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Optical Coherence Tomography Angiography Biomarkers Changes After Cataract Surgery on Macula in Diabetic Retinopathy with No Diabetic Macular Edema: An Interventional Study

Dr. Sandeep Parwal[1], Dr. Kavita Bajiya[2], Dr. Sahil Jain[3], Dr. Sunil Gurjar[4]

[1] Professor, SMS Medical College and Attached Hospitals, Jaipur, Rajasthan
[2] Senior Resident, SMS Medical College and Attached Hospitals, Jaipur, Rajasthan
[3] Senior Resident, SMS Medical College and Attached Hospitals, Jaipur, Rajasthan
[4]3rd Year Resident, SMS Medical College and Attached Hospitals, Jaipur, Rajasthan

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Corresponding Author
Dr. Kavita Bajiya
Senior Resident, SMS Medical College and Attached Hospitals, Jaipur, Rajasthan

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ABSTRACT

Background: Diabetic retinopathy (DR) patients undergoing cataract surgery face potential microvascular complications, but the precise impact on macular perfusion remains unclear. This study aimed to evaluate postoperative changes in retinal microvasculature using optical coherence tomography angiography (OCTA) in DR patients without diabetic macular edema (DME) compared to non-diabetic controls.
Methods: A prospective interventional study was conducted on 108 eyes (54 DR patients and 54 controls) undergoing phacoemulsification. OCTA parameters—macular thickness (MT), superficial capillary plexus vessel density (SCP VD), perfusion density (SCP PD), and foveal avascular zone (FAZ) area—were analyzed preoperatively and 3 months postoperatively. Statistical comparisons employed paired and independent t-tests (*p* < 0.05 significant).
Results: **MT** increased significantly in both groups postoperatively (*p* < 0.001), with no intergroup difference in magnitude. **SCP VD** and **SCP PD** rose significantly in DR patients (*p* < 0.001) but remained unchanged in controls. **FAZ area** expanded in DR patients (*p* < 0.001), while controls showed no significant change.
Conclusion: Cataract surgery induces distinct microvascular remodeling in DR patients, characterized by increased SCP perfusion and FAZ enlargement, which may signal subclinical DR progression. OCTA demonstrates utility in detecting these early changes, advocating for tailored postoperative surveillance in diabetic populations to preempt vision-threatening complications.

Keywords: Diabetic retinopathy, phacoemulsification, OCT angiography, macular perfusion, foveal avascular zone, postoperative monitoring.

INTRODUCTION

Diabetic retinopathy (DR) is a leading cause of vision impairment and blindness among working-age adults globally. It is a microvascular complication of diabetes mellitus, characterized by progressive retinal alterations resulting from chronic hyperglycemia-induced vascular damage.

Cataract formation is another common issue in diabetic patients, occurring at an earlier age and progressing more rapidly compared to non-diabetic individuals. Cataract surgery, while improving visual acuity by replacing the opacified lens, can influence ocular structures and hemodynamics. Postoperative inflammatory responses and changes in intraocular cytokine levels may affect both the retina and the choroid. Understanding these changes is crucial, as they may have implications for postoperative management and the progression of DR.(1-2)

There are some reports of DR progression after cataract surgery. This progression may be due to increased release of pro-inflammatory mediators such as vascular endothelial growth factors (VEGFs), interleukin 1 (IL-1), and hepatocyte growth factor (HGF) into the aqueous humor. These postoperative inflammations may have resulted in vascular abnormalities in the retina and choroidal layers and exacerbated the diabetic retinopathy (DR) after cataract surgery in patients with diabetes mellitus (DM.)

A special algorithm is used to perform a continuous optical coherence tomography (OCT) scan and obtain blood flow signals, which leads to better visualization and quantification of the retinal vessels in different layers and nonperfused areas of the macula and nerve (3-4) .Optical coherence tomography angiography(OCTA) has been used to In this study, we used optical coherence tomography angiography (OCTA) to assess the macular thickness, superficial vascular densities, foveal avascular zone (FAZ) area and chorodial thickness in diabetic and nondiabetic patients after cataract surgery. The aims of our study were to compare the optical coherence tomography angiography (OCTA) parameters obtained from patients with or without diabetes after uncomplicated cataract surgery and to analyze the effects of phacoemulsification surgery on progression of diabetic retinopathy detect microvascular changes early in diabetic patients, even before clinical signs appeared (5).

MATERIALS AND METHODS

Study Design and Setting

This prospective interventional study was conducted at the Upgraded Department of Ophthalmology, S.M.S. Medical College and Hospital, Jaipur, Rajasthan, India, from December 2022 to December 2023, following approval from the Institutional Ethics Committee (IEC).

Study Population

The study included male and female patients aged between 50 and 80 years who presented to the Ophthalmology Outpatient Department (OPD) at S.M.S. Medical College and Hospital and met the inclusion and exclusion criteria. All participants provided written informed consent prior to enrollment.

Inclusion Criteria

- **For Diabetic Patients (Case Group):**
    1. Patients diagnosed with diabetic retinopathy without diabetic macular edema, possessing immature senile cataract requiring phacoemulsification surgery.
    2. Intraocular pressure (IOP) between 10–21 mmHg.
    3. Age between 50–80 years.
    4. Provided written informed consent.
- **For Non-Diabetic Patients (Control Group):**
    1. Patients with immature senile cataract requiring phacoemulsification surgery.
    2. Intraocular pressure (IOP) between 10–21 mmHg.
    3. Age between 50–80 years.
    4. Provided written informed consent.

Exclusion Criteria

1. Eyes with diabetic macular edema.
2. Eyes with intraocular pressure greater than 21 mmHg.
3. Eyes with mature, posterior subcapsular, or posterior polar cataract.
4. History of retinal laser therapy or intravitreal injections.
5. History of ocular trauma, uveitis, or prior intraocular surgery.
6. Patients with Optical Coherence Tomography Angiography (OCTA) images with a signal strength less than 2 due to severe cataract or unstable fixation.

Sample Size Calculation

The sample size was calculated based on a confidence level of 95% and an alpha error of 0.05. Using observations of the foveal avascular zone (FAZ) following cataract surgery at 3 months postoperatively in diabetic and non-diabetic patients—reported as 0.289 mm^2 and 0.366 mm^2, respectively, in a reference study1—we aimed to detect a mean difference of at least 0.08 mm^2 in postoperative FAZ between the two groups. With a standard deviation of 0.146 mm^2 and a study power of 80%, the sample size was calculated to be 54 patients in each group.

Study Procedure

All eligible patients underwent a comprehensive ophthalmic examination, which included:

- **Best-Corrected Visual Acuity (BCVA):** Assessed using a Snellen chart.
- **Slit-Lamp Biomicroscopy:** For anterior segment evaluation.
- **Indirect Ophthalmoscopy:** Using a 20-diopter lens for fundus examination.
- **Intraocular Pressure Measurement:** Using applanation tonometry.

Imaging Assessments

- **Spectral-Domain Optical Coherence Tomography (SD-OCT):** Performed to measure macular thickness and choroidal thickness.
- **Optical Coherence Tomography Angiography (OCTA):** Conducted using the Zeiss Cirrus 5000 AngioPlex system to evaluate retinal vascular parameters, including superficial capillary plexus vessel density (SCP VD), perfusion density (SCP PD), and foveal avascular zone (FAZ) area.

Surgical Procedure

Patients in both groups underwent standard phacoemulsification cataract surgery with intraocular lens implantation performed by an experienced surgeon. Postoperative care included topical antibiotics and steroids as per institutional protocol.

Outcome Measures

- **Primary Outcome:** Change in choroidal thickness at 3 months postoperatively.
- **Secondary Outcomes:** Changes in macular thickness, SCP VD, SCP PD, FAZ area, and BCVA.

Follow-Up

Measurements were recorded preoperatively and at 3 months postoperatively. OCT and OCTA scans were performed at each visit to assess structural and vascular changes.

Statistical Analysis

Data were analyzed using statistical software (e.g., SPSS version 25.0). Continuous variables were expressed as mean ± standard deviation (SD). Paired t-tests were used to compare preoperative and postoperative measurements within groups, while independent t-tests were employed for comparisons between groups. Pearson correlation coefficients assessed relationships between continuous variables. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations

The study adhered to the tenets of the Declaration of Helsinki. Ethical approval was obtained from the Institutional Ethics Committee of S.M.S. Medical College and Hospital, Jaipur. All participants were informed about the nature and purpose of the study, and written informed consent was obtained prior to enrollment.

RESULTS

A total of 108 eyes from 108 patients were included in the study, with 54 eyes in the case group (diabetic retinopathy patients without macular edema) and 54 eyes in the control group (non-diabetic patients). The mean age and sex distribution between the two groups were comparable ($p > 0.05$), ensuring homogeneity in baseline characteristics.

Table 1: Comparison of Demographic and Clinical Characteristics Between Case and Control Groups

	Case		Control		P value
	Mean	**Std. Dev.**	**Mean**	**Std. Dev.**	
Age	65.370	6.913	67.537	6.906	0.106
FBS	98.746	6.974	80.130	8.720	p<0.001
PPS	139.222	9.430	120.259	11.146	p<0.001
Hb1AC	6.828	0.624	5.389	0.642	p<0.001
Sex (F/M)	27/27		18/36		0.118

Tale 2: MT

	Case		Control	
	Mean	**Std. Dev.**	**Mean**	**Std. Dev.**
Pre Op	277.426	16.514	272.852	13.876
After 3 months	292.500	22.133	291.352	15.206
P value	p<0.001		p<0.001	

MT significantly increased in both the case and control groups after 3 months compared to pre-op levels. Statistical analysis confirmed significant differences in MT before and after three months in both groups (p<0.001).

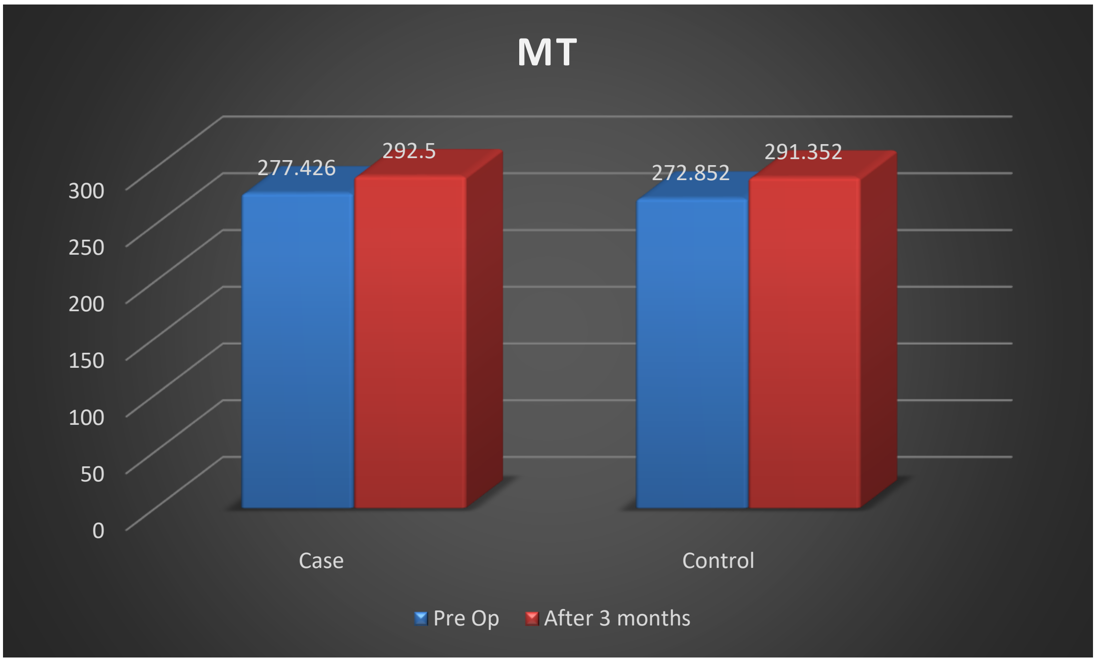


Table 3: SCP VD (mm/mm2)

	Case		Control	
	Mean	**Std. Dev.**	**Mean**	**Std. Dev.**
Pre Op	14.640	3.391	16.096	2.117
After 3 months	18.712	2.794	16.360	2.416
P value	p<0.001		0.133	

The mean SCP VD significantly increased from pre-operation to after 3 months in the case group ($p < 0.001$), indicating a positive effect of the intervention on SCP VD. In the control group, there was no statistically significant change in SCP VD from pre-operation to after 3 months ($p = 0.133$)

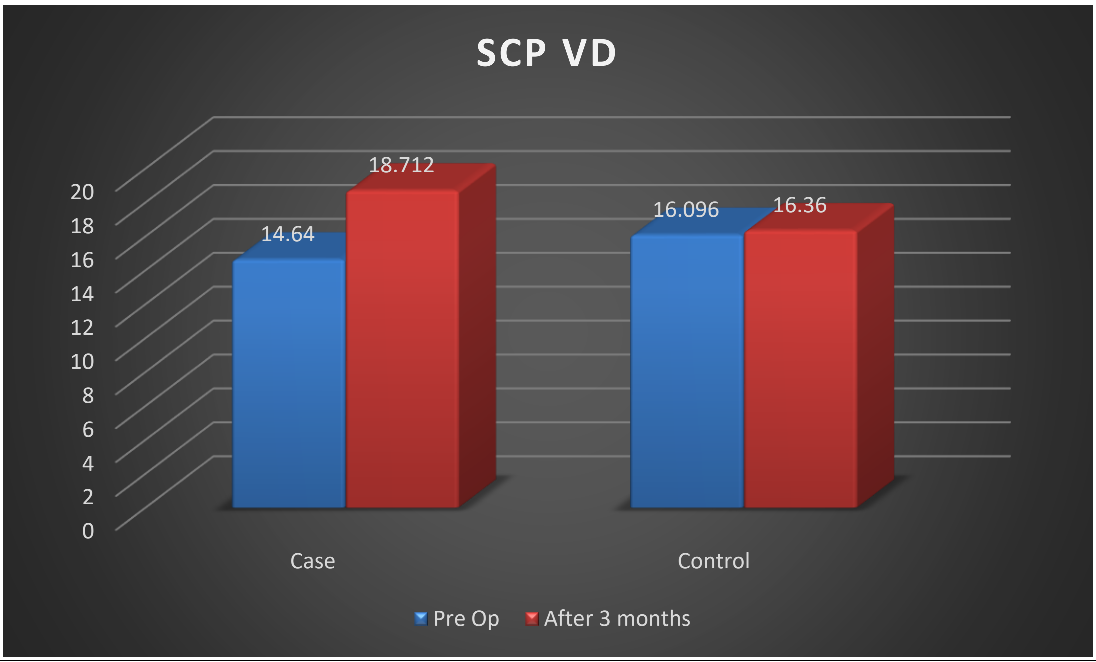


Table 4: SCP PD (%)

	Case		Control	
	Mean	**Std. Dev.**	**Mean**	**Std. Dev.**
Pre Op	22.478	5.300	22.361	5.600
After 3 months	28.905	5.125	22.609	5.669
P value	p<0.001		0.103	

The mean SCP PD (%) significantly increased from pre-operation to after 3 months in the case group ($p < 0.001$), indicating a positive effect of the intervention on SCP PD (%). In the control group, there was no statistically significant change in SCP PD (%) from pre-operation to after 3 months ($p = 0.103$)

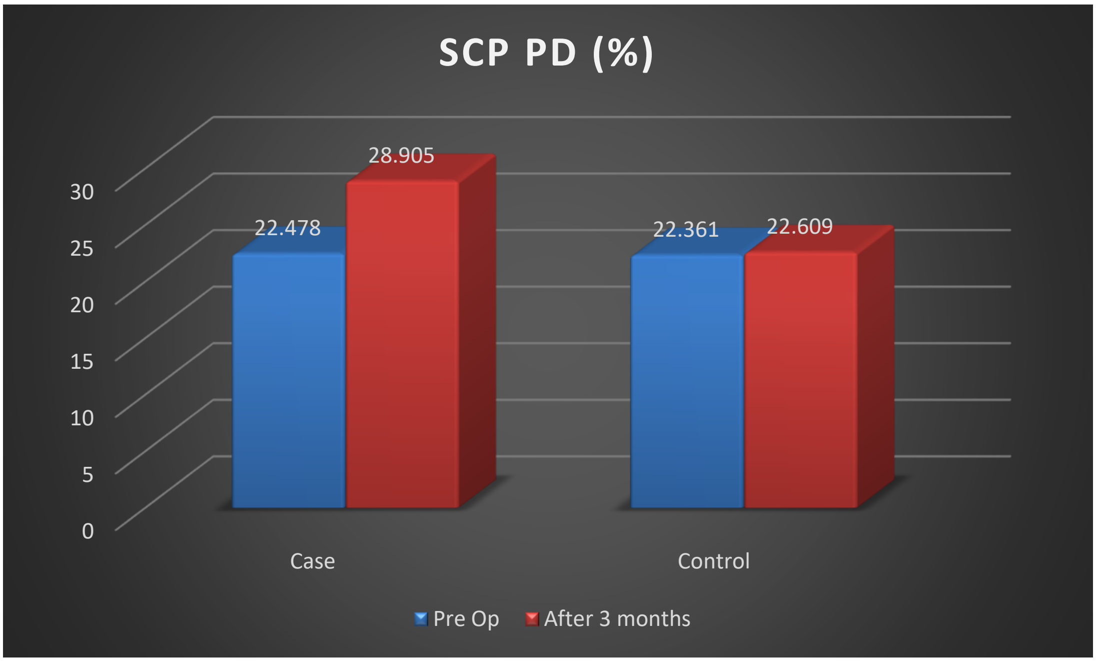
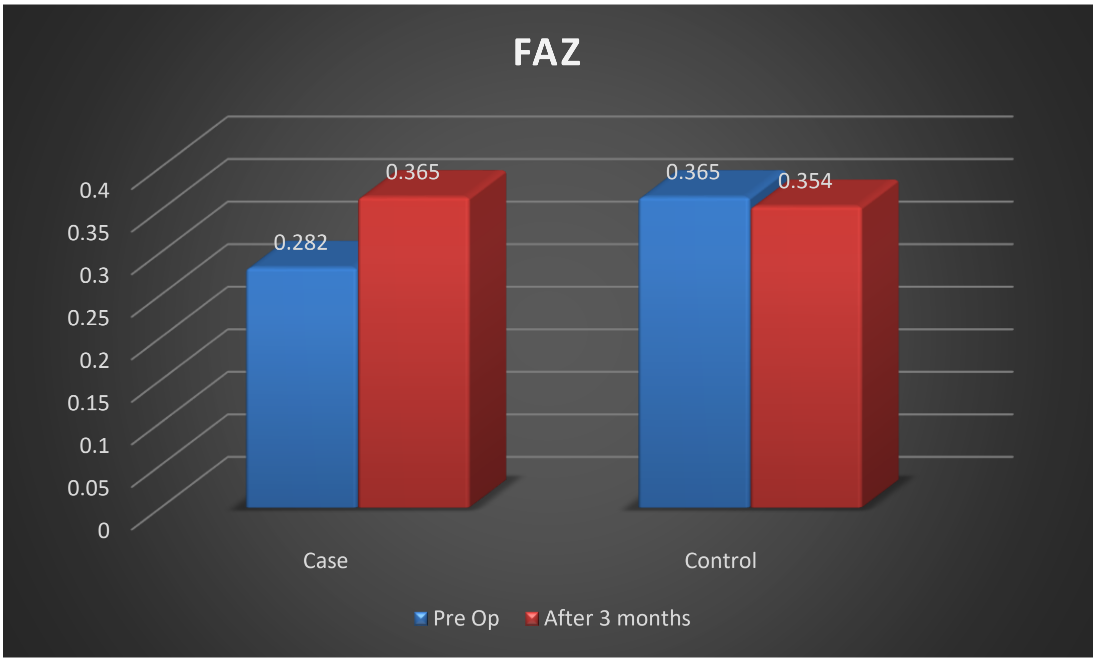


Table 5: FAZ (mm2)

	Case		Control	
	Mean	**Std. Dev.**	**Mean**	**Std. Dev.**
Pre Op	0.282	0.193	0.365	0.083
After 3 months	0.365	0.207	0.354	0.080
P value	p<0.001		0.119	

The mean FAZ significantly increased from pre-operation to after 3 months in the case group ($p < 0.001$). In the control group, there was no statistically significant change in FAZ from pre-operation to after 3 months ($p = 0.119$).



DISCUSSION

OCT angiography has been an effective and non-invasive tool for investigating retinal vascular diseases such as DR. In this study, we first assessed the changes in OCTA parameters before and after 3 months after cataract surgery on individual level and also correlated them with visual and anatomic outcomes in the form of BCVA and MT, SCP VD, SCPPD, FAZ respectively.

To the best of our knowledge, there are few observational follow-up studies about macular microvasculature changes after phacoemulsification in this specific population of patients with mild to moderate DR using the OCTA-based VD and PD calculation and analysis. SCP-VD and PD in the macula increased at 3 months postoperatively compared with baseline in patients with DR in this study.

Our study, changes in MT in patients with DR were significantly greater than those in controls at 3 months postoperatively; changes in SCP-VD and PD in patients with DR were significantly greater than those in the control group at 3 months postoperatively. Presumably, it was suggested that cataract surgery might increase the risk of macular edema in patients with mild/ moderate DR compared with patients without diabetes, which may be due to defects in blood-retinal barrier function in those patients with more advanced vascular changes caused by microvascular destruction in DR than in normal individuals.

The presence of diabetes was a risk factor of pseudophakic macular edema (PME) and the risk increased approximately linearly with the severity of retinopathy (6).

At present, cataracts and diabetes very commonly coexist. Some studies have shown that phacoemulsification can accelerate diabetic retinopathy (7-9). Other studies suggest that the development of DR and DME after cataract surgery is part of the natural history of the disease and that cataract surgery does not cause the progression of diabetic retinopathy (10-11).

In our study, we used OCTA to quantitatively investigate the differences in MT and SCP between diabetic and nondiabetic patients in the short term after phacoemulsification. Our results indicate that OCTA can effectively show retinal micro vascular changes after cataract surgery in diabetic patients. We found a significant increase in MT from baseline to 3 months postoperatively in both groups. However, there was no significant difference in the magnitude of change between the two groups. Therefore, in our short-term observation, both diabetic and nondiabetic patients exhibited an increase in MT. It can be considered that the surgery itself did not increase the risk of DME.

Cong et al.(11) summarized the possible mechanisms of macular thickness changes after cataract surgery, and the mechanisms included the release of local inflammatory mediators caused by surgical stimulation, tissue damage caused by ultrasound energy and radiation effects, surgical perfusion fluid damage, and light exposure. Although the loss of pericytes, endothelial cells, and hemodynamic abnormalities in diabetic patients can also cause postoperative macular thickness increase and even macular edema, this study did not find the difference between diabetic and nondiabetic groups from statistical analysis. This is similar to the results reported in previous studies in nondiabetic patients.

This is similar to the results reported in previous studies in non diabetic patients. George et al. observed hyper fluorescence of the macula and optic disc postoperatively on fluorescein angiography in the surgical eyes, which was greater than that in the nonsurgical eyes (12). Moreover, increased macular thickness has previously been reported in surgical diabetic eyes (13) which are similar to the results of our research.

Kurt and Kilic(14) showed a decrease in MT on the first postoperative day, increases at week 1 and months 1 and3,and a relative decrease at month 6, although MT did not return to preoperative levels. Zhao et al.(15) also reported that at 1 month and 3 months after surgery, the full retina of the fovea, parafovea, and perifovea increased significantly, and this change was more obvious in the inner layer.

Yu et al.(16) reported a significant increase in perfusion and vessel densities in both the SCP and the DCP after cataract surgery in 3×3mm images. The authors considered that inflammation may impact the assessment of density parameters. Pilotto et al.(17) found that macular intermediate retinal capillary (ICP) and DCP perfusion increased at 1 day after uncomplicated cataract surgery, whereas the extent of macular SCP perfusion did not change, and all parameters almost reached baseline levels after 90 days, which seems to confirm their inflammatory nature. In our results, the diabetes group began to show a significant increase in SCP at 3 months after surgery.

Haleem et al.(18) showed that cystoid macular edema after phacoemulsification wase equally present in both diabetic and nondiabetic patients without any retinopathy. There have been no reports on postoperative SCP and DCP in diabetic patients. We also observed a significant increase in FAZ area in diabetic group after 3 months of cataract surgery.

In a study including 205 eyes, an increase in FAZ size significantly predicted the progression of DR ($p < 0.001$). In addition, the FAZ shows a higher degree of irregularity in patients with severe DME compared with those with earlier-stage DME.(19)

In conclusion we can say that macular thickness increased in both diabetic and nondiabetic patients at 3 months after cataract surgery, and the SCP increased only in diabetic patients at 3 months after cataract surgery. OCTA found that SCP increased in diabetic patients 3 months after cataract surgery, which may have a predictive effect on the progression of postoperative DR.

Our study also concludes that increase FAZ area can also be used as a predictive factor for progression of disease severity of DR in comparison to normal eyes.

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