Diabetic Macular Ischemia: Influence of Optical Coherence Tomography Angiography Parameters on Changes in Functional Outcomes Over One Year

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Purpose. To prospectively evaluate whether diabetic macular ischemia detected with coherence tomography angiography (OCTA) is associated with change in functional outcomes over a period of one year.

Methods. This is a one-year prospective, observational study that included 56 eyes with varying levels of diabetic retinopathy. All participants underwent best corrected visual acuity evaluation, swept-source OCTA and microperimetry at baseline and repeated at one year. Parafoveal vessel densities (VD) and foveal avascular zone (FAZ) areas were generated from OCTA in the superficial and deep vascular plexuses. The influence of baseline and change in OCTA parameters on change in visual acuity and retinal sensitivity over one year was evaluated.

Results. Over the one-year follow-up period, 16% (9) of eyes had at least one line worsening in BCVA and 7% (4) of eyes had at least 5% decrease in retinal sensitivity compared to baseline. Diabetic retinopathy progressed in 12.5%. Mean superficial vascular plexus (SVP) FAZ area increased (0.32 ± 0.15 to 0.39 ± 0.18 mm^2, $P = 0.003$) and parafoveal VD in deep vascular plexus (DVP) decreased ($49.8 \pm 3.7\%$ to $48.8 \pm 2.9\%$, $P = 0.040$) at one year compared to baseline. In the multivariate regression analysis, larger baseline DVP FAZ area was associated with worsening of BCVA over one year ($\beta = 0.16$ logMAR per mm^2, 95% CI 0.02 to 0.31, $P = 0.032$). In addition, larger decreases in SVP VD ($\beta = -4.18$ db per 10% decrease, 95% CI -6.55 to -1.80, $P = 0.002$) was associated with worsening of retinal sensitivity over one year.

Conclusions. Progression of parafoveal microvasculature changes over one year can be detected using OCTA. Larger baseline DVP FAZ area on OCTA is predictive of worsening in visual outcomes, and larger decreases in SVP VD were associated with worsening of retinal sensitivity over a course of one year in diabetic individuals.

Keywords: diabetic macular ischemia, diabetic retinopathy, microperimetry, optical coherence tomography angiography, retinal sensitivity

Diabetic macular ischemia (DMI) is one of the irreversible and vision-threatening complications of diabetic retinopathy.[1] With the advent of optical coherence tomography angiography (OCTA), it is now possible to diagnose and monitor the progression of DMI noninvasively in asymptomatic patients. Another key advantage of OCTA over fluorescein angiography the ability to generate depth resolved quantitative measurements such as vessel densities (VD), foveal avascular zone (FAZ) areas, and FAZ circularity throughout the layers of the retina.[2]

The use of OCTA in the evaluation of diabetic macular ischemia has been previously demonstrated in several previous studies.[3,4] Changes in the FAZ area and VD had been reported in diabetic patients even before the development of frank diabetic retinopathy using OCTA, suggesting that these alterations are potential early biomarkers for diabetic retinopathy (DR).[5–7] The FAZ area has also been correlated with varying levels of DR severity.[2,7] Cross-sectional OCTA studies have found that the FAZ area and VD in the deep vascular plexus correlated with visual acuity.[8,9] Additionally, our group previously demonstrated that retinal sensitivity, as evaluated by microperimetry, may be a more sensitive measure of retinal function than BCVA and that alterations in parafoveal VD and FAZ area correlated with DR severity and reduction of macular sensitivity but not BCVA in patients with diabetic retinopathy.[10] A key limitation in the current body of knowledge is the lack of longitudinal data, because most previous studies have been cross-sectional in nature. An important clinical question that remains is whether deficits detected on OCTA may predict

progression of functional loss and identify a group of individuals at increased risk of visual loss longitudinally.

In this prospective study, we aimed to evaluate the influence of baseline macular OCTA parameters on change in functional parameters over a period of one year. Specifically, we examined whether the OCTA metrics provided additional predictive value for functional outcomes beyond established risk factors (age, cardiovascular disease, total cholesterol, duration of diabetes, and DR severity).

Methods

This was a prospective observational study of participants with type 2 diabetes mellitus and varying levels of diabetic retinopathy recruited from Singapore National Eye Centre clinics over a one-year period from September 2017 to September 2018. Written, informed consent was obtained from each participant. The principles of the Declaration of Helsinki were followed, and approval from the Singapore Eye Research Institute's institutional review board was obtained. The baseline characteristics have previously been reported.[10] The current analysis reports the one-year follow-up results.

Participants were included if there was no media opacity affecting OCT capture. We excluded subjects with coexisting or previous ocular disease, and media opacities that could potentially confound study findings or precluded OCT image capture. Participants with evidence of diabetic macular edema or epiretinal membranes on OCT B scan were also excluded because this may produce artefacts that can affect acquisition and assessment of vascular perfusion through OCT angiography.

Clinical and Imaging Protocol

All participants underwent standard ophthalmic examinations at every study visit. BCVA was obtained after manifest refraction using a Snellen chart and converted in LogMAR notation at baseline and at one-year follow-up. Severity of DR at baseline and at one-year follow-up was assessed and categorized into mild nonproliferative DR (NPDR), moderate NPDR, severe NPDR, and proliferative DR based on the International Clinical Diabetic Retinopathy Severity Scales.[11] At baseline, clinical information collected included history of cardiovascular disease, hypercholesterolemia, glycated hemoglobin (%), total cholesterol (μmol/L), creatinine (μmol/L) and duration of diabetes (years). OCTA and microperimetry were performed at baseline and repeated at the one-year follow-up. Ocular therapeutic intervention and metabolic control were given as per standard of care.

OCTA Measurement

OCTA was performed with Triton (Topcon, Japan) using a scanning area of 3 × 3 mm centered on the fovea and segmented using the-in software (Fastmap Version 10.12, IMAGEnet 6 Ver.1.21). The enface OCT image was segmented with an inner boundary at 2.6 μm below the internal limiting membrane and the outer boundary at 15.6 μm below the inner plexiform layer to obtain images of the superficial vascular plexus (SVP). For the deep vascular plexus (DVP), the image was segmented at 15.6 μm below the inner plexiform layer, and the outer boundary was set at 70.2 μm below the inner plexiform layer. Automated segmentation was verified for all cases, and manual correction was performed in cases with segmentation errors. We applied quality control criteria as elucidated previously by Fenner et al.[12] to include images. Scan parameters assessed included fine vessel visibility, scan centration, image tilt, motion and segmentation artefacts, B-scan quality, and image quality scores.

We used proprietary software to obtain automated parafoveal VD (%).[13] We used the built-in projection artifact removal application to the DVP slab (see Fig. 1A). The mean superficial and deep parafoveal VD was calculated from the vessel densities of the superior, nasal, inferior, and temporal quadrants, respectively. The FAZ area was measured in both SVP and DVP. The FAZ area was redrawn if the automated tracing was erroneous.

Retinal Sensitivity Measurement Using Microperimetry

We used the Nidek MP-3 microperimeter (MP3, Nidek Co, Japan) to measure retinal sensitivity. A 4-2-staircase strategy with Goldmann III size stimulus was used. The specific protocol used included a 13-stimuli grid that covered an area of 1500 μm x 1500 μm centered on the fovea (see Fig. 1B). Retinal sensitivity was calculated as the average sensitivity from these 13 points. This was based on pilot data that this area will cover the majority of participants with parafoveal capillary loss. The stimulus luminance was 31.4 asb, and duration was 200 ms with a dynamic range of 34 dB.[10]

Statistical Analysis

Main outcome measures include change in LogMAR BCVA and retinal sensitivity (dB) over one-year follow-up. Data from clinical assessment and imaging protocols were obtained at baseline and repeated at one year as previously reported.[10] Statistical analysis was performed using Stata version 15 (Statacorp, Lake Station, TX, USA). Data were presented in means ± standard deviations (SD) and number (%). Between-group comparison of continuous variables and categorical variables was done using Student's *t*-test and χ^2 statistics, respectively. Standard errors were adjusted for between-eye correlation of observations made on the same patient when comparing eye-level characteristics. Baseline and one-year measurements of functional and anatomic parameters were compared using paired *t*-tests.

Multivariable regression analysis assessed associations between baseline characteristics, anatomical parameters (baseline and change of vessel density index and FAZ area), and change in functional outcomes (BCVA and retinal sensitivity) over a period of one year. We constructed a base model of sociodemographic and clinical covariables (age, baseline BCVA or baseline retina sensitivity, total cholesterol, history of cardiovascular disease, duration of diabetes, DR severity and lens status), selected by clinical relevance and/or individual association with change in each functional outcomes at one year. We then added each OCTA anatomical parameter (vessel density index and FAZ area) and determined whether the parameter was independently associated with change in functional outcomes over one year while controlling for the variables included in the base model. We also assessed changes to the coefficient of determination (R^2) to see whether any of the baseline or change in OCTA anatomical parameters explained additional variation in one

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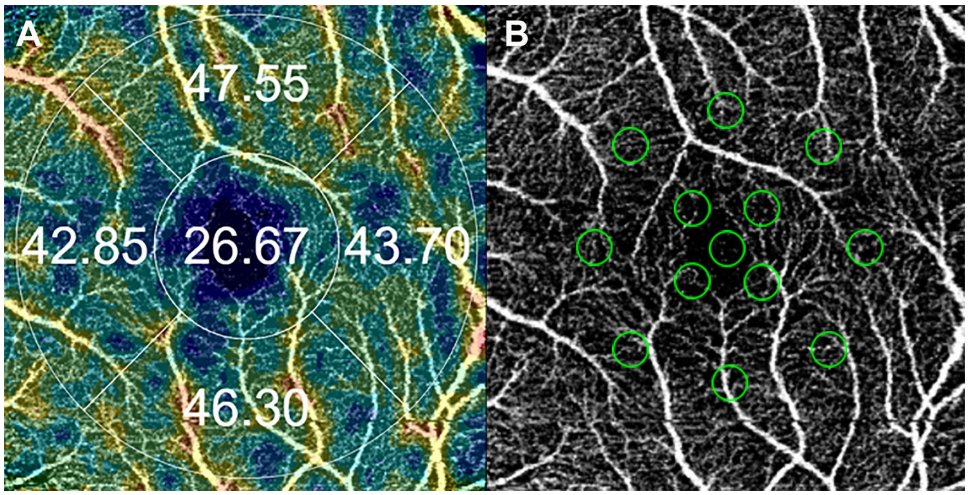

Figure 1. **(A)** OCTA Vessel density grid. (**B**) Microperimetric protocol. A 13-stimuli microperimetric grid (1500 µm × 1500 µm) superimposed on a 3 mm × 3 mm enface OCTA scan centered on the fovea.

year change in functional parameters. Regression coefficient standard errors were adjusted for between-eye correlation of measurements made on the same patient. P values < 0.05 were considered statistically significant.

Results

A total of 60 eyes (31 participants) had OCTA at baseline and one year. We excluded four eyes (three participants) because of poor quality scan. Fifty-six eyes from 28 type-2 diabetic subjects were included in the one-year analysis. Overall, the mean age of these 28 subjects at baseline was 62.5 ± 8.4 years, and 53.6% were males. The mean HbA1C% level was 7.4 ± 1.4 at baseline, and duration of diabetes was 13.9 ± 8.6 years. At baseline, 33 of 56 eyes (59%) were phakic, and 23 of 56 eyes were pseudophakic (41%), and the mean spherical equivalent (SE) of manifest refraction was −0.50 ± 1.25 D (Diopters) [range +2.25 to −4.00 D]. Baseline demographic characteristics and DR severity of subjects are summarized in Table 1.

Comparison of baseline and one-year functional and anatomic parameters of 56 eyes are detailed in Table 2. There was no significant change in mean BCVA (0.16 ± 0.16 logMAR at baseline versus 0.13 ± 0.14 logMAR at one year, $P = 0.100$) and mean retinal sensitivity (22.27 ± 4.36 dB at baseline vs. 22.92 ± 4.04 db at one year, $P = 0.405$). However, 16% (9) of eyes had at least one line worsening in BCVA, and 7% (4) of eyes had at least 5% decrease in retinal sensitivity compared at one year compared to baseline. Severity of DR progressed in seven eyes and was unchanged or improved in the remaining 49 eyes. Comparing OCTA at one year to baseline, there was a significant increase in the FAZ area in the SVP (0.32 ± 0.15 mm^2 to 0.39 ± 0.18 mm^2, $P = 0.003$) and reduction in DVP parafoveal VD (49.8% ± 3.7% to 48.8% ± 2.9%, $P = 0.040$). The reduction in the DVP parafoveal VD was mainly seen in the superior (52.2% ± 6.3% to 49.5% ± 5.4%, $P = 0.009$) and temporal (49.2% ± 3.8% to 47.5% ± 3.9%, $P = 0.009$) quadrants.

During the one-year study period, one patient had progression of cataract in one eye and underwent uncomplicated cataract surgery. None of the eyes developed incident diabetic macular edema that required intravitreal anti-VEGF therapy. Four eyes from three patients progressed to PDR and received pan retinal photocoagulation within the study period.

Table 1. Demographics and DR Severity at Baseline

N = 56 Eyes of 28 Subjects	Baseline
Demographics	
Age (years)	62.5 ± 8.4
Gender (male)	15 (53.6%)
Cardiovascular disease	2 (7.1%)
Hypercholesterolemia	23 (79.3%)
HbA1C (%)	7.4 ± 1.4
Creatinine (µmol/L)	87.0 ± 26.4
Total cholesterol (mmol/L)	4.6 ± 2.6
Duration of diabetes (years)	13.9 ± 8.6
Spherical equivalent (D)	−0.50 ± 1.25 [−4.00 to +2.25]
Lens status (phakic)	33 (59%)
DR severity per eye	
No DR	21 (37.5%)
Mild	10 (17.9%)
Moderate	5 (8.9%)
Severe	11 (19.6%)
PDR	9 (16.1%)

Data are presented in mean ± SD [range]/number (%).

Associations Between OCTA Parameters and Change in Functional Outcomes Over One Year

In the base model of the multivariable regression analysis (See Table 3), baseline factors associated with change in BCVA (logMAR) over one year include cardiovascular disease ($\beta = 0.10$, 95% CI 0.06 to 0.14, $P < 0.001$) and DR severity, mild/moderate DR ($\beta = 0.09$, 95% CI 0.03 to 0.16, $P = 0.005$) and severe DR or PDR ($\beta = 0.15$, 95% CI 0.05 to 0.24, $P = 0.005$). When we added OCTA parameters to the base model, larger baseline DVP FAZ area was associated with worsening in BCVA over one year ($\beta = 0.16$ logMAR per mm^2, 95% CI 0.02 to 0.31, $P = 0.032$). Some improvement in the coefficient of determination (R^2) from 0.34 to 0.40 was observed after adding DVP FAZ size to the base model.

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Table 2. Functional and Anatomic Parameters at Baseline and One Year

N=56 Eyes	Baseline	1 Year	Change	P*
Functional parameters				
Best corrected VA (logMAR)	0.16 ± 0.16	0.13 ± 0.14	−0.03	0.100
Retinal Sensitivity (dB)	22.27 ± 4.36	22.92 ± 4.04	0.65	0.405
Anatomic (OCTA) parameters				
Superficial vascular plexus				
FAZ area (mm^2)	0.32 ± 0.15	0.39 ± 0.18	0.07	**0.003**
Parafoveal vessel density (%)	46.4 ± 4.0	47.2 ± 3.3	0.80	0.267
Superior quadrant	48.1 ± 5.0	47.4 ± 4.8	−0.74	0.329
Inferior quadrant	47.3 ± 5.5	48.1 ± 7.3	0.81	0.496
Nasal quadrant	44.4 ± 5.7	46.1 ± 3.9	1.71	0.078
Temporal quadrant	45.8 ± 4.4	46.6 ± 4.5	0.86	0.282
Deep vascular plexus				
FAZ area (mm^2)	0.46 ± 0.19	0.48 ± 0.21	0.02	0.757
Parafoveal vessel density (%)	49.8 ± 3.7	48.8 ± 2.9	−1.00	**0.040**
Superior quadrant	52.2 ± 6.3	49.5 ± 5.4	−2.63	**0.009**
Inferior quadrant	49.4 ± 6.1	50.8 ± 6.4	1.40	0.279
Nasal quadrant	48.8 ± 5.3	47.6 ± 4.7	−1.13	0.124
Temporal quadrant	49.2 ± 3.8	47.5 ± 3.9	−1.69	**0.008**

Data are presented in mean ± SD.
* Paired T-Test, significant *P*-values in bold.
VA = visual acuity; OCTA = ocular coherence tomography angiography; FAZ = foveal avascular zone

Table 3. Association Between Baseline OCTA Anatomical Parameters and Change in Functional Outcomes Over One Year

	Change in Best-Corrected VA (logMAR)†			Change in Average Retinal Sensitivity (dB)‡		
	Beta (95% CI)	P	Adjusted R^2	Beta (95% CI)	P	Adjusted R^2
Base model						
Baseline BCVA (per line increase)	−0.03 (−0.07 to 0.01)	0.117	0.34	NA		0.39
Baseline retinal sensitivity (per db increase)	NA			−0.57 (−0.93 to −0.21)	**0.004**	
Age (per 10 years increase)	0.02 (−0.04 to 0.08)	0.438		−0.36 (−1.63 to 0.91)	0.558	
Total cholesterol (per 10 µmol/L increase)	−0.05 (−0.15 to 0.04)	0.280		0.73 (−2.72 to 4.18)	0.665	
Cardiovascular disease	0.10 (0.06 to 0.14)	**<0.001**		−10.79 (−13.01 to −8.57)	**<0.001**	
Diabetes duration (per 10 years increase)	−0.00 (−0.03 to 0.03)	0.737		0.29 (−2.02 to 2.60)	0.794	
DR severity						
No DR	Reference			Reference		
Mild or moderate DR	0.09 (0.03 to 0.16)	**0.005**		−0.30 (−3.29 to 2.69)	0.838	
Severe DR or PDR	0.15 (0.05 to 0.24)	**0.005**		−1.78 (−5.17 to 1.61)	0.286	
Lens Status (Pseudophakic)	−0.01 (−0.08 to 0.07)	0.874		1.22 (−1.10 to 3.54)	0.286	
Baseline anatomical parameters*						
Superficial vascular plexus						
FAZ (per mm^2 increase)	0.11 (−0.13 to 0.36)	0.351	0.35	−7.55 (−19.47 to 4.37)	0.201	0.43
Parafoveal VD (per 10% decrease)	0.01 (−0.07 to 0.09)	0.805	0.32	1.33 (−2.52 to 5.17)	0.480	0.38
Deep vascular plexus						
FAZ (per mm^2 increase)	0.16 (0.02 to 0.31)	**0.032**	0.40	1.43 (−10.93 to 13.79)	0.812	0.37
Parafoveal VD (per 10% decrease)	0.02 (−0.06 to 0.11)	0.541	0.33	0.04 (−3.71 to 3.80)	0.981	0.37
Change in anatomic parameters—Baseline to month 12*						
Superficial vascular plexus						
FAZ (per mm^2 increase)	−0.01 (−0.26 to 0.24)	0.960	0.26	−3.50 (−14.05 to 7.06)	0.497	0.43
Parafoveal VD (per 10% decrease)	0.02 (−0.06 to 0.10)	0.606	0.26	−4.18 (−6.55 to −1.80)	**0.002**	0.57
Deep vascular plexus						
FAZ (per mm^2 increase)	−0.03 (−0.13 to 0.06)	0.508	0.26	−5.14 (−12.92 to 2.63)	0.182	0.49
Parafoveal VD (per 10% decrease)	0.01 (−0.07 to 0.08)	0.839	0.26	−0.62 (−4.40 to 3.16)	0.735	0.43

Significant *P* values in bold.
* Each anatomic parameter is controlled for variables in the core model.
† Positive Beta is interpretable as worsening of logMAR visual acuity over one year per unit change in a continuous variable or presence/level of a categorical variable against the reference level.
‡ Negative Beta is interpretable as worsening of retinal sensitivity over one year per unit change in a continuous variable in a continuous variable or presence/level of a categorical variable against the reference level.

Figure 2 shows a patient with smaller DVP FAZ at baseline that maintained stable vision until one-year follow-up (patient A) and conversely a patient with larger FAZ at baseline who developed worsening of vision at one year (patient B).

Baseline factors associated with change in retinal sensitivity (dB) over one year include baseline retinal sensitivity ($\beta = -0.57$ per dB, 95% CI −0.93 to −0.21, $P = 0.004$) and presence of cardiovascular disease ($\beta = -10.79$, 95% CI −13.01 to −8.57, $P < 0.001$). None of the baseline OCTA

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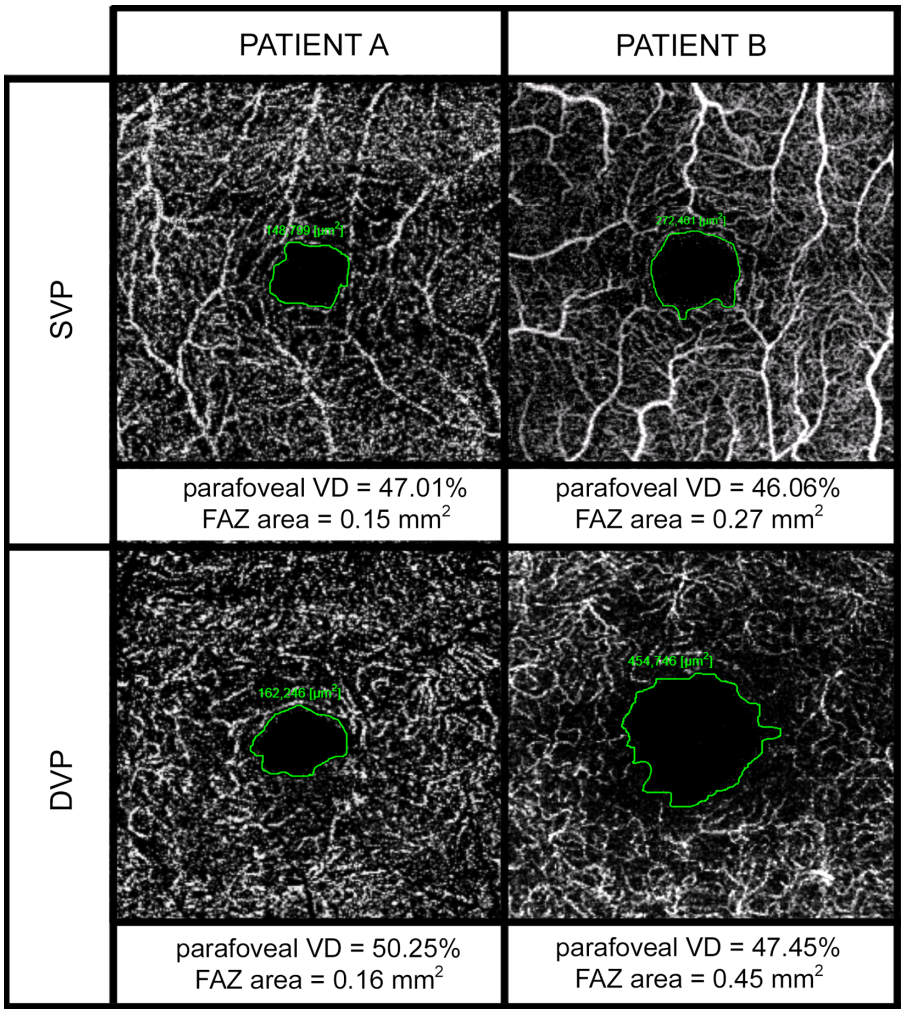

Figure 2. Representative cases. **(A)** Patient A is a type 2 diabetic for 23 years, diagnosed with mild NPDR in the right eye. She presented with acceptable parafoveal VD and FAZ areas in both the SVP and DVP at baseline. OCTA metrics was associated with a good vision of 0.1 logMAR at baseline that was maintained at one-year follow-up. (**B**) Conversely, Patient B, is a type 2 diabetic for 12 years, diagnosed with moderate NPDR in the left eye. He presented with a larger FAZ area in the DVP which was associated with poorer vision of 0.2 logMAR at baseline, which further deteriorated to 0.3 at one-year follow-up despite no progression of DR.

parameters showed significant influence on change in retinal sensitivity over a period of one year. Larger decreases in SVP VD between baseline and one year ($\beta = -4.18$ db per 10% decrease, 95% CI -6.55 to -1.80, $P = 0.002$) was significantly associated with worsening of retinal sensitivity over one year.

Diabetic Retinopathy Progression

Among the 56 eyes, DR progression was noted in seven eyes of participants who had no DR to severe DR at baseline. In the remaining 49 eyes, DR was stable in 47 eyes and regressed in two eyes. None of the eyes developed diabetic macular edema. There were no significant differences in baseline characteristics and OCTA parameters between eyes that progressed and did not progress in DR severity (see Supplementary Table 1).

Discussion

In this prospective observational study over a one-year follow-up period, a significant deterioration in two OCTA parameters: DVP parafoveal VD and SVP FAZ area was observed in participants with various severity of DR at baseline. Importantly, larger DVP FAZ area at baseline was associated with significant worsening of BCVA over one year, beyond other significant risk factors such as age, cholesterol levels, cardiovascular disease, lens status, duration and severity of diabetic retinopathy in our study. During the same follow-up period, there was no significant change in DR severity, BCVA or retinal sensitivity on average, although 16% of eyes did experience worsening of BCVA by one line or more. These results suggest that OCTA may be a more sensitive predictive tool for visual outcomes added to other known clinical parameters for identifying this group of patients at higher risk of developing functional loss.

One of the key advantages of OCTA over fluorescein angiography is the ability to detect diabetic macular ischemia (DMI) noninvasively.[14] It is therefore possible to identify DMI even in eyes with relatively few symptoms. We have previously reported that FAZ area in both SVP and DVP increased with DR severity, and FAZ area (SVP) correlated with retinal sensitivity at baseline. However, an important clinical question remains as to whether eyes with DMI detected on OCTA are at higher risk of progressive visual

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loss longitudinally and whether the OCTA findings continue to deteriorate with time.

Significant deterioration in OCTA parameters over time in diabetic retinopathy patients has previously been described. For instance, Kim et al.[15] recently reported that microvascular impairment is progressive even in early stages of diabetic retinopathy. Among 40 eyes with no DR or mild NPDR, vessel density loss was observed in the SVP over a period of two years. However, DVP vessel density was not studied in this report.[15]

In our prospective study, we found that baseline DVP FAZ size was associated with worsening of vision over one year. This not only provided evidence that OCTA parameters are able to predict visual outcomes in DR participants but is also in keeping with previous reports that suggest the importance of detection and monitoring of DVP parameters in ischemic conditions such as in DR. Previous cross-sectional studies have correlated central visual loss in diabetic eyes with degree of parafoveal capillary loss,[8,16] and that such associations are more prominent with alterations in the DVP than the SVP.[9,17] Changes in the DVP have also been found to correlate better with DR severity than the SVP.[18] These observations are supported by histologic studies which show higher vulnerability of the deep foveal plexus to endothelial injury.[19] Furthermore, ischemic changes in the DVP are more likely to result in macular photoreceptor disruptions than changes in the SVP, thereby contributing to the central vision loss in DMI.[20]

The correlation between OCTA metrics and microperimetry has been established in previous cross-sectional reports.[10,21] In this analysis we evaluated the association of baseline and change in OCTA parameters to prospective retinal sensitivity outcomes over the one-year follow-up. Although we expected the influence of baseline OCTA metrics on longitudinal change in retinal sensitivity to mirror that of BCVA, we did not find such an association. It is possible that the lack of the association could be related to the small microperimetric area analyzed. We did, however, find that larger decreases in parafoveal VD in the SVP was associated with worsening of retinal sensitivity over one year. To the best of our knowledge, this association between deterioration in superficial VD with retinal sensitivity loss over time in diabetic eyes has not been previously reported.

In terms of DR severity, only 12.5% (seven of 56 eyes) had progression of DR severity over one year. This rate is lower than that from a recent prospective study by Sun and colleagues,[22] in which a total of 28 (13.5%) of 205 eyes showed a two-step progression in DR during two years of follow-up. Additionally, they have demonstrated that OCTA parameters predict DR progression longitudinally wherein larger FAZ areas and lower vessel density in DVP at baseline increases likelihood of DR progression within two years.[22] The differences may be due to differences in patient characteristics in the two population, as well as the smaller sample size with shorter follow-up in our series.

The prospective nature of the study allowed us to use a predetermined uniform imaging and clinical examination protocol which adds strength to our results. Additionally, the use of a commercially available automated software increases the applicability of our results in a clinical setting. However, we acknowledge the several limitations we had during the conduct of the study. In terms of imaging, we intentionally excluded participants with diabetic macular edema as the presence of cyst affects quantification of OCTA metrics focused in this study, which is an innate limitation of this imaging.[23] It is possible that different OCTA parameters may be differently affected at different severity stages. Future studies with larger sample size will be able to study the effects of OCTA while stratifying according to DR severity. Directions of future studies might want to include wide field OCT angiography, to explore correlations between degree of peripheral changes with central vascular changes and its influence on functional changes prospectively. Another important limitation is that lack of magnification correction for OCTA parameters as we did not measure axial length.[24,25] However, we did not include any eyes with spherical equivalent refraction of more than −4D, and thus the potential effect of variation in magnification should be limited. Also, the number of participants were limited, therefore further longitudinal studies on larger cohorts are still necessary to further validate our results and explore these associations in different patient groups according to DR severity.

In conclusion, we demonstrated the predictive value of structural OCTA parameters in relation to visual outcomes beyond current established systemic risk factors. Larger baseline FAZ areas in the deep vascular plexus were associated with worsening of visual outcomes, and larger decreases in SVP VD were associated with worsening of retinal sensitivity over one year. These associations support the use of OCTA in the early detection and monitoring of diabetic macular ischemia.

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