Retinal microvascular alterations after phacoemulsification in patients with diabetes evaluated using optical coherence tomography angiography

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Research article

Keywords: retinal microvasculature, phacoemulsification, diabetes, OCT angiography

Posted Date: August 26th, 2019

DOI: <https://doi.org/10.21203/rs.2.13588/v1>

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Abstract

Purpose: To quantify changes in retinal microvasculature in diabetic patients after phacoemulsification by using optical coherence tomography angiography (OCTA). **Methods:** Macular thickness (MT), superficial capillary plexus (SCP), deep capillary plexuses (DCP) and foveal avascular zone (FAZ) measurements of the 3×3 mm macular images were obtained by OCTA at baseline, 1 day, 1 week, 1 month, and 3 months after cataract surgery in diabetic and non-diabetic patients. **Results:** There was a significant increase in MT at 1 month and 3 months after surgery in both groups (all $P < 0.05$), but no significant difference between the two groups ($p = 0.217$). At 3 months postoperatively, the SCP increase was significantly higher compared with baseline in diabetic group ($P < 0.05$). The MT and SCP was negatively correlated with logMAR best corrected visual acuity (BCVA), while the FAZ area and perimeter were positively correlated with logMAR BCVA in diabetic group. **Conclusions:** Cataract surgery can increase macular thickness in both diabetic and non-diabetic patients, and also increase the SCP in diabetic patients. Whether these changes will persist a longer period still needs to be followed up.

Background

Diabetes mellitus (DM) is one of the most prevalent diseases affecting 425 million people worldwide[1]. Diabetes can cause many ocular complications such as cataracts and diabetic retinopathy, which are the main causes of decreased vision in diabetic patients and often coexist[2]. Cataract occurs more frequently and earlier in diabetic patients than non-diabetic patients. Phacoemulsification surgery can not only improve visual acuity but also help doctors to detect diabetic retinopathy in early stage[3]. However, some studies have found that cataract surgery can accelerate the progression of diabetic retinopathy (DR), and the incidence of macular edema is significantly higher in diabetic patients[4, 5]. Studies have reported the use of anti-VEGF therapy to prevent post-cataract surgery diabetic macular edema in diabetic patients and achieved good results[6-8]. However, the reasons for the risk of DR and diabetic macular edema (DME) progression after cataract surgery are still unclear.

Optical coherence tomography (OCT angiography, OCTA) is a new and noninvasive vascular imaging technique developed in recent years. It uses a special algorithm to calculate the continuous scan OCT and obtain blood flow signals, which allows better visualization and quantification of retinal vessels in different layers, and non-perfused areas of the macula and nerve[9, 10]. OCTA was found to detect microvascular changes early in diabetic patients, even before clinical signs appeared[11]. In this study, we used OCTA to study the macular thickness, superficial, deep vascular density, and foveal avascular zone (FAZ) Area, perimeter, and acircularity index (AI) in diabetic and non-diabetic patients after cataract surgery.

Methods

Patients and setting

This prospective study enrolled cataracts patients with or without diabetics, who planned to undergo routine phacoemulsification surgery with intraocular lens (IOL) implantation between October 2017 and March 2018. Patients undergoing cataract surgery with or without nonproliferative diabetic retinopathy (NPDR), intraocular pressure (IOP) between 10 mm and 21 mm Hg and axial length (AL) between 20.0 mm and 26.0 mm were included in this study. The exclusion criteria were as follows: (1) patients with proliferative diabetic retinopathy (PDR) or clinically significant diabetic macular edema (CSDME); (2) patients treated with intravitreal anti-VEGF drugs or panretinal photocoagulation (PRP); (3) patients with history of ocular trauma, intraocular surgery, glaucoma and uveitis; (4) low quality OCT images due to severe cataracts or unstable fixation. This study was approved by the Institutional Review Board and followed the tenets of the Declaration of Helsinki. All patients provided written informed consent.

All patients had complete ophthalmologic examinations, including the measurement of best-corrected visual acuity (BCVA) in logarithm of the minimum angle of resolution (logMAR), slit lamp examination, intraocular pressure measurement, and dilated fundus examination by indirect ophthalmoscope and +90 non-contact lens. Cataract severity was assessed using the Lens Opacities Classification system III (LOCS scale). We also recorded the blood pressure, total cholesterol level, and the duration of diabetes and hemoglobin A1c (HbA1c) level. All cataract surgeries are performed using Infiniti® vision system (Alcon Laboratories, Inc., USA), performed by one surgeon. All the enrolled patients in this study underwent implantation of aspheric posterior chamber IOL ((Tecnis ZCB00, Abbott Medical Optics, Inc., USA) with phacoemulsification. The bottle height and cumulative dissipated energy (CDE) data in each surgery were recorded. The bottle height is set between 60-90 cm, according to the stability of the anterior chamber during surgery and the patient's subjective comfort. Patients were followed up and examined at baseline (up to two weeks before surgery), one day, one week, one month and three months after surgery.

OCTA Data collection

The OCTA images were obtained using a spectral-domain OCT device (RTVue-XR Avanti, version 2017.1, OptoVue, Inc., USA). Macular OCTA images of 3 × 3 mm were obtained. Macular thickness (MT) was obtained by the same OCT system at the same time as the retinal vasculature. The full retinal thickness was measured from inner limiting membrane (ILM) to retinal pigment epithelium (RPE). Vessel density of SCP and DCP were measured, and DCP parameters were calculated after removing the projection artifacts from the SCP. Measurement of the foveal avascular zone (FAZ) are FAZ area (in mm²), perimeter (in mm) and a-circularity. The acircularity index (AI) is defined as the ratio of the perimeter of the FAZ and the perimeter of a circle with equal area.

Statistical analysis

All data were analyzed using SPSS 17.0 for Windows statistical software (SPSS, Inc., Chicago, IL, USA), and expressed as the mean $\pm$ standard deviation (SD). The preoperative and postoperative measurements were compared using repeated measures analysis of variance. Pearson's correlation analyses were performed to determine the relationships between the magnitude of the changes in MT, SCP, DCP from baseline and related factors, including duration of DM, HbA1C, cumulative dissipated energy (CDE) and bottle height during cataract surgery. Correlations between BCVA and MT, SCP, DCP, FAZ were analyzed by Spearman's correlation. $P < 0.05$ was considered statistically significant.

Results

In total, 32 eyes of 32 type 2 diabetic patients and 40 eyes of 40 non-diabetic patients were included in this study. In diabetic group, there were 3 mild NPDR, 1 moderate NPDR, 1 severe NPDR and 27 background DR. All patients had no CSDME. Baseline characteristics of the patients in both groups are shown in Table 1. Subjects within the diabetic and non-diabetic groups were not significantly different in any of the demographic or baseline characteristics.

All microvasculature parameters obtained using OCTA at baseline, one day, one week, one month and three months after cataract surgery are presented in Table 2. The changes in MT, SCP and DCP were also shown in Figure 1. Mean MT changed from 302.09 ± 23.07 and 289.33 ± 23.06 at baseline to 312.64 ± 24.98 and 313.27 ± 30.98 at 1 month, 313.00 ± 28.16 and 311.67 ± 28.16 micron at 3 months in diabetic and non-diabetic groups respectively (all $P < 0.05$) (Fig. 1A). There was no significant difference between the two groups ($p = 0.217$). The SCP had significantly increased from 38.47 ± 4.37 at baseline to 44.96 ± 4.52 at 3 months after the surgery only in diabetic group ($P < 0.05$) (Fig. 1B). There was no statistical difference at any postoperative timepoints and between the two groups in DCP (Fig. 1C).

The magnitude of the changes in MT, SCP, DCP from baseline did not have significant correlation with the factors such as duration of DM, HbA1C, cumulative dissipated energy (CDE) and bottle height during cataract surgery. (Fig. 2).

The Spearman's correlation coefficients (ρ) with BCVA and MT, SCP, FAZ, PERIM in DM group were respectively -0.382 ($P = 0.045$), -0.476 ($P = 0.012$), 0.426 ($P = 0.027$), 0.382 ($P = 0.045$), which shown in Table 3. The MT and SCP was negatively correlated with logMAR best corrected visual acuity (BCVA), while the FAZ area and perimeter were positively correlated with logMAR BCVA in diabetic group.

Discussion

At present, the co-existence of cataract and diabetes is a very common situation. The conclusions of the study on the development of DR and DME after cataract surgery are controversial. Some studies have shown that phacoemulsification can accelerate diabetic retinopathy [4, 5, 12]. Other studies suggest that the development of DR and DME after cataract surgery are only the natural history of the disease, and

cataract surgery does not cause the progression of diabetic retinopathy[13, 14]. Although this question still has no answer, one thing is basically certain. Many studies have found macular thickness increase after cataract surgery[15-17], whether this change is different between diabetic and non-diabetic patients is not clear. Cong et al[18]summarized of possible mechanisms of macular thickness changes after cataract surgery in diabetic patients, which included the release of local inflammatory mediators caused by surgical stimulation, the tissue damage caused by ultrasound energy and radiation effects, the surgical perfusion fluid damage , the increase in light exposure surgery, deletion of perivascular cells, endothelial cells and hemodynamic abnormalities in diabetic patients.

Previous studies have generally suggested that the macular thickness has a significant increase in the short term after phacoemulsification, but very little research on changes in postoperative SCP and DCP. The study of differences in MT, SCP, and DCP between diabetic and non-diabetic patients is also very limited.

In our study, we found a significant increase in MT at 1 month and 3 months postoperative compared with baseline in both groups. However, there was no significant difference in the magnitude of the change between the two groups. Also, the SCP was significantly higher at 3 months after surgery than baseline only in the diabetic group. No significant changes were found in DCP.

In non-diabetic patients, Kurt A et al.[19] showed a decrease in MT at the first postoperative day visit and then increasing at week 1, and months 1 and 3, and then relatively decreasing at month 6 although not returning to preoperative levels. Zhao et al.[20] also reported at 1 month and 3 months after surgery, the full retinal the fovea[10] , parafovea, and perifovea increased significantly and this change was is more obvious in the inner layer. Yu et al.[21] reported a significant increase of perfusion and vessel densities in both the SCP and the DCP after cataract surgery within the 3×3 mm images. They considered the inflammation may impact the assessment of density parameters. Pilotto E et al.[22] found macular intermediate retinal capillary (ICP) and DCP perfusion increased at 1 day after uncomplicated cataract surgery, whereas macular SCP perfusion did not change, and all parameters had almost reached baseline levels after 90 days ,which seems to confirm their inflammatory nature.

Are there any differences between diabetic and non-diabetic patients in MT, SCP and DCP after cataract surgery? Giansanti F et al.[23] measured MT by OCT preoperatively and 1, 6, 15, 30, 60, 90, and 360 days after surgery, and found that MT significant increased from day 30 after surgery in diabetic patients, reaching its maximum thickness at day 60, while it was observed only on day 360 in healthy subjects. Haleem A et al.[24] showed that Cystoid macular oedema after phacoemulsification was equally present in both diabetics and non-diabetics without any retinopathy. There was no report on postoperative SCP and DCP in diabetic patients.

In our study, most of the diabetic patients we enrolled have background and mild retinopathy. This may cause no significant difference in the macular thickness between the two groups. Interestingly, we found a significant increase in SCP 3 months after surgery in diabetic group, but not in control group. There was no significant change in DCP at each time point after surgery in both groups. We thought postoperative

inflammatory response should not be the main factors [associated with](#) SCP change after 3 months. This may be a compensatory increase in superficial vasculature due to retinal microcirculatory disorders in diabetic patients under surgical stimulation, which may be beneficial for diabetic patients. However, there is choroid-rich blood supply in the deep retina, so that surgery has little effect on DCP.

We also tried to explore factors related to postoperative MT, SCP and DCP changes. The magnitude of the changes in MT, SCP, DCP from baseline did not have significant correlation with the factors such as duration of DM, HbA1C, cumulative dissipated energy (CDE) and bottle height during cataract surgery. Denier C et al.[25]also found there is no linear correlation between HbA1C and CRT after cataract surgery in diabetic patients. About bottle height and CDE, we did not find the relationship unfortunately. In our study, the bottle height was mostly set between 75-90cm in order to ensure the stability of the anterior chamber, and may be the difference is too small to cause the change of the MT. For OCTA data collection, we did not include cataract patients with severe opacity, which may not be enough to have an impact. Therefore, we need further research to avoid these limitations to explore the factors that affect the thickness of the macula.

Our preliminary findings have shown the MT and SCP was negatively correlated with logMAR best corrected visual acuity(BCVA), while the FAZ area and perimeter were positively correlated with logMAR BCVA in diabetic group. This provides direction for us to further study in the future. The shortcoming of this study is that the patient sample is small, and most of the diabetic patients have background or only mild retinopathy. The retinal function is still in the compensatory period, so the difference is not obvious compared with non-diabetic patients. We will continue to supplement the sample and increase patients with different stage of DR to get more comprehensive results.

Conclusions

In summary, our preliminary findings have shown that macular thickness increased in both diabetic and non- diabetic patients at 1 month and 3 months after cataract surgery, and the SCP increased only in diabetic patients at 3 months after cataract surgery. Whether these changes will persist a longer period still needs to be followed up.

Abbreviations

OCTA: optical coherence tomography angiography; MT: Macular thickness; SCP: superficial capillary plexus; DCP: deep capillary plexuses; FAZ: foveal avascular zone; DM: diabetes mellitus; DR: diabetic retinopathy; BCVA: best corrected visual acuity; CDE: cumulative dissipated energy; PERIM: perimeter in mm; AI: acircularity index

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Shanghai Tenth People's Hospital and followed the tenets of the Declaration of Helsinki. All patients provided written informed consent.

Consent for publication

Not applicable.

Availability of data and materials

Available upon request from the corresponding author.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was supported by Shanghai Municipal Health and Planning Commission Foundation (Grant No. 201540046), Bethune Langmu Young Ophthalmology Research Fund of China (Grant No. BJ-LM2016006J) and Shanghai Tenth People's Hospital Climbing Talent Program (Grant No. 2018SYPDRC029).

Authors' contributions

Concept and design (LF, FL); data acquisition (GA, TL); data analysis/interpretation (LF, GA, FL); drafting of the manuscript (LF); critical revision of the manuscript (FL); statistical analysis (LF, GA, TL); securing funding: (LF, FL); supervision (FL); All authors read and approved the final manuscript.

Acknowledgements

We thank all the patients who participated in this study.

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Tables

Table 1. Baseline characteristics of in both groups

	Diabetic group (n=32)	Non-diabetic group (n=40)	P
Age, y	68.31±9.42	71.60±6.85	0.103
Male patients, n (%)	31.25%	32.5%	0.318
Right eyes, n (%)	50%	52.5%	0.566
Duration of DM, y	10.38±6.67	-	-
HbA1C, %	7.39±1.24	-	-
BCVA , LogMAR	0.35±0.22	0.27±0.14	0.059
MT, µm	302.09±23.07	289.33±23.06	0.998
SCP, %	38.47±4.37	39.05±6.45	0.077
DCP, %	46.68±5.42	46.17±3.74	0.972
FAZ, mm ²	0.287±0.120	0.389±0.120	0.180
PERIM, mm	2.263±0.527	2.254±0.477	0.224
AI	1.20±0.11	1.17±0.08	0.258

Data in the table are presented as means ± standard deviation

DM = diabetes mellitus; HbA1c = hemoglobin A1c; BCVA = best corrected visual acuity; MT=macular thickness; SCP = superficial capillary plexus; DCP = deep capillary plexus; FAZ = fovea avascular zone; PERIM = FAZ perimeter in mm; AI= Acircularity index: ratio between the measured perimeter and the perimeter of the same size circular area

Table 2. Comparison of pre- and post-operative microvasculature parameters

Parameter	Baseline	1 Day	1 Week Postop	1 Month Postop	3 Months Postop
vPostop					
MT, μm	302.09 $\pm$ 23.07	301.45 $\pm$ 22.37	306.00 $\pm$ 20.70	312.64 $\pm$ 24.98*	313.00 $\pm$ 28.16*
SCP, %	38.47 $\pm$ 4.37	40.09 $\pm$ 5.59	42.67 $\pm$ 3.22	42.11 $\pm$ 3.40	44.96 $\pm$ 4.52*
DCP, %	46.68 $\pm$ 5.42	48.48 $\pm$ 3.81	49.13 $\pm$ 3.57	47.04 $\pm$ 3.50	48.00 $\pm$ 2.37
FAZ, mm^2	0.287 $\pm$ 0.120	0.253 $\pm$ 0.094	0.282 $\pm$ 0.153	0.290 $\pm$ 0.129	0.289 $\pm$ 0.146
PERIM, mm	2.263 $\pm$ 0.527	2.060 $\pm$ 0.535	2.145 $\pm$ 0.580	2.220 $\pm$ 0.468	2.242 $\pm$ 0.565
AI	1.20 $\pm$ 0.11	1.16 $\pm$ 0.10	1.17 $\pm$ 0.05	1.18 $\pm$ 0.11	1.15 $\pm$ 0.06
MT, μm	289.33 $\pm$ 23.06	295.80 $\pm$ 20.21	299.87 $\pm$ 22.66	313.27 $\pm$ 30.98*	311.67 $\pm$ 28.16*
SCP, %	39.05 $\pm$ 6.45	38.59 $\pm$ 6.59	41.70 $\pm$ 7.33	41.61 $\pm$ 7.07	40.39 $\pm$ 6.36
DCP, %	46.17 $\pm$ 3.74	47.75 $\pm$ 4.02	48.68 $\pm$ 4.37	46.96 $\pm$ 2.87	48.10 $\pm$ 2.75
FAZ, mm^2	0.389 $\pm$ 0.120	0.343 $\pm$ 0.128	0.374 $\pm$ 0.142	0.363 $\pm$ 0.136	0.366 $\pm$ 0.124
PERIM, mm	2.254 $\pm$ 0.477	2.377 $\pm$ 0.463	2.448 $\pm$ 0.514	2.430 $\pm$ 0.543	2.443 $\pm$ 0.480
AI	1.17 $\pm$ 0.08	1.17 $\pm$ 0.06	1.14 $\pm$ 0.04	1.15 $\pm$ 0.09	1.15 $\pm$ 0.06

Data in the table are presented as means $\pm$ standard deviation

* P<0.05

Table 3. The result of Spearman's correlation analysis

group			MT	SCP	DCP	FAZ	PERIM	AI
DM	BCVA	rho	-0.382*	-0.476*	0.224	0.426*	0.382*	-0.023
		P	0.045*	0.012*	0.242	0.027*	0.045*	0.904
non-DM	BCVA	rho	0.028	-0.118	-0.250	-0.018	-0.054	0.031
		P	0.884	0.541	0.19	0.926	0.782	0.193

*P<0.05

Figures

Figure 1

The changes in MT, SCP and DCP after cataract surgery

Figure 2

Pearson's correlation analyses between the magnitude of the changes in MT, SCP, DCP from baseline and related factors

Supplementary Files

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