical value of measuring RT in type 1 diabetic patients is still limited. Moreover, the usefulness of this procedure in the diagnosis of retinopathy has not been fully elucidated.

TABLE 1 Clinical characteristics of the study group

Characteristics	Diabetic patients, n = 77	Healthy subjects, n = 31	*P*
age, y	35 (29–42)	46 (25–50)	0.33
sex, male/female	39/38	13/18	0.52
duration of diabetes, y	10 (9–14)	–	–
smoking	20 (26)	8 (26)	0.99
SBP, mmHg	120 (110–130)	120 (110–128)	0.82
DBP, mmHg	76 (70–80)	75 (70–80)	0.81
HbA_{1c}, %	7.9 (7.0–9.2)	–	–
retinopathy	23 (29)	–	–
nephropathy	14 (18)	–	–
neuropathy	15 (19)	–	–

Data are presented as median (IQR) or number (%) of patients.

Abbreviations: DBP – diastolic blood pressure, HbA_{1c} – hemoglobin A_{1c}, IQR – interquartile range, SBP – systolic blood pressure

The aim of the study was to compare RT, retinal nerve fiber layer (RNFL) thickness, and ganglion cell layer (GCL) thickness measured by OCT in type 1 diabetic patients with and without retinopathy. Moreover, we assessed the potential correlations between RT and metabolic parameters as well as duration of the disease.

PATIENTS AND METHODS We recruited 77 consecutive patients with type 1 diabetes (39 men and 38 women), hospitalized in the Department of Internal Medicine and Diabetology in Poznań, Poland. The patients were admitted to the hospital for education, adjustment of appropriate insulin dose, and assessment of late diabetic complications. The median age of the patients was 35 years (interquartile range [IQR], 29–42); median disease duration was 10 years (IQR, 9–14). All subjects were informed about the aim of the study and gave their written consent. The study was conducted according to the guidelines of the Helsinki Declaration and was approved by the local Ethics Committee.

The exclusion criteria were as follows: proliferative retinopathy after laser treatment, myopia bigger than 2 diopters, and diabetic clinical signs of macular edema observed on ophthalmoscopy. A total of 31 age- and sex-matched controls were recruited from the staff members of the ophthalmology clinic and their families. Controls had no history of refractive errors, diabetes, or other chronic diseases.

The participants completed a standardized questionnaire including data on sex, age, medical history, duration of diabetes, treatment, smoking status, and blood glucose self-control. All patients underwent complete physical examination with anthropometric and blood pressure measurements. Blood samples were collected in a fasting state after a period of rest, with minimal occlusion of the vein using the S-Monovette blood collection system. Hemoglobin A_{1c} (HbA_{1c}) was measured using high-performance liquid chromatography with the Variant Hemoglobin A_{1c} Program (Bio-Rad Laboratories, Hercules, California, United States). The clinical characteristics of the study group are presented in **TABLE 1**.

During ophthalmological examination, patients were asked about previous ocular diseases, visual symptoms, and ophthalmic treatment. Best-corrected visual acuity was measured using the standard methods. The pupils were dilated on both eyes using 1% tropicamide and 10% phenylephrine eye drops. Fundus examinations were performed using ophthalmoscopy as well as slit lamp and indirect Volk lens. Subsequently, using a 45-degree digital camera VISUCAM (Zeiss, Germany), 2 fundus photographs were taken of each eye, one centered on the fovea and the other on the optic disc. The evaluation of opthalmoscopy results and fundus photographs was performed for the entire group by the same ophthalmologist with experience in diabetic retinopathy.

Diabetic retinopathy was graded according to the classification of the American Academy of Ophthalmology as no retinopathy, mild nonproliferative, moderate nonproliferative, severe nonproliferative, and proliferative retinopathy.[12] We divided diabetic patients into 2 subgroups: with diabetic retinopathy and without retinopathy according to clinical examination and fundus photographs. One microaneurysm was enough to assign a patient to the subgroup with retinopathy.

We performed OCT in the study group with the RTVue model version 3.5 (Optovue Inc., Canada). RTVue OCT is a modern equipment with ultra-high speed (26,000 A-scn/s), high scan resolution (5 μm), and high transverse scan resolution (15 μm). As Biallosterski et al.[7] showed a significant correlation between RT in the left and right eye of the study population, we chose the right eyes of the patients and performed 5 scans in each.[7] There were 3 retinal scan patterns: high-definition B-scan, horizontal and vertical scans, and dense thickness/elevation maps. We measured RT: in the fovea (the central circle of 1 mm in diameter), in the parafovea (the circle of 1 mm in the inner diameter and 3 mm in the outer diameter), and in the perifovea (the circle of 3 mm in the inner diameter and 6 mm in the outer diameter). There were 2 glaucoma scan patterns: 3.45 mm RNFL thickness and GCL thickness. The measurements of RNFL thickness were obtained along a 360° path for 4 quadrants of the optic disc and as a mean value. The quadrants were defined as follows: superior (46°–135°), inferior (226°–315°), temporal (316°–45°), and nasal (136°–225°).

Statistical analysis Statistical analysis was performed using the Statistica PL version 8.0 (Stat Soft Inc., Tulsa, United States). The results of continuous variables are shown as median values and IQR or the number and percentage of patients. Comparisons between the subgroups with and without retinopathy were performed using the *t* test for normally distributed variables, the Mann-Whitney *U* test for continuous

TABLE 2 Comparison of retinal thickness, retinal nerve fiber layer thickness, and ganglion cell layer thickness between diabetic patients and healthy subjects

		Diabetic patients, n = 77	Healthy subjects, n = 31	*P*
RT	foveal	270 (254–288)	271 (254–280)	0.38
	parafoveal	333 (321–341)	328 (321–333)	0.15
	perifoveal	310 (301–317)	305 (296–309)	0.05
RNFL	mean	112.9 (105.8–119.5)	105.9 (97.7–113.1)	0.002
	superior	132.7 (123.2–145.2)	132.0 (114.7–140.7)	0.30
	inferior	156.2 (143.0–165.5)	135.7 (125.7–144.7)	<0.0001
	temporal	83.6 (77.7–90.7)	79.7 (74.0–89.2)	0.35
	nasal	78.0 (66.7–85.5)	77.7 (73.2–85.7)	0.50
GCL	superior	102.1 (95.9–106.9)	99.1 (93.7–101.4)	0.05
	inferior	102.8 (98.1–108.2)	100.1 (95.2–103.6)	0.04

Data are presented as median (IQR), μm.

Abbreviations: GCL – ganglion cell layer, RNFL – retinal nerve fiber layer, RT – retinal thickness, others – see TABLE 1

variables with skewed distributions, and the Fisher's exact test for categorical data. Pearson's correlation coefficients were calculated to assess the association between the continuous variables. All tests were performed with the significance level of 0.05 (two-sided).

RESULTS **Comparison between diabetic subjects and controls** We observed thicker perifoveal retina ($P = 0.05$), mean RNFL ($P = 0.002$), inferior RNFL ($P < 0.0001$), and superior and inferior GCL ($P = 0.05$ and $P = 0.04$, respectively) in diabetic subjects compared with controls (TABLE 2).

Comparison between type 1 diabetic patients with and without retinopathy We detected retinopathy in 23 diabetic patients (29%); 19 patients had mild nonproliferative retinopathy and 4 subjects moderate nonproliferative retinopathy. The results of RT, RNFL thickness, and GCL thickness in diabetic patients are shown in TABLE 3. Compared with patients without retinopathy, subjects with retinopathy had thinner parafoveal retina ($P = 0.05$), mean RNFL ($P = 0.002$), inferior and nasal RNFL ($P = 0.002$, $P = 0.03$), superior ($P = 0.05$) and inferior GCL ($P = 0.006$).

We also compared diabetic subjects without retinopathy with the control group (TABLE 3). Subjects without retinopathy had thicker perifoveal retina ($P = 0.048$), mean RNFL ($P < 0.0001$), inferior RNFL ($P < 0.0001$), as well as superior and inferior GCL ($P = 0.007$ and $P = 0.003$, respectively).

Associations between clinical characteristics and retinal thickness, retinal nerve fiber layer thickness, and ganglion cell layer thickness RT, RNFL thickness, and GCL thickness in diabetic patients were

TABLE 3 Comparison of retinal thickness, retinal nerve fiber layer thickness, and ganglion cell layer thickness between healthy subjects, diabetic patients without retinopathy, and diabetic patients with retinopathy

		Healthy subjects, n = 31	Diabetes without retinopathy, n = 54	P^a	Diabetes with retinopathy, n = 23	P^b
RT	foveal	271 (254–280)	271 (258–290)	0.22	261 (250–285)	0.25
	parafoveal	328 (321–333)	335 (322–342)	0.054	329 (313–336)	0.05
	perifoveal	305 (296–309)	310 (301–321)	0.048	310 (298–316)	0.52
RNFL	mean	105.9 (97.7–113.1)	115.2 (108.8–120.8)	<0.0001	109.4 (101.1–115.1)	0.002
	superior	132.0 (114.7–140.7)	133.7 (126.0–149.6)	0.11	131.5 (118.2–141.7)	0.08
	inferior	135.7 (125.7–144.7)	162.5 (149.0–167.7)	<0.0001	148.2 (138.0–161.0)	0.002
	temporal	79.7 (74.0–89.2)	85.0 (79.1–91.5)	0.25	80.8 (72.5–89.5)	0.21
	nasal	77.7 (73.2–85.7)	79.2 (72.2–87.7)	0.69	72.0 (64.7–81.5)	0.03
GCL	superior	99.1 (93.7–101.4)	102.5 (96.6–107.1)	0.007	97.6 (92.1–104.2)	0.05
	inferior	100.1 (95.2–103.6)	104.8 (99.7–109.6)	0.003	98.8 (93.9–104.6)	0.006

Data are presented as median (IQR), μm.

a differences between diabetic patients without retinopathy and healthy subjects
b differences between diabetic patients with retinopathy and without retinopathy

Abbreviations: see TABLES 1 and 2

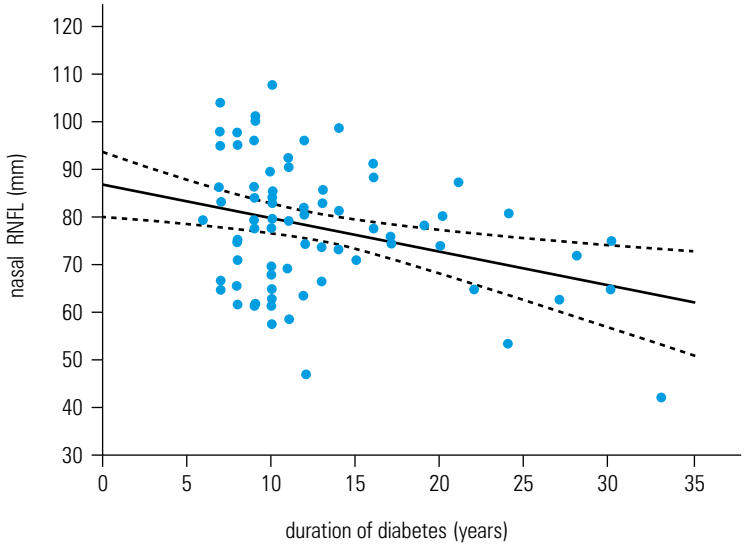

FIGURE 1 Correlation between retinal nerve fiber layer (RNFL) thickness in the nasal quadrant of the right eye and duration of diabetes; Pearson's $r = -0.32$, $P = 0.004$

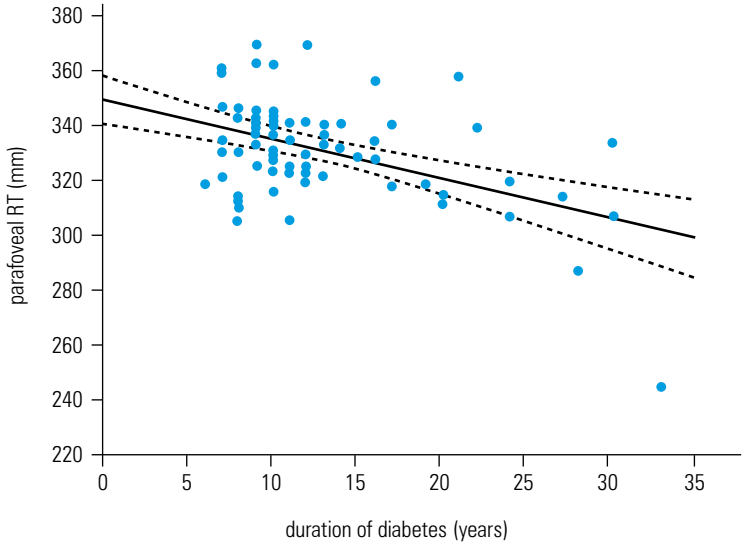

FIGURE 2 Correlation between parafoveal retinal thickness (RT) of the right eye and duration of diabetes; Pearson's $r = -0.47$, $P < 0.001$

analyzed along with various clinical parameters. A significant correlations were found between the duration of diabetes and nasal RNFL thickness ($r = -0.32$, $P = 0.004$) and parafoveal RT ($r = -0.47$, $P < 0.001$) (FIGURES 1 and 2).

There were no significant correlations between RT, RNFL thickness, and GCL thickness and glycemic control of diabetes.

DISCUSSION The main finding of the study is that RT measured by OCT is higher in type 1 diabetic patients compared with controls. Interestingly, however, the retina becomes thinner if diabetic retinopathy is present. The results of our study show that OCT could help identify early changes in the neural layers of the retina in diabetic patients. The measurement of RNFL and GCL thickness could serve as the early sign of neurodegeneration in diabetic retina. In diabetic patients, increased retinal vascular permeability related to hyperglycemia leads to the leakage of serum proteins and lipids into the intraretinal space.[13] This may result in higher values observed on OCT in diabetic patients compared with controls, as observed in our study. However, in subjects with recognized retinopathy, we also noted significant thinning of the retina. Several studies conducted in experimental animal models have recently indicated that neuroglial tissue loss may occur at the early stages of diabetic retinopathy and even precede vascular changes.[8,14,15] It has also been postulated that diabetic retinopathy should be considered as a disease that involves vascular pathology and retinal neurodegeneration.[8] OCT is a noninvasive and sensitive method that might help identify the thinning of particular retinal layers. Segmentation of the intraretinal layers obtained by OCT could lead to an earlier detection of diabetic retinal damage and facilitate the understanding of its pathogenesis. Cabrera et al.[8] showed reduced RNFL and GCL thickness in diabetic patients with mild retinopathy compared with subjects without retinopathy. However, the study group of Cabrera et al.[8] was not homogeneous – there was a wide range of patients' age. There have been studies on type 2 diabetic subjects that revealed RNFL defect in patients with early diabetic retinopathy.[3] However, the studies using OCT in type 2 diabetes focused mostly on the assessment of macular edema.[16-18] The knowledge on clinical usefulness of RT measurement in type 1 diabetes is still limited. However, we would like to emphasize that the group of type 1 diabetic subjects seems to be much more homogenous than that of type 2 diabetic patients with well-defined onset of the disease. Ciresi et al.[19] found no difference between type 1 diabetic patients with and without diabetic retinopathy and the control group for all OCT parameters. The authors suggested that retinopathy without macular edema in type 1 diabetic patients cannot be detected with OCT.[19] On the other hand, Biallosterski et al.[7] showed significantly decreased pericentral RT in patients with retinopathy compared with controls. Similarly, Van Dijk et al.[20] compared type 1 diabetic subjects with retinopathy with the control group and showed thinning of the total retina. We detected the thinning of the retina and of particular neuroglial layers in type 1 diabetic subjects with retinopathy compared with those without retinopathy.

Interestingly, we observed negative correlations between all studied OCT parameters and the duration of the disease. The results are consistent with those reported by Asefzadeh et al.[21] (who, however, investigated type 2 diabetes) and those reported by Biallosterski et al.[7] (whose study involved type 1 diabetic patients). Similarly, in the study by Chihara et al.,[3] the risk factors for nerve fiber layer thinning were the degree of diabetic retinopathy, high systolic blood pressure, and patient's age, but not HbA_{1c} levels.[3]

It seems that degeneration of the neurons and ganglion cells is a gradual process, which pccurs over time. In the present study, we did not find any correlations between RT, RNFL thickness, and GCL thickness and glycemic control of diabetes. However, it is possible that HbA_{1c} reflects only the mean values of glycemia from the last 3 months without showing the fluctuations of glycemia, and it is just not the perfect determinant of good metabolic control.[22] Moreover, the activation of adenosine monophosphate-activated protein kinase and metabolic stress in diabetic patients probably occurs as a result of hyperglycemia, hypoglycemia, and hypoxia.[23] There is strong evidence that the combination of high metabolic demand and minimal vascular supply may limit the ability of intraretinal neural tissue to adapt to the metabolic stress of diabetes.[24] These aspects may partially explain the pathogenesis of neurodegeneration as an additional component to microvascular pathomechanism of diabetic retinopathy as well as the lack of correlation between HbA_{1c} and OCT parameters observed in our study.

The results of RT measurements in diabetic patients without retinopathy compared with healthy subjects presented in the literature are inconsistent. A number of studies have been conducted in type 2 diabetes and the results cannot be compared to type 1 diabetes. Asefzadeh et al.[21] performed a study in type 2 diabetic patients and found no significant differences between RT in controls, in subjects with mild retinopathy, and those without retinopathy.[21] Van Dijk et al.[20] showed no statistically significant differences in RT between diabetic patients without retinopathy and the control group.[20] Similarly to our study, Biallosterski et al.[7] divided patients into 3 subgroups, but they only found a difference in RT in the pericentral ring between diabetic patients with retinopathy and the control group.[7] However, there are some data suggesting the thinning of the retina even in type 1 diabetic subjects without retinopathy. Lopes de Faria et al.[25] showed significant nerve fiber loss in some segments of the retina only in 12 patients without retinopathy compared with controls.[25] The inconsistent data might result from the early functional and hemodynamic changes in the retina observed as a result of hyperglycemia. There is evidence of vascular dysfunction and abnormal autoregulation of retinal circulation in diabetes that can lead to retinal hyperperfusion.[26] This high level of retinal perfusion is assumed to induce endothelial damage and increased permeability of the capillaries due to increased shear stress.[27,28] This hypothesis is in line with the observation that systemic hypertension increases the frequency and rate of progression of diabetic retinopathy.[29] This might result in the accumulation of extracellular fluid and retinal thickening observed in OCT in the group without retinopathy. It has been shown that the total retinal blood flow and blood velocity are increased in early diabetic retinopathy even before the clinical onset visible on fundus examination.[30] Moreover, we cannot exclude that other mechanisms leading to increased permeability of the endothelium could be stimulated early in diabetes. The formation of advanced glycation end-products and oxidative stress associated with hyperglycemia lead to the thickening of the capillary basement membrane and pericyte loss, preceding clinically visible retinopathy.[31,32]

The study has several limitations. First, we observed thinner retina in diabetic patients with retinopathy only in some quadrants and layers. Although the results of OCT seem to be reproducible, the future studies are needed with more than 1 OCT measurement in the same group of patients. Second, based on our results, the process of retinal thinning seems to be selective and limited. The nature of this process in type 1 diabetes requires further research.

In conclusion, the results might suggest the loss of intraretinal neural tissue in type 1 diabetic patients with retinopathy. Neurodegeneration in diabetic retinopathy is strongly associated with disease duration. OCT might be valuable in the assessment of diabetic retinopathy.

REFERENCES

1 Cheung N, Wong TY. Diabetic retinopathy and systemic vascular complications. Prog Retin Eye Res. 2008; 27: 161-176.

2 Photocoagulation for diabetic macular edema. Early Treatment Diabetic Retinopathy Study report number 1. Early Treatment Diabetic Retinopathy Study Research Group. Arch Ophthalmol. 1985; 103: 1796-1806.

3 Chihara E, Matsuoka T, Ogura Y, Matsumura M. Retinal nerve fiber layer defect as an early manifestation of diabetic retinopathy. Ophthalmology. 1993; 100: 1147-1151.

4 Gardner TW, Antonetti DA, Barber AJ, et al. Diabetic retinopathy: more than meets the eye. Surv Ophthalmol. 2002; 47: S253-S262.

5 Peng PH, Lin HS, Lin S. Nerve fibre layer thinning in patients with preclinical retinopathy. Can J Ophthalmol. 2009; 44: 417-422.

6 Park SH, Park JW, Park SJ, et al. Apoptotic death of photoreceptors in the streptozotocin-induced diabetic rat retina. Diabetologia. 2003; 46: 1260-1268.

7 Biallosterski C, van Velthoven M, Michels R, et al. Decreased optical coherence tomography-measured pericentral retinal thickness in patients with diabetes mellitus type 1 with minimal diabetic retinopathy. Br J Ophthalmol. 2007; 91: 1135-1138.

8 Cabrera DeBuc D, Somfai GM. Early detection of retinal thickness changes in diabetes using Optical Coherence Tomography. Med Sci Monit. 2010; 16: MT15-M21.

9 Ceklic L, Maár N, Neubauer AS. Optical coherence tomography fast versus regular macular thickness mapping in diabetic retinopathy. Ophthalmic Res. 2008; 40: 235-240.

10 Bressler NM, Edwards AR, Antoszyk AN, et al.; Diabetic Retinopathy Clinical Research Network. Retinal thickness on Stratus optical coherence tomography in people with diabetes and minimal or no diabetic retinopathy. Am J Ophthalmol. 2008; 145: 894-901.

11 Yeung L, Lima VC, Garcia P, et al. Correlation between spectral domain optical coherence tomography findings and fluorescein angiography patterns in diabetic macular edema. Ophthalmology. 2009; 116: 1158-1167.

12 Wilkinson CP, Ferris FL 3rd, Klein RE, et al.; Global Diabetic Retinopathy Project Group. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology. 2003; 110: 1677-1182.

13 Ehrlich R, Harris A, Ciulla TA, et al. Diabetic macular oedema: physical, physiological and molecular factors contribute to this pathological process. Acta Ophthalmol. 2010; 88: 279-291.

14 Barber AJ. A new view of diabetic retinopathy: a neurodegenerative disease of the eye. Prog Neuropsychopharmacol Biol Psychiatry. 2003; 27: 283-290.

15 Martin PM, Roon P, Van Ells TK, et al. Death of retinal neurons in streptozotocin-induced diabetic mice. Invest Ophthalmol Vis Sci. 2004; 45: 3330-3336.

16 Lattanzio R, Brancato R, Pierro L et al. Macular thickness measured by optical coherence tomography (OCT) in diabetic patients. Eur J Ophthalmol. 2002; 12: 482-487.

17 Goebel W, Kretzchmar-Gross T. Retinal thickness in diabetic retinopathy: a study using optical coherence tomography (OCT). Retina. 2002; 22: 759-767.

18 Yang CS, Cheng CY, Lee FL, et al. Quantitative assessment of retinal thickness in diabetic patients with and without clinically significant macular edema using optical coherence tomography. Acta Ophthalmol Scand. 2001; 79: 266-270.

19 Ciresi A, Amato MC, Morreale D, et al. OCT is not useful for detection of minimal diabetic retinopathy in type 1 diabetes. Acta Diabetol. 2010; 47: 259-263.

20 Van Dijk HW, Kok PH, Garvin M, et al. Selective loss of inner retinal layer thickness in type 1 diabetic patients with minimal diabetic retinopathy. Invest Ophthalmol Vis Sci. 2009; 50: 3404-3409.

21 Asefzadeh B, Fisch BM, Parenteau CE, Cavallerano AA. Macular thickness and systemic markers for diabetes in individuals with no or mild diabetic retinopathy. Clin Experiment Ophthalmol. 2008; 36: 455-463.

22 Homa K, Majkowska L. Difficulties in interpreting HbA(1c) results. Pol Arch Med Wewn. 2010; 120: 148-154.

23 Hardie DG, Hawley SA, Scott JW. AMP-activated protein kinase – development of the energy sensor concept. J Physiol. 2009; 574: 7-15.

24 Antonetti DA, Barber AJ, Bronson SK, et al.; JDRF Diabetic Retinopathy Center Group. Diabetic retinopathy: seeing beyond glucose-induced microvascular disease. Diabetes. 2006; 55: 2401-2411.

25 Lopes de Faria JM, Russ H, Costa VP. Retinal nerve fibre layer loss in patients with type 1 diabetes mellitus without retinopathy. Br J Ophthalmol. 2002; 86: 725-728.

26 Pemp B, Polska E, Garhofer G, et al. Retinal blood flow in type 1 diabetic patients with no or mild diabetic retinopathy during euglycemic clamp. Diabetes Care. 2010; 33: 2038-2042.

27 Schmetterer L, Wolzt M. Ocular blood flow and associated functional deviations in diabetic retinopathy. Diabetologia. 1999; 42: 387-405.

28 Kohner EM, Patel V, Rassam SM. Role of blood flow and impaired autoregulation in the pathogenesis of diabetic retinopathy. Diabetes. 1995; 44: 603-607.

29 Knowler WC, Bennett PH, Ballintine EJ. Increased incidence of retinopathy in diabetics with elevated blood pressure. A six-year follow-up study in Pima Indians. N Engl J Med. 1980; 302: 645-650.

30 Grunwald JE, DuPont J, Riva CE. Retinal haemodynamics in patients with early diabetes mellitus. Br J Ophthalmol. 1996; 80: 327-331.

31 Arden GB, Sivaprasad S. Hypoxia and oxidative stress in the causation of diabetic retinopathy. Curr Diabetes Rev. 2011; 7: 291-304.

32 Samborski P, Naskręt D, Araszkiewicz A, et al. Assessment of skin autofluorescence as a marker of advanced glycation end product accumulation in type 1 diabetes. Pol Arch Med Wewn. 2011; 121: 67-72.

ARTYKUŁ ORYGINALNY

Neurodegeneracja siatkówki u chorych na cukrzycę typu 1

Aleksandra Araszkiewicz[1], Dorota Zozulińska-Ziółkiewicz[1], Mikołaj Meller[2], Jadwiga Bernardczyk-Meller[2], Stanisław Piłaciński[1], Anita Rogowicz-Frontczak[1], Dariusz Naskręt[1], Bogna Wierusz-Wysocka[1]

1 Katedra i Klinika Chorób Wewnętrznych i Diabetologii, Uniwersytet Medyczny im. K. Marcinkowskiego, Poznań
2 Specjalistyczny Okulistyczny Niepubliczny Zakład Opieki Zdrowotnej „OCU SERVICE" Poznań

SŁOWA KLUCZOWE

cukrzyca typu 1, grubość siatkówki, neurodegeneracja, optyczna koherentna tomografia, retinopatia cukrzycowa

STRESZCZENIE

WPROWADZENIE Ostatnio podkreśla się rolę zwyrodnienia neuronów siatkówki oraz komórek glejowych w patogenezie retinopatii cukrzycowej. Za pomocą optycznej koherentnej tomografii (*optical coherence tomography* – OCT) można wykonywać jakościowe i ilościowe pomiary grubości siatkówki (*retinal thickness* – RT) z identyfikacją poszczególnych warstw siatkówki.

CELE Porównanie RT, grubości warstwy włókien nerwowych siatkówki (*retinal nerve fiber layer* – RNFL) oraz warstwy komórek zwojowych (*ganglion cell layer* – GCL) mierzonych za pomocą OCT u chorych na cukrzycę typu 1 bez retinopatii oraz z klinicznie rozpoznaną retinopatią.

PACJENCI I METODY Do badania włączono 77 kolejnych chorych na cukrzycę typu 1 (39 mężczyzn, 38 kobiet; mediana wieku – 35 lat [rozstęp międzykwartylowy (*interquartile range* – IQR): 29–42]; mediana czasu trwania cukrzycy – 10 lat [IQR: 9–14]) oraz 31 osób zdrowych dobranych pod względem wieku i płci do grupy badanej. Zmierzono RT w centrum dołka, okołodołkowo i pozadołkowo, a także grubość RNFL i GCL. Podzielono chorych na cukrzycę na 2 podgrupy: z retinopatią cukrzycową i bez retinopatii.

WYNIKI Stwierdzono grubszą siatkówkę okołodołkowo ($p = 0,05$), średnią RNFL ($p = 0,002$), RNFL w dolnym kwadrancie ($p < 0,0001$) oraz GCL w górnym i dolnym kwadrancie ($p = 0,05$; $p = 0,04$) u chorych na cukrzycę w porównaniu z grupą kontrolną. Retinopatię rozpoznano u 23 pacjentów z cukrzycą (29%). W porównaniu z osobami bez retinopatii, u pacjentów z retinopatią stwierdzono cieńszą siatkówkę okołodołkowo ($p = 0,05$), mniejszą średnią grubość RNFL ($p = 0,002$), mniejszą grubość RNFL w dolnym i nosowym kwadrancie ($p = 0,002$, $p = 0,03$) oraz grubość GCL w górnym ($p = 0,05$) i dolnym kwadrancie ($p = 0,006$). Stwierdzono istotne statystycznie korelacje między czasem trwania cukrzycy a grubością RNFL w kwadrancie nosowym ($r = –0,32$; $p = 0,004$) i RT okołodołkowo ($r = –0,47$; $p < 0,001$).

WNIOSKI Wyniki mogą sugerować utratę komórek tkanki nerwowej w obrębie siatkówki u chorych na cukrzycę typu 1 z retinopatią cukrzycową. Neurodegeneracja występująca w retinopatii cukrzycowej jest ściśle związana z czasem trwania choroby.

Adres do korespondencji:
dr med. Aleksandra Araszkiewicz, Katedra i Klinika Chorób Wewnętrznych i Diabetologii, Uniwersytet Medyczny im. K. Marcinkowskiego, ul. Mickiewicza 2, 60-834 Poznań, tel./fax: 61-847-45-79, e-mail: olaaraszkiewicz@interia.pl

Praca wpłynęła: 20.07.2012.
Przyjęta do druku: 22.08.2012.
Publikacja *online*: 22.08.2012.
Nie zgłoszono sprzeczności interesów.
Pol Arch Med Wewn. 2012; 122 (10): 464-470