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Anatomical and functional testing in diabetic patients without retinopathy: results of optical coherence tomography angiography and visual acuity under varying contrast and luminance conditions

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Abstract

Purpose—To assess early retinal microvascular and functional changes in diabetic patients without clinical evidence of diabetic retinopathy (DR) with optical coherence tomography angiography (OCTA) and central visual analyzer (CVA).

Methods—This was an observational case-control study of diabetic patients without DR and non-diabetic controls. Patients underwent OCTA imaging and visual acuity testing using the CVA. The foveal avascular zone (FAZ) area and the capillary density (CD) in the superficial and deep capillary plexuses were measured manually by a masked grader.

Results—Sixty eyes from 35 diabetic patients were included in the study group and 45 eyes from 31 non-diabetic patients were included in the control group. FAZ area was not significantly different between the diabetic group and controls (both $p > 0.05$). The mean CD in the deep capillary plexus was significantly lower in diabetic eyes compared with control eyes ($p = 0.04$).

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The study was conducted and completed in the Jacobs Retina Center at the Shiley Eye Institute, University of California San Diego, La Jolla, California.

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The mean visual acuity in all CVA modules was significantly decreased in diabetic patients compared with controls (all $p < 0.05$).

Conclusion—OCTA was able to detect retinal microvascular changes in the deep capillary plexus and the CVA showed signs of decreased visual acuity under conditions simulating suboptimal contrast and glare in diabetic patients without DR.

Keywords

diabetes mellitus; diabetic retinopathy; optical coherence tomography angiography; contrast sensitivity

Introduction

Diabetic retinopathy (DR), is the most common cause of visual impairment and blindness in working-age individuals.[1,2] Early detection and screening for retinopathy is important to decrease the risk of vision loss.[3] Diagnosis of DR is usually based on clinical examination and manual or automated analysis of color fundus photographs, fluorescein angiography images and optical coherence tomography (OCT) scans.[4,5] However, this approach can detect DR only after the development of clinical signs, such as microaneurysms, retinal hemorrhages or macular edema, and cannot recognize preclinical retinal microvascular changes or functional deficits. We aimed to evaluate new diagnostic methods to detect early anatomical and functional changes in diabetic patients without DR.

OCT angiography (OCTA) is a relatively new imaging method that can be used to assess and quantify the retinal and choroidal microcirculation noninvasively. It generates highly detailed, high resolution image of the macular microvascular networks in a depth-resolved fashion, allowing each capillary layer to be studied separately.[6,7] OCTA has been shown to be useful in detecting retinal microcirculatory disturbance in diabetic patients with retinopathy.[8–17] The foveal avascular zone (FAZ) area in both the superficial and deep capillary plexuses is enlarged in diabetic eyes compared to healthy eyes and significantly correlates with visual acuity.[8–11] Macular capillary density has been reported to progressively decrease as the DR severity worsens, and vessel density measurements are able to distinguish healthy eyes from eyes with DR.[11–15] Furthermore, macular photoreceptor disruption on OCT in patients with DR has been shown to correspond to areas of capillary nonperfusion at the deep capillary plexus (DCP) on OCTA.[16] These findings suggest that OCTA is very sensitive to microcirculatory abnormalities in DR and may be useful to detect early anatomical changes prior to the onset of clinical retinopathy.[8,17–19]

Another approach to early DR diagnosis is through functional tests. Retinal neurodegeneration is an important and early component of diabetic retinopathy that may precede detectable microcirculatory abnormalities.[20,21] As a result of neurodegeneration, there have been reports showing early functional deficits in contrast sensitivity and color discrimination in diabetic patients that occur prior to clinical retinopathy.[22,23] Utilizing measures such as contrast sensitivity may assist physicians in the earlier detection of patients in the initial stages of retinopathy.

The central visual analyzer (CVA) (Sinclair Technologies, LLC, Media, Pennsylvania, USA) is an FDA-approved device that enables testing of central vision under a variety of surroundings that resemble varying contrast and luminance conditions.[24] The CVA has previously been used to assess time-dependent visual acuity, contrast sensitivity, and photopic glare in patients with age-related macular degeneration and patients after cataract surgery using realistic scenarios mimicking different lighting situations.[24,25]

The aim of this study was to assess early retinal microvascular and functional changes in diabetic patients without clinical evidence of DR using OCTA and CVA, respectively. In addition, we sought to determine if anatomical changes identified by OCTA correlated with functional alterations by CVA in these patients.

Methods

An observational case-control study was conducted according to the principles of the Helsinki Declaration. Institutional Review Board (IRB) approval was acquired from the University of California San Diego for the review and analysis of patients' data. The study complied with the Health Insurance Portability and Accountability Act of 1996.

Consecutive patients with diabetes mellitus (DM) type 1 or 2 seen between June 2015 and August 2017 by 2 retina specialists (W.R.F, E.N.) at the Shiley Eye Institute, University of California, San Diego, were enrolled prospectively in this study. Inclusion criteria for the study group was patients with a diagnosis of diabetes but without any clinical signs of diabetic retinopathy on funduscopic examination such as dot blot hemorrhages or microaneurysms; no signs of diabetic retinopathy on fluorescein angiography (FA) such as microaneurysms, capillary non-perfusion or leakage; normal retinal layers without edema on spectral-domain optical coherence tomography (SD-OCT); and visual acuity of 20/25 or better. Exclusion criteria were age less than 18 years, any history of prior treatment for diabetic retinopathy such as laser or anti-vascular endothelial growth factor therapy, and other ocular pathology except for mild cataract. During the study enrollment period, 38 diabetic patients had no clinical signs of retinopathy on funduscopic examination. Three of them were excluded from the study based on diabetic retinopathy signs on FA. Age-matched non-diabetic patients without any retinal pathology or history of ocular trauma were included in this study as controls.

Patients meeting the inclusion criteria underwent a comprehensive ophthalmic evaluation, including manifest refraction (MR), slit-lamp biomicroscopy examination and full dilated funduscopic examination. Measurement of distance best corrected visual acuity (BCVA) was tested with existing corrective lenses (if worn) or trial frames according to the result of the MR using the Early Treatment for Diabetic Retinopathy Study (ETDRS) chart. The FDA-approved CVA was used to assess central visual acuity (CVA-VA) under a variety of contrast and luminance conditions. The patients used the correction obtained from the MR in their glasses or trial frames when the CVA was performed. All testing conditions, including room illumination, distance between subject and eye chart or CVA device, visual acuity and refractive error measurements were kept identical for all subjects. The logarithm of the

minimum angle of resolution (logMAR) results for both BCVA and CVA-VA were used for statistical analysis.

The clinical evaluation also included imaging with either intravenous or oral FA, SD-OCT (Heidelberg Spectralis HRA+OCT, Heidelberg Engineering, Heidelberg, Germany) and OCTA (Optovue RTVue XR Avanti, Optovue, Inc, Fremont, CA). Demographic and clinical information including DM duration, hemoglobin A1c (HbA1c) level, hypertension, hyperlipidemia and smoking status was obtained from the medical charts.

OCTA Imaging Protocol

A split-spectrum amplitude-decorrelation angiography was obtained with the Optovue RTVue XR Avanti device (70,000 A-scan/second, wave length of 840 nm). A 3×3-mm scanning area, centered on the fovea, was performed. Each OCTA volume contained 304×304 A-scans with 2 consecutive B-scans captured at each fixed position before proceeding to the next sampling location. Two orthogonal OCTA volumes were acquired to minimize motion artifacts and fixation changes. Image segmentation was performed using the built-in ReVue software version 2015.100.0.35. The superficial capillary plexus (SCP) image was automatically segmented with an inner boundary at 3 μm beneath the internal limiting membrane and an outer boundary set at 16 μm beneath the inner plexiform layer (IPL), whereas the deep capillary plexus (DCP) image had its inner boundary at 16 μm beneath the IPL and an outer boundary at 72 μm beneath the IPL.

Foveal Avascular Zone Measurement

Measurement of the FAZ area in each layer was performed by a single masked grader (A.M.) using the ImageJ software version 1.50i (National Institutes of Health, Bethesda, MD). The image size was 304 × 304 pixels. The magic wand tool was used to manually demarcate the boundaries of the FAZ after the innermost capillaries in the fovea were identified. A tolerance of 15 was used. Fine tuning of the FAZ boundaries was done with the oval selections tool (Figure 1A). The area measurement function was then used to determine the FAZ area in pixels and this value was converted to millimeters squared (mm^2) using scale conversion.

Capillary Density Measurement

Image analysis to measure capillary density (CD) in each layer was done by a single masked grader (A.M.) using Adobe Photoshop CS6 (Adobe Systems Inc, San Jose, CA), as previously described.[26] CD was defined as the percentage of the scan area occupied by capillaries. Each en face image was opened and rendered in Adobe-RGB color scheme, and the color range selector was used to select the color black, defined by the color scheme as RGB = 0-0-0. The inverse button was used to deselect black and select all other colors outside the black region. This was presumed as the amount of capillaries within the image. A fuzziness factor, which sets the tolerance of the color range included in the selection, was set to 140. This value yielded the most accurate vessel detection and used in all image analyses for standardization. The amount of capillaries selected was expressed in pixels in the histogram, and capillary density was expressed as percent capillaries occupied in one

image (Figure 1B). This was calculated as the amount of pixels selected divided by the total pixels (92,416 pixels) in each en face image.

Central visual analyzer test

The CVA measures central vision for six sequential modules that emulate activities of daily living that patients may experience on a routine basis. The mesopic modules, M1-3, simulate conditions with varying contrast and the photopic modules, G1-3, simulate conditions with glare. Real-life conditions simulated include high contrast situations (M1), reading in a dimly-lit environment (M2), driving at dusk (M3), reading high contrast optotypes with glare (G1), being outside with direct overhead sunlight (G2), and being outside with off-axis sunlight (G3). The modules are timed and each letter is presented for less than a second (900 milliseconds). Each module takes two minutes to complete. The patient is first presented with sequential 98% Michelson contrast white Landolt C's on a background luminance of 1.6 cd/m^2 to determine best visual acuity. The modules then vary the Michelson contrast from 8% to 98% and the background luminance from 1.6 to 220 cd/m^2 and progressively diminishing steps of 0.05 logMAR are used to determine a threshold for that contrast setting. Following the six modules, a repeat test of high contrast letters is performed to evaluate reliability.

The module that most closely simulates conventional acuity is G1 as it reflects photopic VA under high contrast conditions but the CVA is a timed test unlike the ETDRS where there is no time constraint. The mean logMAR G1 CVA-VA was worse than the mean logMAR BCVA in both groups (Tables 1 and 2), although this difference was statistically significant only in the diabetic group (diabetics $p < 0.001$, controls $p = 0.20$). This difference represents the effect timing has on the visual acuity test.

Statistical analysis

For continuous variables, data were presented as means with standard deviations or 95% confidence interval, while categorical variables were expressed in fractions or percentages. The parameters from the OCTA and CVA were used as response variables and group as main independent variable along with the other independent variables including age, sex, refraction, and lens status. Some independent variables such as diabetic duration, HbA1C, hypertension and hyperlipidemia were only available in diabetic group or significantly more with the diabetic group. These parameters were not included in the multivariable regression analysis to avoid the collinearity issue. In addition, two eyes of the same patient were studied; therefore, patient ID was assigned as random effect when the linear regression was performed using Jumper statistical software version 13. The Pearson correlation coefficient of the OCTA and CVA parameters between the right and left eyes in patients where both eyes were tested ($n = 39$) is presented in table 3. A pairwise correlations among the available parameters within each study group were also examined. P value smaller than 0.05 was considered statistically significant.

Results

Sixty eyes from 35 diabetic patients (51.4% male, 83% DM type 2) of average age 58.5 years (range 34–93) were included in the study group. These patients had an average HbA1c level of 6.75% (range 5.6%–9.3%) and a diagnosis of diabetes for approximately 9 years (range 1–39 years). For the control group, 45 eyes from 31 non-diabetic patients (38.7% male) of average age 59 years (range 40–75) were analyzed. The mean BCVA was approximately −0.025 logMAR (Snellen equivalent, 20/19; range, 20/12.5–20/25) in both groups. The mean spherical equivalent refraction was −0.75 (range −6.25 to +3.13) in the study group and −0.66 (range −7.50 to +2.00) in the control group. There was no significant difference in the mean age, gender, mean BCVA, mean spherical equivalent refraction, smoking status or lens status between the two groups (Table 1). There were significantly more patients with hypertension and hyperlipidemia in the study group than in the control group (both $p < 0.02$).

OCTA parameters

Measurements of the FAZ area and CD in the superficial and deep capillary plexuses in the diabetic and control groups are presented in Table 2. The comparison between the groups was controlled for age, sex, refraction and lens status and the use of 2 eyes from the same patient was accounted for. The superficial and deep FAZ areas were not significantly different between the diabetic group and control group (SCP: $p = 0.36$, DCP: $p = 0.46$). The mean superficial CD was not significantly different between the groups ($p = 0.71$), whereas the mean deep CD was significantly lower in diabetic eyes (52.74%, range 37.03%–65.15%) compared with control eyes (55.45%, range 45.82%–65.12%) ($p = 0.04$).

Pairwise correlation analysis did not show any significant correlation between FAZ area and age, BCVA, HbA1c level and diabetes duration. However, the superficial and deep CDs were negatively correlated with age and logMAR BCVA in both the diabetic and control groups (Table 4) (Figure 2). No correlation was found between CD and HbA1c level or diabetes duration.

CVA parameters

The logMAR VA measurements of the 6 modules of the CVA for the diabetic and control groups are shown in Table 2. The mean logMAR CVA-VA in all modules was significantly higher (worse) in diabetic eyes compared with control eyes (all $p < 0.05$) (Figure 3). Pairwise correlation analysis did not show any significant correlation between the CVA modules and HbA1c level, diabetes duration or OCTA parameters.

Discussion

Here we report a series of diabetic patients without retinopathy that showed significant anatomical and functional changes measured with OCTA and CVA, respectively. The CD in the DCP was lower and the visual acuities obtained with the CVA were worse in all the modules measured in the diabetic group compared to age-matched non-diabetic controls. These results suggest that diabetic patients may develop an early capillary dropout at the DCP level and experience a decline in contrast sensitivity and visual acuity under glare

conditions prior to the clinical expression of retinopathy compared to patients without diabetes.

Enlargement of the FAZ area in patient with DR has been well documented with FA[27,28] and OCTA[8,9,11] imaging. However, in this study, the superficial and deep FAZ areas in diabetic patients without retinopathy were not significantly different from controls. Two previous studies reported on the early retinal microvascular changes in OCTA in type 1 DM patients without or early retinopathy.[18,19] Consistent with our results, neither study found a significant difference in FAZ area in the SCP and DCP between diabetic patients and controls. However, several reports have shown evidence of OCTA FAZ area enlargement in diabetic eyes without retinopathy compared with normal eyes.[8,29,30] De Carlo et al[29] measured the FAZ area in 61 eyes of 39 type 1 and type 2 DM patient using the full-thickness OCTA image. They found that the average FAZ area was larger in diabetic patients (0.348 ± 0.10 mm^2) compared with controls (0.288 ± 0.14 mm^2). This difference was weakly significant ($p = 0.04$). Dimitrova et al[30] found that the FAZ area was larger only in the SCP, but not in the DCP, in 29 type 2 diabetic patients with no retinopathy. Although our study population had a majority of type 2 DM patients, our results support the evidence against significant FAZ area changes prior to development of DR. Perhaps, FAZ area remodeling and enlargement appear at a later and more advanced stage of DR. Additionally, normal FAZ area may indicate that in eyes without apparent retinopathy, early microvascular changes may be reversible with good control of diabetes, as our patients had low HbA1c levels. It would be of interest in the future to correlate FAZ area and remodeling with other microvascular changes commonly affected by diabetes, i.e. microalbuminuria, presence of peripheral neuropathy, as well as changes associated with diabetes control in the same patient.

Retinal capillary density measured by OCTA was shown to be adversely affected in DR eyes and was correlated with disease severity.[9,11–15] We found that the CD was decreased in the DCP in diabetic patients even before the clinical signs of retinopathy despite some overlap with the control group. Half of the eyes in the diabetic group were within 1 standard deviation of the mean deep CD value of the control group. This overlap may be due to the relatively small difference between healthy and well controlled diabetic patients and the large standard deviation. A larger sample size would help to differentiate these group more accurately.

Decrease of retinal vessel density in OCTA was previously reported for both type 1[18,19] and type 2[30,31] DM patients without retinopathy. Chen et al[31] quantified the density of retinal capillary layers by fractal analysis in 48 type 2 DM patients with no retinopathy. They found that the fractal dimensional parameter of the capillary layer was decreased in the deep retinal capillary layer, but not in the superficial layer. Similarly, CD was decreased only in the DCP in type 1 DM patients without retinopathy.[18,19] These findings suggest that CD decrease is an early process in diabetic eyes and may initially occur in the DCP. Animal models also demonstrated more vascular abnormalities in the deep vascular network than in the superficial network in diabetic mice.[32] Thus, CD in the DCP may serve as an early and sensitive indicator of microvascular loss in diabetic patients.

We found no correlation between the FAZ area or the CD and diabetes duration or hemoglobin A1c level. This was consistent with previous reports in the literature in both type 1 and type 2 DM patients.[8,14,18,19] The lack of correlation between retinal microvascular measurements and clinical diabetic parameters suggests that OCTA is not a good indicator for diabetes duration or glycemic control. In this study, CD, but not FAZ area, was significantly correlated with BCVA and age in both diabetics and controls. Recent studies found that OCTA FAZ size was correlated with BCVA in eyes with diabetic retinopathy and was a significant predictor of vision in such eyes.[10,11] In our cohort, all patients had good BCVA with a small standard deviation, which may explain the absence of such correlation in our study. However, CD at both the superficial and deep capillary plexuses did show correlation with BCVA despite the narrow range of visual acuities. Similarly, Samara et al[11] found an association between vascular density and visual acuity in diabetic patients. Further study is needed to elucidate whether CD measured by OCTA could predict visual function independently.

Several groups have evaluated contrast sensitivity in diabetics without retinopathy. Stavrou et al[33] reported decreased contrast sensitivity using the Pelli-Robson chart but normal high contrast visual acuity in patients with early or no retinopathy. Sokol et al[34] found decreased contrast sensitivity at one higher spatial frequency in non-insulin dependent diabetics without retinopathy. Using the Arden grading test, Ghafour et al[23] found decreased sensitivities at higher spatial frequencies in diabetic patients without clinical retinopathy.

The decreased contrast sensitivity in diabetic patients may be linked to early retinal neuronal degeneration. Decreased thickness of the radial nerve fiber layer (RNFL) and ganglion cell complex have been described using SD-OCT in both type 1 and type 2 diabetic eyes prior to funduscopic evidence of retinopathy.[35,36] Neriyanuri et al[37] reported RNFL thinning, impaired color vision and reduced contrast and retinal sensitivity in type 2 DM subjects with no DR. In type 1 diabetes, Stem et al[38] found a direct correlation between inner nuclear layer thickness on OCT imaging with contrast sensitivity after controlling for age. Furthermore, a functional decrease in the magnocellular ganglion cell response, which is important in contrast discrimination, has been documented in diabetic patients with and without retinopathy when compared to controls.[39] The neuronal degeneration that precedes microvascular degeneration clinically manifests as impaired visual response to low-contrast stimuli.

Our results validate the clinical significance of decreased visual acuity under varied lighting conditions that may result in glare or decreased contrast. Moreover, while visual acuity remained unchanged in our patients, our results suggest that there is significant deterioration in the quality of vision under varying light conditions. In module M3 of the CVA, simulating driving at dusk, there was a statistically significant difference between the control group and the diabetic group with logMAR CVA-VA of 0.38 (Snellen equivalent, 20/48) and 0.55 (Snellen equivalent, 20/71), respectively. Our results show that diabetic patients before evidence of retinopathy may suffer from greater deterioration of visual acuity when driving at or after dusk when compared to non-diabetic patients. Similarly, results from module M2 suggest diabetic patients may suffer from decreased visual acuity in dim-light reading

conditions even prior to the onset of retinopathy. These patients may benefit from maximized lighting conditions while reading or minimizing driving at nighttime.

It is believed that retinal neurodegeneration is an early component of DR which may precede visible vasculopathy.[40] Both anatomical and functional alterations were found in our non-retinopathy diabetic patients. To the best of our knowledge, this is the first time that both retinal microvascular degeneration and decreased visual function are reported in diabetic patients without retinopathy. This anatomical-functional coupling is best explained by considering the retinal neurons, glial cells and blood vessels as an integrated neurovascular unit.[41] An example of this neurovascular unit dysfunction in diabetic patients is the impairment of vascular autoregulation mechanisms in response to flickering light stimulation.[42,43] The high resolution and segmentation abilities of OCTA and the high sensitivity of CVA allowed us to demonstrate that vascular and functional impairment coexisted in DM patients with no overt retinopathy. However, no correlation was found between the OCTA parameters and the CVA modules. The degree of decrease in contrast sensitivity and visual acuity under glare conditions was more significant than the retinal capillary damage in our patients. This may imply that visual function impairment is an earlier manifestation and a more sensitive indicator for neurovascular damage in DM.

Limitations of our study include pooling of both type 1 and type 2 diabetic patients, the relatively small sample size, OCTA parameters measurement by a single grader and lack of scotopic glare testing by the CVA. Moreover, patients in the diabetic group had significantly more hypertension and hyperlipidemia than patients in the control group. These comorbidities might have contributed to the retinal vascular changes. Projection artifact is another issue that might have influenced our results. Projection of the SCP may appear on the reconstruction of the DCP. A commercial software version that eliminate such artifacts was not available for the Optovue OCTA device when the study was conducted.

In conclusion, deep capillary density and visual acuity in simulated conditions with low contrast and glare were decreased in diabetic patients without evidence of retinopathy. This early neurovascular damage may help in counseling diabetic patients, including those without evidence of retinopathy. Further studies including these pre-clinical markers are needed to evaluate their prognostic power to predict the development of overt diabetic retinopathy.

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Summary statement

Diabetic patients may develop an early capillary dropout at the deep capillary plexus and experience a decline in contrast sensitivity and visual acuity under glare conditions prior to the clinical expression of retinopathy.

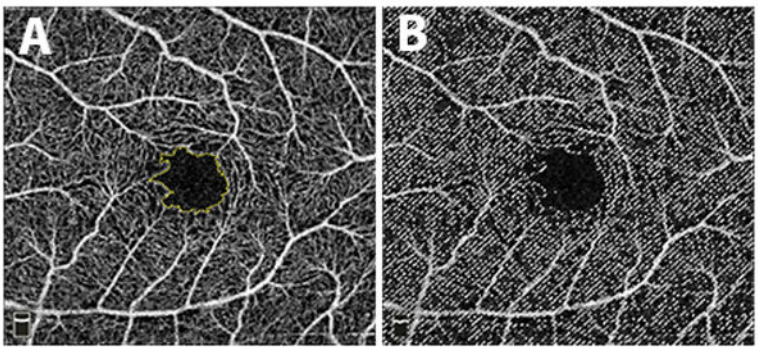

Figure 1.

Measurement of the foveal avascular zone (FAZ) area and capillary density (CD) in the en face optical coherence tomography angiography (OCTA) image. **A.** The boundaries of the FAZ (yellow line) were manually demarcated and the FAZ area was measured with the ImageJ software. **B.** The retinal capillaries were selected with Adobe Photoshop software by deselecting the black color. The amount of capillaries selected was expressed in pixels in the histogram and divided by the total number of pixels to calculate the CD.

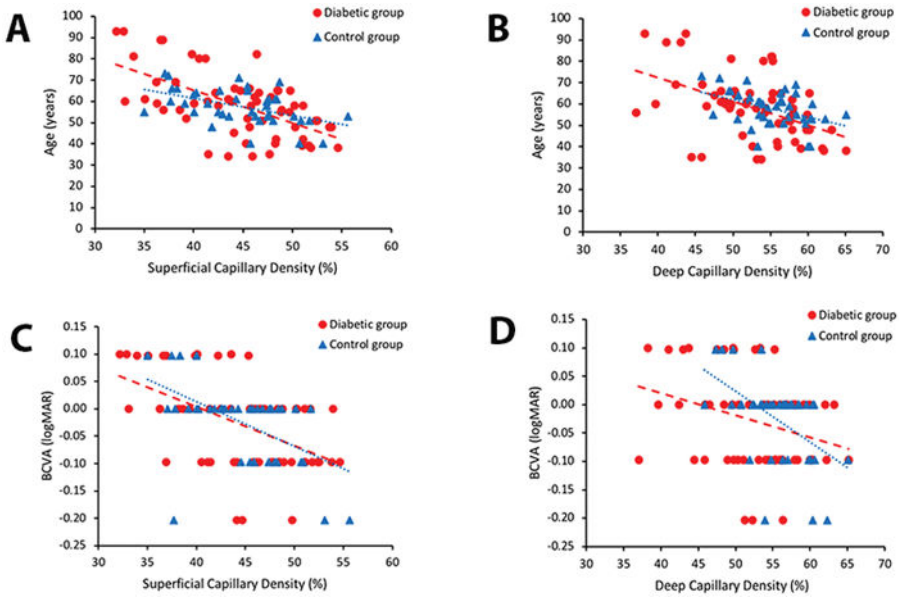

Figure 2.

Scatterplots showing correlation between capillary density (CD), age and best corrected visual acuity (BCVA) in the diabetic (red) and control (blue) groups. A trend line is presented for the diabetic group (dashed line) and control group (dotted line). A significant negative correlation between CD and age is present in both the superficial (A) and deep (B) networks in the two groups. Similarly, a significant negative correlation is present between CD and BCVA in both the superficial (C) and deep (D) networks in the two groups. The correlation coefficients are presented in Table 4.

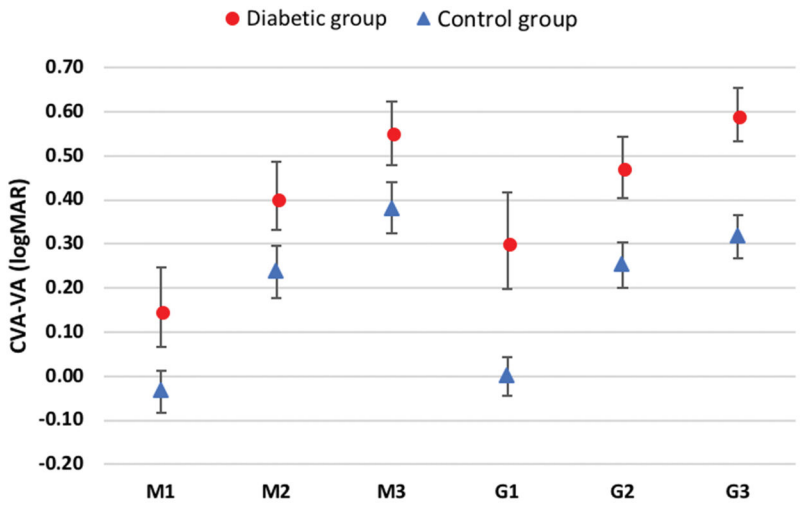

Figure 3.

Comparison of central visual analyzer (CVA) logarithm of the minimum angle of resolution (logMAR) visual acuity (CVA-VA) between the diabetic and control groups. The markers represent the mean logMAR visual acuity as tested on the 6 modules of the CVA (M1, M2, M3, G1, G2, G3). The bars represent 95% confidence interval.

Table 1

Demographic and clinical characteristics.

	Diabetic group (n = 35)	Control group (n = 31)	P value
Number of eyes	60	45	
Mean age, year ± SD (range)	58.5 ± 14.6 (34–93)	58.9 ± 9.0 (40–75)	0.89
Gender, male, n (%)	18 (51.4)	12 (38.7)	0.33
Diabetes mellitus type 2, n (%)	29 (82.9)	n/a	
Mean diabetes duration, year ± SD (range)	9.23 ± 9.3 (1–39)	n/a	
Mean HbA1c level, % ± SD (range)	6.75 ± 0.9 (5.6–9.3)	n/a	
Hypertension, n (%)	22 (66.7)	10 (33.3)	**0.01**
Hyperlipidemia, n (%)	25 (75.8)	7 (23.3)	< **0.001**
Smoking, n (%)	7 (21.9)	1 (3.4)	0.06
Mean BCVA, logMAR ± SD (Snellen equivalent; range)	−0.03 ± 0.08 (20/18.5; 20/12.5–20/25)	−0.02 ± 0.07 (20/19; 20/12.5–20/25)	0.40
Mean refraction (SE), diopters ± SD (range)	−0.75 ± 1.95 (−6.25 – +3.13)	−0.66 ± 2.46 (−7.50 – +2.00)	0.43
Lens status			0.77
Clear crystalline lens, n (%)	21 (35)	16 (35.6)	
Mild cataract, n (%)	31 (51.7)	25 (55.6)	
Pseudophakia, n (%)	8 (13.3)	4 (8.8)	

SD = standard deviation, HbA1c = hemoglobin A1c, BCVA = best corrected visual acuity, logMAR = logarithm of the minimum angle of resolution, SE = spherical equivalent.

Table 2

Comparison of optical coherence tomography angiography and central visual analyzer parameters between the diabetic and control groups.

	Diabetic group	Control group	p value
OCTA parameters			
Mean superficial FAZ area, mm^2 ± SD (range)	0.251 ± 0.09 (0.099–0.556)	0.261 ± 0.11 (0.095–0.539)	0.36
Mean deep FAZ area, mm^2 ± SD (range)	0.311 ± 0.09 (0.129–0.597)	0.320 ± 0.11 (0.102–0.556)	0.46
Mean superficial CD, % ± SD (range)	44.61 ± 5.9 (32.18–54.63)	44.75 ± 4. 9 (35.03–55.61)	0.71
Mean deep CD, % ± SD (range)	52.74 ± 6.3 (37.03–65.15)	55.45 ± 4.3 (45.82–65.12)	**0.04**
CVA parameters			
Mean M1 CVA-VA, logMAR ± SD (Snellen equivalent; range)	0.150 ± 0.35 (20/28; 20/8–20/225)	−0.034 ± 0.17 (20/18.5; 20/8–20/36)	**0.02**
Mean M2 CVA-VA, logMAR ± SD (Snellen equivalent; range)	0.405 ± 0.32 (20/51; 20/8–20/285)	0.239 ± 0.21 (20/35; 20/8–20/100)	**0.008**
Mean M3 CVA-VA, logMAR ± SD (Snellen equivalent; range)	0.553 ± 0.28 (20/71; 20/17–20/400)	0.380 ± 0.20 (20/48; 20/25–20/112)	**0.003**
Mean G1 CVA-VA, logMAR ± SD (Snellen equivalent; range)	0.304 ± 0.43 (20/40; 20/8–20/225)	0.001 ± 0.14 (20/20; 20/8–20/36)	**0.004**
Mean G2 CVA-VA, logMAR ± SD (Snellen equivalent; range)	0.473 ± 0.27 (20/60; 20/17–20/400)	0.253 ± 0.19 (20/36; 20/10–20/90)	**0.001**
Mean G3 CVA-VA, logMAR ± SD (Snellen equivalent; range)	0.593 ± 0.25 (20/78; 20/28–20/400)	0.317 ± 0.17 (20/41; 20/20–20/142)	**<0.0001**

OCTA = optical coherence tomography angiography, FAZ = foveal avascular zone, SD = standard deviation, CD = capillary density, CVA = central visual analyzer, CVA-VA = central visual analyzer visual acuity, logMAR = logarithm of the minimum angle of resolution.

Table 3

Pearson correlation of the OCTA and CVA parameters between the right and left eyes.

n = 39	Correlation coefficient	95% CI	p value
Superficial FAZ area	0.94	0.89–96	< **0.001**
Deep FAZ area	0.80	0.60–0.91	< **0.001**
Superficial CD	0.59	0.32–0.79	< **0.001**
Deep CD	0.76	0.61–0.89	< **0.001**
LogMAR M1 CVA-VA	0.65	0.21–86	< **0.001**
LogMAR M2 CVA-VA	0.66	0.36–0.83	< **0.001**
LogMAR M3 CVA-VA	0.57	0.27–0.77	< **0.001**
LogMAR G1 CVA-VA	0.73	0.48–0.86	< **0.001**
LogMAR G2 CVA-VA	0.56	0.07–0.87	< **0.001**
LogMAR G3 CVA-VA	0.53	0.25–0.78	< **0.001**

CI = confidence interval, FAZ = foveal avascular zone, CD = capillary density, LogMAR = logarithm of the minimum angle of resolution, CVA-VA = central visual analyzer visual acuity.

Table 4

Pairwise correlation of capillary density with age and best corrected visual acuity.

	Correlation coefficient	95% CI	p value
CD x Age			
SCP – diabetic group	−0.600	−0.736 – −0.430	< **0.0001**
SCP – control group	−0.492	−0.699 – −0.227	**0.001**
DCP – diabetic group	−0.464	−0.678 – −0.211	**0.0002**
DCP – control group	−0.425	−0.674 – −0.010	**0.007**
CD x BCVA (logMAR)			
SCP – diabetic group	−0.514	−0.679 – −0.299	< **0.0001**
SCP – control group	−0.536	−0.728 – −0.265	**0.0004**
DCP – diabetic group	−0.304	−0.518 – −0.055	**0.018**
DCP – control group	−0.524	−0.721 – −0.250	**0.0006**

CI = confidence interval, CD = capillary density, SCP = superficial capillary plexus, DCP = deep capillary plexus, BCVA = best corrected visual acuity, logMAR = logarithm of the minimum angle of resolution.