Research paper

Cite as: Pauk-Domańska M, Wilczewska A, Jaguś D, Kaczyński B, Jakubowski W: Doppler ultrasound-based evaluation of hemodynamic changes in the ophthalmic artery and central retinal artery in patients with type 1 diabetes mellitus without retinopathy and with mild non-proliferative retinopathy. J Ultrason 2024; 24: 9. doi: 10.15557/JoU.2024.0009.

Submitted: 25.01.2023
Accepted: 06.07.2023
Published: 29.02.2024

Doppler ultrasound-based evaluation of hemodynamic changes in the ophthalmic artery and central retinal artery in patients with type 1 diabetes mellitus without retinopathy and with mild non-proliferative retinopathy

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DOI: 10.15557/JoU.2024.0009

Keywords
diabetes mellitus; diabetic retinopathy; color Doppler imaging; blood flow velocities

Abstract

Aim: Determination of blood flow parameters in the ophthalmic artery and central retinal artery using Doppler ultrasound in patients with type 1 diabetes mellitus without fundus signs of diabetic retinopathy and with mild non-proliferative retinopathy. **Material and methods:** To eliminate the impact of other systemic factors on vascular flow, the study enrolled a total of 80 patients with type 1 diabetes mellitus, aged between 18 and 45 years. The study participants did not have any diabetic complications or other systemic or ocular comorbidities. The control group comprised 81 healthy individuals within a similar age range. Color Doppler ultrasound examinations of the ophthalmic artery and central retinal artery were performed to evaluate selected blood flow parameters including peak systolic velocity, end-diastolic velocity, and resistance index. **Results:** Patients with type 1 diabetes mellitus exhibited statistically significant decrease in both systolic and end-diastolic velocities in the central retinal artery, accompanied by an elevation in resistance index, compared to the control group. The study revealed differences in blood flow parameters between the patients without fundus changes and those exhibiting mild non-proliferative retinopathy. Specifically, patients with retinopathy showed a significant decrease in both systolic velocity and end-diastolic velocity in the central retinal artery. No differences were observed for the same parameters in the ophthalmic artery. When analyzing the patients' blood flow parameters in relation to the degree of diabetes control, as determined by glycated hemoglobin levels, a statistically significant reduction in systolic velocity was identified in both the ophthalmic and central retinal arteries in the group with poorly controlled diabetes. **Conclusions:** Examination of the orbital vessels using Doppler ultrasound in patients with type 1 diabetes mellitus holds promise as an effective method for early detection of vascular abnormalities.

Introduction

In view of the rising incidence of diabetes mellitus the search is on for new diagnostic methods to serve as markers of early diabetic changes. Diabetic retinopathy is the primary microvascular and neurodegenerative complication of diabetes. It is also the main ocular complication of diabetes and the most common reason behind vision loss among individuals between 20 and 74 years of age[(1)]. Concurrently with the rise in the incidence of diabetes, there is a noticeable increase in the occurrence of chronic microvascular complications. After 20 years, diabetic retinopathy develops in nearly all patients with type 1 diabetes mellitus and in 60% of individuals with type 2 diabetes[(2,3)]. A key role is attributed to chronic hyperglycemia leading to microcirculation disorders. Other contributory factors

include duration of the disease, comorbid hypertension, hyperlipidemia, smoking, and pregnancy. While the risk factors are well-documented, the exact pathogenesis of diabetic retinopathy is not fully understood, and the mechanisms causing vascular damage are multifaceted. The onset of the disease is influenced by a variety of aspects, including genetics, and metabolic and vascular conditions.

Evaluation of vascular flow in the retina and its supplying blood vessels by color Doppler ultrasound could serve as a valuable tool in expanding our understanding of the progression of diabetic retinopathy.

Doppler ultrasound imaging is a non-invasive diagnostic procedure used in ophthalmology to evaluate changes in blood flow in the orbital blood vessels.

The most commonly assessed vessels include the ophthalmic artery (OA), the central retinal artery (CRA), and the temporal posterior ciliary arteries (TPCA), while the main studied parameters comprise peak systolic velocity (PSV), end-diastolic velocity (EDV), and resistance index (RI), which is a measure of peripheral vascular resistance. While it is possible to determine blood velocity in these vessels, direct measurement of their diameter poses a challenge because of their small size. Despite this limitation, velocity is regarded as a good indicator of blood flow[4,5].

There are only scarce reports in the literature that specifically address blood flow in the orbital vessels in diabetic patients. Most measurements are carried out in small, heterogeneous patient groups, which diminishes the diagnostic value of results. In addition, discrepancies in the findings are frequently noted. Some sources have reported a decrease in PSV, EDV and RI in retrobulbar blood vessels in patients with diabetes, while other authors have presented opposing observations[6–12]. The discrepancies in findings might be due to differences in patient selection criteria and heterogeneity of study groups in terms of diabetes type, patient age, duration of diabetes, control of metabolic parameters, stage of retinopathy, and treatment method.

The aims of the study were to assess the blood flow parameters in the orbital vessels in the OA and CRA in patients with type 1 diabetes mellitus without changes in the fundus and with mild non-proliferative retinopathy, to compare the parameters with a control group of healthy individuals, and to examine the correlations between the blood flow values in the orbital vessels and the duration and metabolic control of diabetes measured by the level of glycated hemoglobin (HbA_{1c}).

Material and methods

The study included a total of 161 participants, with 80 individuals aged 18–45 diagnosed with type 1 diabetes mellitus and 81 healthy individuals of a similar age range, serving as the control group. The study exclusion criteria included comorbidities, systemic diabetic complications, obesity, smoking, medications other than insulin, vision defects (up to ±3.0 diopters (D)), current or past eye conditions that may affect ocular vascular flow, ocular trauma, and history of ophthalmic surgery.

The participants gave their informed consent to take part in the study, which was approved by the Ethics Committee (decision No. KB/217/2016).

The study encompassed individuals aged 18–45 years who had been diagnosed with type 1 diabetes mellitus and treated for a period ranging from one to 25 years. The patients were divided into groups based on the presence or absence of diabetic fundus changes. Another classification was determined by the degree of diabetes control, as assessed by the level of HbA_{1c}: group HbA_{1c} 5.0–7.0%, group HbA_{1c} 7.1–13.0%. The third criterion was the duration of diabetes (evaluated in increments of five years).

All participants in the study underwent a general medical assessment and laboratory tests. The results, including renal function and lipid profile, fell within the normal range for all subjects. A full ophthalmic examination with pupil dilation and indirect ophthalmoscopy using a Volk +90D focusing lens in white and red-free light were performed. Color and red-free fundus images were taken using a Topcon TRC-NW7SF Mark II fundus camera at 30° and 45°. Optical coherence tomography (OCT) was performed along with fluorescein angiography (FA) in the participants who consented to the examination with a contrast agent. Diabetic alterations were assessed according to the ETDRS (Early Treatment Diabetic Retinopathy Study) scale. Depending on the findings of the fundus examination, diabetic patients were allocated to a group without retinopathy or with mild non-proliferative retinopathy.

Doppler ultrasound examinations of blood flow in the orbital vessels were carried out using a Siemens Acuson X300 ultrasound system equipped with a VF10-5 linear transducer. Blood flow was assessed in the OA and CRA. During the examination, the patients were positioned lying on their back with closed eyelids. A linear probe with ultrasound gel was used, with no pressure applied to the eyeball. By capturing an image of the eye in B-scan presentation, the optic nerve was identified, serving as a reference point for the retrobulbar vessels. The visualization of the ophthalmic and central retinal arteries was routinely achieved with the eye positioned in a straight-ahead gaze. The OA was typically identified nasal to the optic nerve, following its path towards the medial part of the optic nerve. The CRA was visualized along with the homonymous vein in the lumen of the optic nerve, with measurements conducted prior to its passage through the lamina cribrosa. Adopting an appropriate scan depth, a narrow sampling gate (1.5 mm) was set in the vessel lumen, with an angle correction of 0–30°. In this set-up, a flow velocity spectrum was recorded for the OA (Fig. 1) and CRA (Fig. 2).

The following blood flow parameters were analyzed:

- peak systolic velocity (PSV, m/s), i.e. maximum velocity of blood flow during the systolic phase of the cardiac cycle (heart contraction);
- end-diastolic velocity (EDV, m/s), i.e. minimum velocity of blood flow during the diastolic phase before the onset of heart contraction;
- vascular resistance index (RI), or Pourcelot index, i.e. ratio of the difference between systolic and diastolic velocities to the systolic velocity of blood flow.

Statistical methodology

Upon preliminary examination, the variables were found to deviate significantly from a normal distribution, prompting the adoption

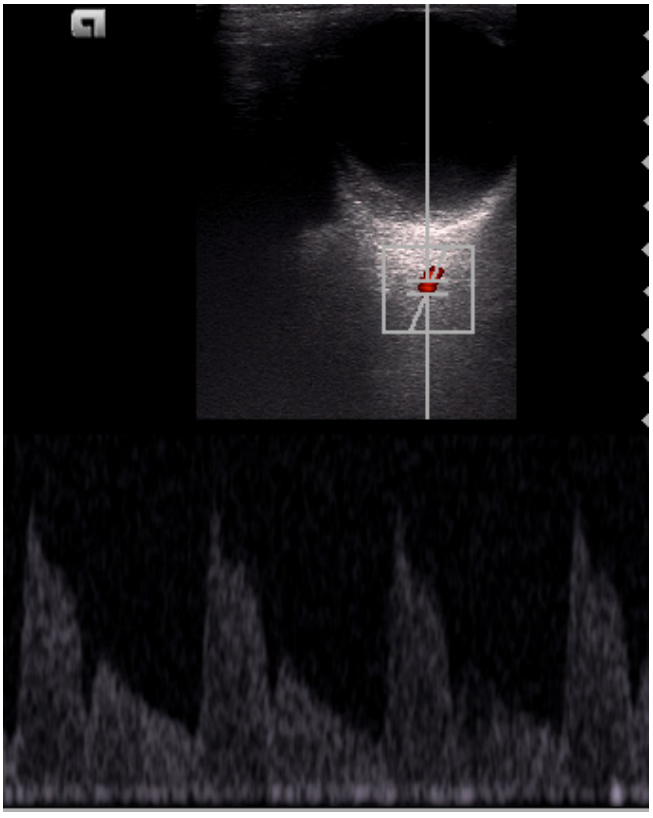

Fig. 1. *Flow velocity spectrum in the ophthalmic artery*

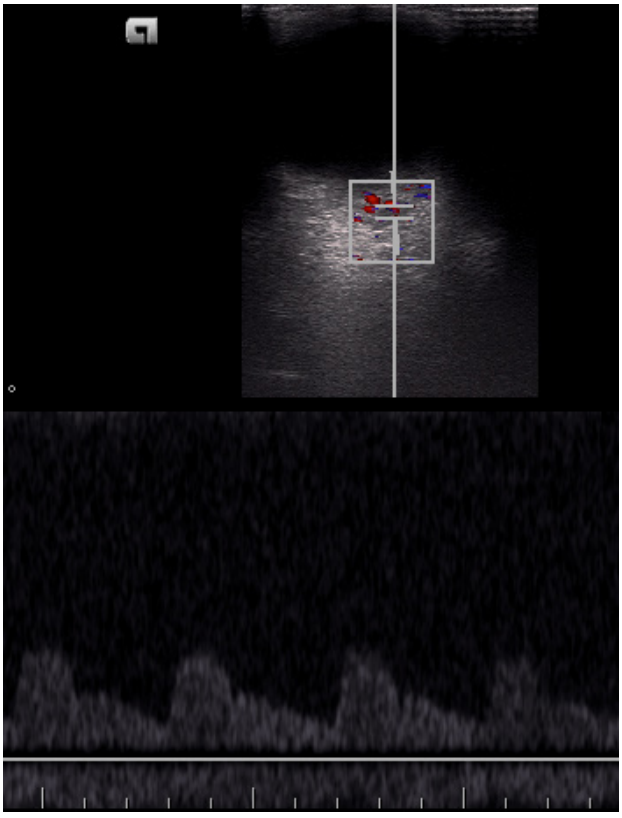

Fig. 2. *Flow velocity spectrum in the central retinal artery*

of non-parametric methods for the analysis. The basic descriptive statistics used in the study included the median and mean values, standard deviation (SD), confidence interval for the mean (95% CI), interquartile range (25–75P), and the minimum and maximum values. The primary measure compared was the median with interquartile range.

The level of statistical significance was set at $\alpha = 0.05$, and compared with the test probability '*p*' values derived from tests and correlation analysis. On that basis, it was determined whether to accept the hypothesis suggesting differences, lack thereof, or correlations between variables. All statistical analyses were conducted with the Statistica package (version 13.1PL).

Results

Characteristics of groups

The study involved a cohort of 161 individuals. The type 1 diabetes mellitus group comprised 80 patients, including 34 women and 46 men between the ages of 18 and 45 years (mean age: 28.85 years). The control group consisted of 81 healthy volunteers aged 20–39 years (mean: 26.53 years), including 53 women and 28 men.

In the study group, the duration of diabetes ranged between one and 33 years (mean: 10.4 years). Diabetic control was assessed on the basis of the level of HbA_{1c} and varied from 5.4 to 13.0% (mean: 7.58%). In the group of patients receiving insulin treatment, insulin injection pens and personal insulin pumps were used by 60 and 20 individuals, respectively. All the patients had normal blood pressure readings. The biochemical parameters (lipid, renal, and hormonal profiles) were within the normal ranges. Furthermore, no systemic complications of diabetes were found among the study participants. Aside from insulin, the patients did not use any medications and were non-smokers.

Evaluation of results

Examinations were carried out for the right and left eyes. The right eye was selected for the assessment and analysis of results. However, where the right eye met the study exclusion criteria, the left eye was selected.

Both the healthy subjects and patients had full visual acuity for both distance and near vision, and normal intraocular pressure. Appropriate correction was used to accommodate individuals with visual impairment. In the control group, no abnormalities were noted in the anterior segment and fundus of the eyes.

Patients diagnosed with type 1 diabetes mellitus were classified based on the fundus examination and digital photography, using the ETDRS (Early Treatment Diabetic Retinopathy Study) scale. Two groups were set up: one consisting of patients without clinical fundus lesions, and another with patients presenting with mild non-proliferative retinopathy, with lesions including sparse microaneurysms, petechiae, and isolated hard exudates, without concurrent macular edema.

Tab. 1. Detailed descriptive statistics for blood flow parameters (PSV, EDV, RI in the OA and CRA) in the control group

Variable	*N*	Min.	Max.	Median	25–75 P
OA PSV	80	20.1	54.3	34.4	from 29.05 to 40.10
OA EDV	79	4.3	15.1	8.6	from 6.65 to 10.10
OA RI	80	0.6	0.83	0.75	from 0.73 to 0.77
CRA PSV	80	8.7	14.5	11.1	from 10.30 to 12.00
CRA EDV	80	1.9	5.7	3.8	from 3.30 to 4.35
CRA RI	80	0.52	0.75	0.65	from 0.62 to 0.68
n – number of patients; 25–75 P – interquartile range					

Tab. 2. Detailed descriptive statistics for blood flow parameters (PSV, EDV, RI in the CRA) in the group with type 1 diabetes mellitus

Variable	*N*	Min.	Max.	Median	25–75 P
CRA PSV	80	6	14.7	10.5	from 8.70 to 11.90
CRAEDV	80	1.5	5.3	3	from 2.40 to 3.70
CRA RI	80	0.55	0.82	0.7	from 0.65 to 0.74
n – number of patients; 25–75 P – interquartile range					

Tab. 3. Descriptive statistics for blood flow parameters in the OA in the group with type 1 diabetes mellitus

Variable	*N*	Min.	Max.	Median	25–75 P
OA PSV	80	17.9	73.9	33.9	from 28.95 to 39.95
OA EDV	79	3.2	27.7	7.3	from 5.90 to 10.67
OA RI	79	0.55	0.9	0.78	from 0.71 to 0.81
n – number of patients; 25–75 P – interquartile range					

Tab. 4. Statistical relationships of blood flow parameters in the OA and CRA between the control and type 1 diabetes groups

Variable	Study group			Control group			
	n	median	25–75 P	*n*	median	25–75 P	*p*
OA PSV	80	33.9	from 28.950 to 39.950	80	34.4	from 29.05 to 40.10	0.985
OA EDV	79	7.3	from 5.900 to 10.675	79	8.6	from 6.65 to 10.10	0.1376
OA RI	79	0.78	from 0.712 to 0.810	80	0.75	from 0.73 to 0.77	0.0805
CRA PSV	80	10.5	from 8.700 to 11.900	80	11.1	from 10.30 to 12.00	0.0064
CRA EDV	80	3	from 2.400 to 3.700	80	3.8	from 3.30 to 4.35	<0.0001
CRA RI	80	0.7	from 0.650 to 0.740	80	0.65	from 0.62 to 0.68	<0.0001
n – number of patients; 25–75 P – interquartile range; *p* – test probability							

Hemodynamic parameters

The study determined the values of blood flow parameters (PSV, EDV and RI) in the ophthalmic and central retinal arteries in a group of healthy volunteers and in patients with type 1 diabetes mellitus.

Detailed descriptive statistics for blood flow parameters (PSV, EDV, RI in the CRA and OA) in the control group are shown in Tab. 1.

Detailed descriptive statistics for blood flow parameters (PSV, EDV, RI in the CRA) in the study group are shown in Tab. 2.

Detailed descriptive statistics for blood flow parameters (PSV, EDV, RI in the OA) in the control and study groups are shown in Tab. 3.

Statistical relationships of blood flow parameters in the OA and CRA between the control and study groups are shown in Tab. 4.

Central retinal artery

Among individuals with type 1 diabetes mellitus, there were statistically significant differences in blood flow parameters in the central retinal artery (a decrease in PSV and EDV, and an increase in RI) compared to the control group (p <0.05). Median PSV in the CRA was 10.5 (8.7–11.9) in the study group. In the control group, the value was significantly higher: 11.1 (10.3–12.0; p <0.006). Median EDV in the CRA was also significantly higher, reaching 3.8 (3.3–4.4) in the study group and 3 (2.4–3.7; p <0.0001) in the control group. The value of resistance index in the CRA in the study group was significantly higher at 0.70 (0.65–0.74) than in the control group, where the median was 0.65 (0.63–0.68; p <0.0001) (Tab. 4).

Differences in blood flow parameters were found between the group of patients without fundus changes and the group of subjects with mild non-proliferative retinopathy. The patients with retinopathy

Tab. 5. Statistical comparison of blood flow parameters in the OA and CRA in the group with type 1 diabetes mellitus depending on the presence of mild non-proliferative retinopathy

Variable	No retinopathy			Retinopathy			*p*
	n	median	25–75 P	*n*	median	25–75 P	
OA PSV	65	34.2	from 29.42 to 40.00	15	33.9	from 25.82 to 37.17	0.321
OA EDV	64	7.4	from 5.85 to 10.50	15	7.2	from 6.30 to 11.20	0.822
OA RI	64	0.78	from 0.72 to 0.82	15	0.75	from 0.69 to 0.79	0.220
CRA PSV	65	10.7	from 9.22 to 12.00	15	8	from 6.92 to 10.87	0.016
CRA EDV	65	3.2	from 2.50 to 3.72	15	2.7	from 2.20 to 2.97	0.024
CRA RI	65	0.7	from 0.64 to 0.74	15	0.7	from 0.65 to 0.72	0.917

n – number of patients; 25–75 P – interquartile range; *p* – test probability

Tab. 6. Statistical comparison of blood flow parameters in the OA and CRA in the group with type 1 diabetes mellitus depending on the degree of diabetes control (HbA_{1c})

Variable	>7%			<7%			*p*
	n	median	25–75 P	*n*	median	25–75 P	
OA PSV	46	31.3	from 26.50 to 36.30	34	37.8	from 32.90 to 43.40	0.0024
OA EDV	46	6.8	from 5.80 to 9.20	33	9	from 6.25 to 11.82	0.0514
OA RI	46	0.78	from 0.70 to 0.82	33	0.76	from 0.72 to 0.81	0.7959
CRA PSV	46	9.7	from 8.10 to 11.10	34	11.45	from 9.50 to 12.00	0.0382
CRA EDV	46	2.8	from 2.30 to 3.60	34	3.25	from 2.70 to 3.70	0.0679
CRA RI	46	0.695	from 0.64 to 0.74	34	0.7	from 0.65 to 0.73	0.9418

n – number of patients; 25–75 P – interquartile range, *p* – test probability

showed a significant decrease in PSV and EDV. In patients with mild non-proliferative retinopathy, the median values of maximum and minimum flow in the central retinal artery were significantly lower: 8.0 (6.9–10.8) vs. 10.7 (9.2–12.0; p <0.016) for PSV, and 2.7 (2.2–2.9; p <0.024) for EDV, compared to patients without retinopathy (Tab. 5).

Analyzing the blood flow parameters depending on the degree of diabetes control measured by the level of HbA_{1c}, a statistically significant decrease in PSV was found in the central retinal artery in the group with poorly controlled diabetes, with PSV (p = 0.038); in the subgroup with an elevated HbA_{1c} level, the median was 9.7 (8.1–11.1), while in the group with a normalized level of HbA_{1c} the median was 11.5 (9.5–12.0). The values of end-diastolic velocity (EDV) were close to the significance level (p = 0.07) (Tab. 6).

Furthermore, in the group with poorly controlled diabetes, an additional impact of retinopathy on blood flow parameters in the central retinal artery was observed, manifesting as a decrease in both systolic and diastolic velocities. In the subset of patients with long-term diabetes (over 20 years) and unstable glycemic control, a significant decline in PSV was found in the central retinal artery. There was no link between the methods of insulin delivery (insulin injection pen, personal insulin pump) and blood flow parameters in the examined arteries.

Ophthalmic artery

The ophthalmic artery was characterized by variability of blood flow parameters depending on the level of diabetes control, manifested as a significant reduction in PSV in the group with poorly controlled glycemia, as determined by the level of HbA_{1c}. A statistically significant decrease in PSV was found in the OA, with the PSV values (p <0.01) amounting to 31.3 (26.5–36.3 in the group above 7% HbA_{1c}) vs. 37.8 (32.9–43.4 in the group up to 7% HbA_{1c}). The diastolic velocity of blood flow was close to the significance level (p = 0.051).

Discussion

The assessment of blood flow parameters in the orbital vessels was carried out in a cohort of young patients with type 1 diabetes mellitus, without comorbidities, who had not yet developed diabetic changes in the fundus or exhibited early signs of mild non-proliferative diabetic retinopathy. By selecting this group of patients, it was possible to eliminate potential factors contributing to changes in the characteristics of blood flow in the orbital vessels in patients with type 1 diabetes mellitus, and to determine whether alterations in blood flow parameters in the CRA and OA could be seen in this group of patients despite the absence of changes or early changes in the fundus of the eye.

The study involved patients with a diagnosis of type 1 diabetes mellitus who exhibited changes in blood flow parameters compared to the control group, specifically a statistically significant reduction in PSV and EDV in the central retinal artery along with an increase in RI in relation to the control group.

A correlation was found between the blood flow parameters and the progression of changes in the eye fundus in this group. Alterations in blood flow parameters were evident already in individuals without diabetic changes in the fundus. However, the presence of retinopathy further decreased the blood flow velocity (specifically PSV and EDV) in the central retinal artery compared to the group

of patients where no retinal changes were observed. The findings obtained in the study point to the early onset of hemodynamic alterations in the CRA, preceding the emergence of clinical abnormalities in the fundus.

Depending on the level of glycated hemoglobin (HbA_{1c}) which serves as an indicator of diabetes control, changes in blood flow values in the OA and CRA were noted. In the group of patients with uncontrolled diabetes, significant reductions in PSV were observed both in the OA and CRA.

The duration of diabetes was found to have an impact on changes in blood flow parameters in the CRA, manifesting as a decrease in PSV, in patients who had diabetes for more than 20 years. In this group, a significant difference was observed between the individuals with stable glycemia compared to those with elevated levels of HbA_{1c}.

The ophthalmic artery was characterized by variability of blood flow parameters depending on the level of diabetes control, manifested as a significant reduction in PSV in the group with poorly controlled glycemia.

Chronic hyperglycemia disturbs the body's autoregulatory mechanisms, contributing to the onset of diabetic retinopathy by altering the diameter of blood vessels, reducing the perfusion pressure, and inducing changes in peripheral resistance[13,14]. The authors' research suggests that changes in blood flow within the orbital vessels occur in patients without and with retinopathy. Major abnormalities in blood flow parameters, specifically a significant decrease in the measured values of PSV and EDV, are noted in the central retinal artery. The deviations correlate with the severity of fundus lesions, metabolic control of diabetes, and duration of the condition. In the OA, variability in blood flow parameters was shown, depending on diabetes control, with a decrease in PSV observed in patients with elevated levels of HbA_{1c}. Hemodynamic changes observed in the central retinal artery among the study participants with type 1 diabetes mellitus without evident fundus lesions and with mild non-proliferative retinopathy might, therefore, reflect early vascular changes. The central retinal artery seems to hold particular significance as a vessel for evaluating these initial alterations. As a branch of the ophthalmic artery, the central retinal artery is anatomically terminal, and studies have found significant changes in blood flow parameters in this vessel.

Blood flow in the vessels is contingent upon both perfusion pressure and vascular resistance. These two parameters, in turn, are influenced by a range of hyperglycemia-sensitive local factors encompassing blood vessel structure and diameter, obstacles in the flow path, neurogenic and angiogenic factors, and blood rheology[15,16].

The outcomes derived from this study, including diminished PSV and EDV levels in the CRA compared to the healthy group, might suggest that ischemia and inadequate perfusion precede the onset of clinical signs of retinopathy, and increased RI in the CRA may be linked to elevated peripheral vascular resistance.

A review of publications addressing the application of Doppler ultrasound for evaluating blood flow in the orbital vessels in diabetic patients reveals discrepancies in study findings. They may be due to the absence of standardized eligibility criteria across the study groups, including variations in age ranges[7–9,17] and type of diabetes (most publications focus on correlations with type 2 diabetes or combined diabetes types)[18,19]. The groups under comparison also exhibited variations in the duration of the disease and the advancement of fundus lesions. The most commonly described hemodynamic parameters of the orbital vessels include PSV, EDV, and RI. A number of authors have reported a decrease in orbital blood flow velocity in diabetic patients, while others have observed an increase in blood flow. Vascular resistance index demonstrates variability across authors as well.[6,12,13,20].

There are only scarce reports in the literature describing hemodynamic changes in the orbital vessels in young patients with type 1 diabetes mellitus who have not yet developed diabetic changes in the fundus or the abnormalities are still in the early stages. The presence of statistically significant blood flow disruptions in the CRA in patients with type 1 diabetes mellitus without fundus changes and with early signs of retinopathy, as demonstrated in our study, appears to be an important observation, aligned with a limited number of existing reports in the literature and findings from other studies employing alternative measurement techniques for the CRA[21] or based on animal models[22], suggesting that reductions in CRA flow precede ocular fundus changes.

Our study findings align with the results of the metaanalysis of 13 studies conducted by Meng *et al.*[19] in patients without retinopathy and with diabetic retinopathy who had their blood parameters assessed by color Doppler. Just two out of the 13 publications reviewed focused specifically on individuals with type 1 diabetes mellitus. The remaining studies either involved patients with type 2 diabetes or comprised a mixed group, reflecting the scarcity of literature discussing hemodynamic alterations in type 1 diabetes mellitus. Referring to studies involving patients with type 2 diabetes mellitus might result in an inaccurate assessment of hemodynamic changes. Typically, these patients represent a different age group and often present with systemic complications, including vascular abnormalities. Consequently, this particular group, as well as patients with type 1 diabetes mellitus and advanced fundus changes, were excluded from the discussion. In the available literature, some researchers studying patients with type 1 diabetes have reported findings consistent with those observed by the authors of this paper, including an elevation in RI in the OA and CRA, indicating a probable rise in peripheral vascular resistance. Additionally, a significant decline in PSV and EDV in the CRA has been reported, potentially suggesting ischemia and compromised blood perfusion even before the onset of clinical features indicative of diabetic retinopathy. Kawagishi *et al.*[6] assessed the blood flow parameters in the central retinal artery in patients diagnosed with type 1 diabetes mellitus without retinopathy, and compared the measurements with those in the control group. Similar to the authors of this paper, the researchers obtained significantly lower PSV and EDV values in the CRA and increased RI in the CRA, which indicates that hemodynamic changes in the retinal vessels emerge before the onset of clinical symptoms of diabetic retinopathy. Varying results were obtained for the CRA and OA by Ovali *et al.*[20] in young patients diagnosed with type 1 diabetes mellitus but without retinopathy. The study group was characterized by a wide age range (2–20 years). The researchers observed elevated EDV in the OA compared to the control group and reduced RI values in the OA in diabetic patients over five years of age. In cases where diabetes was accompanied by microalbuminuria, there was an observed increase in RI in the CRA. Modrzejewska *et al.*[23] evaluated the retrobulbar arterial flow characteristics in a cohort of young individuals with

type 1 diabetes mellitus but without fundus lesions and in a control group, examining the relationship between these arterial blood flow parameters and serum lipid levels. The study revealed a reduction in PSV in the CRA compared to the control group, and a decrease in RI. A similar relationship was observed in the OA and TPCA. Disturbances in the lipid profile were associated with fluctuations in vascular resistance, primarily in the OA. The authors concluded that reduced values of RI in the CRA and TPCA, and of PI in the TPCA might be linked to the early-onset dilation of retinal arterioles and precapillary vessels resulting from vascular dysregulation. Research conducted by the authors revealed a decrease in blood flow parameters (a significant reduction in PSV in the OA) only in patients with poorly controlled diabetes, with HbA_{1c} >7. A decrease was also noted in EDV (close to the level of significance). Similar associations were reported by Ozates *et al.*[24]. The authors found reduced PSV and EDV values and elevated PI in the OA in patients with type 1 diabetes mellitus without signs of diabetic retinopathy in the fundus, with recently diagnosed type 1 diabetes. The observed decreased blood velocity and increased PI values may be attributed to vascular changes and elevated vascular resistance.

Conclusions

In summary, the findings of the reported study may indicate that alterations in blood flow parameters in the central retinal artery reflect vascular dysfunction preceding the onset of visible signs of retinopathy. Thus, they might serve as sensitive markers of hemodynamic disorders in patients with type 1 diabetes mellitus without fundus changes, and they are more prominent in patients presenting with signs of retinopathy. Uncontrolled diabetes, measured by the level of HbA_{1c}, further decreases vascular flow velocity both in the CRA and OA. The duration of diabetes and the level of glycemic control, which are widely recognized as the most critical risk factors for the development of microangiopathy, were also mirrored in the hemodynamic changes in the orbital vessels found in the study. However, what appears to be particularly important is the fact that changes in blood flow parameters occurred in the early stages of diabetes, even before the onset of retinopathy, which highlights the value of the adopted research methodology and substantiates the need for further studies in this area.

Conflict of interest

The authors do not declare any financial or personal links with other persons or organizations that might adversely affect the content of the publication or claim any right to the publication.

Author contributions

Original concept of study: MPD. Writing of manuscript: MPD, BK. Analysis and interpretation of data: MPD, AW, BK. Final approval of manuscript: MPD, WJ. Collection, recording and/or compilation of data: MPD, AW, DJ. Critical review of manuscript: MPD, WJ.

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