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Optical Coherence Tomography Angiography Assessment of Deep and Superficial Macular Plexus in Diabetes Mellitus Type II before and after Anti-VEGF Injection

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ABSTRACT

Background: Diabetes mellitus (DM) is a multi-system disease with vision-threatening complications such as diabetic retinopathy (DR) and diabetic macular edema (DME), requiring multi-specialist care. In Egypt and the Middle East, DM prevalence and its complications vary widely, with DR being a leading cause of visual impairment. Imaging tools like optical coherence tomography (OCT) and OCT angiography (OCTA) have become essential in detecting and monitoring DME and DR, offering non-invasive, high-resolution evaluation of retinal microvasculature.

Aim: This study aimed to detect changes in the superficial and deep macular plexus in DME before and after injection of anti-vascular endothelial growth factor (anti-VEGF) using OCTA.

Patients and methods: This prospective interventional trial included 50 eyes of 39 patients with DME who were divided into non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) groups. Patients with a history of retinal procedures or non-diabetic causes of macular edema were excluded. All participants underwent standardized ophthalmologic examination and data analysis.

Results: The study did not reveal differences in demographics, glycated hemoglobin (HbA1c), intraocular pressure (IOP), DM duration, and the side of the lesion between NPDR and PDR groups. Significant differences in pre- and post-operative best-corrected visual acuity (BCVA) and central macular thickness (CMT) were noted. Vascular density (VD) of the superficial capillary plexus (SCP) and deep capillary plexus (DCP) in parafoveal areas post-operatively was significantly different between the groups, with each group having distinct intra-group changes in visual and anatomical parameters.

Conclusion: The VD of the SCP and DCP of the fovea and parafoveal area, as well as foveal avascular zone (FAZ) size at baseline were good predictor factors for both anatomical and visual improvement after intravitreal ranibizumab injection in eyes with DME. OCTA offers measurements for VD and FAZ size at the macula and could be used to predict the visual prognosis of anti-VEGF treatment in DME.

Keywords: Diabetic macular edema, Diabetic retinopathy, OCT angiography, Ranibizumab, Vascular density.

INTRODUCTION

Since diabetes mellitus (DM) affects multiple organs, managing its consequences, such as diabetic macular edema (DME), can be challenging and necessitates a multidisciplinary approach [(1).] In developed nations, diabetic retinopathy (DR) is thought to be the primary cause of vision impairment [(2)]. Diabetes mellitus (DM) has become an increasingly significant health concern in Egypt, both clinically and from a public health standpoint. During the 1990s, its prevalence ranged between 5% and 10%. Projections suggest that by 2025, approximately 9 million Egyptians—accounting for more than 13% of adults over the age of 20 will be affected by the disease [(3)]. Research examining the occurrence of DM and DR in Egypt and other Middle Eastern nations reveals wide variations in prevalence rates. These studies report that DM affects between 3.4% and 29% of the population, while DR complications are seen in 7.6% to 60% of cases, with notable differences even within a single country [(4).]

In diabetic macular edema (DME), retinal thickening occurs as a consequence of blood–retinal barrier breakdown and fluid leakage from microaneurysms. VEGF is a central mediator of this vascular leakage, making anti-VEGF agents the first-line therapeutic option. These drugs significantly reduce edema and enhance visual function in many patients [(5)]. Among the traditional imaging modalities for diabetic retinopathy (DR), fluorescein angiography (FA) is widely employed to detect leakage patterns and microaneurysms. However, FA has notable limitations, particularly its poor visualization of the deeper retinal layers where most pathological changes occur [(6)]. Optical coherence tomography (OCT), by contrast, provides detailed cross-sectional images of retinal layers and is a standard tool for assessing diabetic maculopathy [(7)].

Optical coherence tomography angiography (OCTA) introduces a non-invasive approach to evaluate retinal and choroidal vasculature using motion contrast from blood flow, thereby avoiding the use of fluorescent dye [(8)]. Studies have confirmed OCTA's utility in detecting microvascular anomalies in various retinal diseases, including DR [(9)]. Furthermore, OCTA facilitates the measurement of quantitative parameters—such as the FAZ area and capillary vessel and perfusion densities—which are essential for identifying early microvascular changes and monitoring DR progression. These biomarkers may help clinicians detect subclinical disease and intervene before serious visual complications develop [(10)]. Therefore, this study aimed to detect changes in

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superficial and deep macular plexus in DME before and after injection of anti VEGF using OCTA.

PATIENTS AND METHODS

Patients with DME who received intravitreal ranibizumab injections were the subjects of this prospective interventional trial. The study population was sourced from Monofia University Hospitals' Outpatient Clinic, while imaging and investigations were carried out at El Fatah Eye Center in Zagazig, Sharkia. Twenty-five eyes from 39 patients with NPDR and twenty-five eyes with PDR were selected and categorized into two groups. The study was carried out between October 2021 and June 2024. Patients with type 2 DM who were between the ages of 30 and 70, had a CMT more than 300 μm, and had an OCT-proven DME diagnosis were eligible. Best-corrected visual acuity (BCVA) of 2/60 to 6/9 and OCTA scan quality of 5 or above were prerequisites for additional inclusion criterion. Patients who had a history of intravitreal injections, macular laser photocoagulation, vitreoretinal surgery, or other retinal conditions that could impair vascular imaging (such as retinal vein or artery occlusion or choroidal neovascular membranes) were excluded. Patients with severe media opacities (such as thick cataract or vitreous hemorrhage), tractional retinal detachment, vitreomacular traction, intraocular surgery, or non-diabetic macular edema were also excluded.

All participants received informed consent, which included a concise, straightforward explanation of the study's objectives, a guarantee of data confidentiality, and the freedom to discontinue participation at any time without reason. Along with the researcher's contact details, the consent form guaranteed participants that they would be updated on the study's findings. To indicate agreement, each participant signed or left a fingerprint.

Following registration, patients had a thorough ophthalmologic evaluation that included investigative imaging, a clinical examination, and a history. An Auto ref/keratometer (ARK-1, NIDEK Co., Japan, 2013) was used to measure visual acuity and refraction. BCVA values were then recalculated as LogMAR for analysis. The anterior segment was evaluated by slit-lamp biomicroscopic evaluation (SL-D7 Topcon, Japan), and intraocular pressure was measured with a Goldmann applanation tonometer (Shin Nippon, Japan). A +90 diopter Volk lens and an indirect ophthalmoscope (Model AAIO-7, Appasamy Associates, India, 2014) were used for the fundus examination.

OCTA using the RTVue-XR Avanti system enabled detailed imaging of retinal capillary plexuses and FAZ before and after ranibizumab treatment. Pupils were dilated, patients stabilized, and poor-quality scans were excluded or corrected to ensure accurate analysis.

The superficial retinal capillaries (from the inner limiting membrane to the posterior border of the IPL) and the deep retinal capillaries (from the posterior border of the IPL to the outer plexiform layer) were the two layers that were the focus of OCTA imaging. Inbuilt software that used automatic segmentation based on OCT intensity volume was used to quantify the FAZ region and vascular densities (VD). A 6 × 6 mm region centered on the fovea was used to obtain the scans, and segmentation was manually corrected as needed.

Ranibizumab (IVR) was injected intravitreally in compliance with standard sterile procedures. Sterilized gloves, a lid speculum, microforceps, cotton buds, an ophthalmic drape, povidone-iodine solution, and a 30-gauge needle were among the tools utilized. The pars plana was used to inject 0.5 mg dosages of ranibizumab (Lucentis®, Novartis) into the vitreous chamber; for pseudophakic eyes, this was 3.5 mm from the limbus, and for phakic eyes, it was 4.0 mm. Before the injection, 5% povidone-iodine was used for topical anesthesia and antiseptization. A sterile caliper was used to mark the injection location, and the conjunctiva was retracted to prevent direct contact between the vitreous cavity and the ocular surface. After the treatment, antibiotic drops were administered, and a cotton-tipped applicator was placed during the injection to prevent reflux.

Topical antibiotic drops were administered five times a day for a week as part of the post-injection care. Patients were told to come back if they experienced any symptoms, like pain, redness, or visual changes. Following the injection, there were follow-ups on days 1, 1, and 4. A month following the third injection, OCTA imaging was performed again to assess the effectiveness of the treatment. Improvement in BCVA, CMT, FAZ area, and vascular density in the foveal and parafoveal regions' SCP and DCP were the main outcome measures. Anatomical response to IVR was used to classify the eyes: those with a decrease in CMT ≥50 μm following three injections were considered responders, whilst those with less or no improvement were classified as non-responders. These two groups' OCTA results were compared before and after treatment.

The ETDRS grid, which was manually centered on the FAZ, was used to automatically quantify the FAZ and VD in the quantitative OCTA picture analysis. The percentage of pixels in each retinal subfield that were occupied by arteries was used to calculate vascular density. The structural change and treatment response were compared using these measures.

Ethical approval: The Institutional Research Ethics Board Committee of Menoufia University, and Local Research Committee approved this study (IRB approval number: 2/2021 OPHT 5). Before being included in the study, all individuals provided written informed permissions. The study adhered to the Helsinki Declaration throughout its execution.

Statistical analysis

Data were analyzed using SPSS version 26. Descriptive statistics summarized qualitative data as frequencies and percentages, and quantitative data as means, standard deviations and ranges. Group comparisons used the t-test or Mann-Whitney U test based on data distribution. The Chi-squared test assessed associations between categorical variables. Paired t-test or Wilcoxon test was used for within-group comparisons. A p-value < 0.05 was considered significant.

RESULTS

Regarding their sex, age, HbA1c, IOP, length of diabetes, and lesion side, there was no statistically significant difference between the NPDR group and the PDR group. Regarding pre-operative and post-operative BCVA, there was a statistically significant difference between the NPDR group and the PDR group (P value < 0.05), but not with regard to BCVA change (P value >0.05) (Table 1)

Table (1): Comparison between studied groups regarding BCVA (n=50)

Variable	NPDR (n=25)	PDR (n=25)	Test of significance	P value
Pre-operative BCVA			**U=4.40**	**<0.001***
Mean ± SD	**0.64 ± 0.13**	**0.82 ± 0.47**		
Range	**0.5-0.9**	**-1.3 -1.1**		
Post-operative BCVA			**U=4.66**	**<0.001***
Mean ± SD	**0.37 ± 0.15**	**0.67 ± 0.21**		
Range	**0.2-0.7**	**0.3-1.2**		
BCVA change %			**U=0.57**	**0.566 (NS)**
Mean ± SD	**-0.28 ± 0.08**	**-0.15 ± 0.52**		
Range	**-0.40- -0.20**	**-0.40-2.3**		

***:** Statistically significant**, NS:** Non-significant**, SD:** Standard deviation**, U:** Mann-Whitney U test.

Table (2) demonstrated that with regard to pre-operative and post-operative CMT, there was a statistically significant difference between the NPDR group and the PDR group (P value < 0.05), but not with regard to CMT difference (P value > 0.05).

Table (2): Comparison between studied groups regarding CMT (n=50)

Variable	NPDR (n=25)	PDR (n=25)	Test of significance	P value
Pre-operative CMT (µm)				
Mean ± SD	**336.48 ± 67.88**	**408.48 ± 100.84**	**t=2.96**	**0.005***
Range	**254-474**	**249-629**		
Post-operative CMT (µm)				
Mean ± SD	**280.80 ± 34.12**	**338.32 ± 86.26**	**t=3.10**	**0.003***
Range	**230-370**	**223-573**		
CMT difference (µm)				
Mean ± SD	**-55.68 ± 54.03**	**-70.16 ± 92.43**	**U=1.36**	**0.256 (NS)**
Range	**-220-2**	**-220-161**		

***:** Statistically significant**, NS:** Non-significant**, SD:** Standard deviation**, t:** Student t test**, U:** Mann-Whitney U test.

The NPDR group and PDR group did not differ statistically significantly in terms of pre-operative and post-operative FAZ (P value > 0.05), but they did differ statistically significantly in terms of FAZ difference (P value >0.05) Table (3).

Table (3): Comparison between studied groups regarding FAZ (n=50)

Variable	NPDR (n=25)	PDR (n=25)	Test of significance	P value
Pre-operative FAZ (mm)²			**U=1.16**	
Mean ± SD	**0.28 ± 0.14**	**0.24 ± 0.10**		**0.248 (NS)**
Range	**0.052-0.536**	**0.089-0.468**		
Post-operative FAZ (mm)²			**U=1.41**	**0.159 (NS)**
Mean ± SD	**0.25 ± 0.16**	**0.30 ± 0.14**		
Range	**0.036-0.552**	**0.041-0.572**		
FAZ difference (mm)²			**U=2.80**	**0.005***
Mean ± SD	**-0.04 ± 0.15**	**0.06 ± 0.10**		
Range	**-0.32-0.25**	**-0.19-0.26**		

***:** Statistically significant**, NS:** Non-significant**, SD:** Standard deviation**, U:** Mann-Whitney U test

Table (4) showed that there was a statistically significant difference between NPDR group and PDR group regarding post-operative and SCP para VD difference (P value < 0.05). While, there was no statistically significant difference between NPDR group and PDR group regarding pre-operative SCP para VD (P value > 0.05).

Table (4): Comparison between studied groups regarding SCP Para VD (n=50)

Variable	NPDR (n=25)	PDR (n=25)	Test of significance	P value
Pre-operative SCP Para VD%			**t=1.12**	**0.270 (NS)**
Mean ± SD	**45.85 ± 4.89**	**43.80 ± 7.78**		
Range	**36.6-55**	**23.2-55.6**		
Post-operative SCP Para VD%			**t=2.91**	**0.005***
Mean ± SD	**47.62 ± 5.53**	**42.56 ± 6.70**		
Range	**31.5-56.6**	**33.1-56.1**		
SCP Para VD% difference (mm)²			**U=2.96**	**0.003***
Mean ± SD	**1.78 ± 5.31**	**-1.24 ± 6.60**		
Range	**-16.4-11.8**	**-13.6-14.8**		

***:** Statistically significant**, NS:** Non-significant**, SD:** Standard deviation**, t:** Student t test**, U:** Mann-Whitney U test.

Table (5) demonstrated that in the NPDR group, pre- and post-operative BCVA, CMT, and DCP para fovea VD differed statistically significantly (P value <0.05), but pre- and post-operative FAZ, SCP fovea VD, SCP para VD, and DCP fovea VD did not differ statistically significantly (P value > 0.05).

Table (5): Pre- and post-operative parameters in NPDR Group (n=25)

Variable	Pre-operative	Post-operative	Test of significance	P value
	Mean ±SD	Mean ±SD		
BCVA	**0.64 ±0.13**	**0.37 ±0.15**	**W=4.45**	**<0.001***
CMT (µm)	**336.48 ±67.88**	**280.80 ±34.12**	**t=5.15**	**<0.001***
FAZ (mm)²	**0.28 ±0.14**	**0.25 ±0.16**	**W=0.66**	**0.510 (NS)**
SCP fovea VD	**23.69 ±9.22**	**25.52 ±8.85**	**W=1.20**	**0.231 (NS)**
SCP Para VD%	**45.85 ± 4.89**	**47.62 ±5.53**	**t=1.67**	**0.108 (NS)**
DCP fovea VD%	**36.32 ±10.31**	**36.23 ±5.42**	**t=0.05**	**0.964 (NS)**
DCP Para fovea VD	**46.24 ±5.42**	**48.33 ±4.30**	**t=2.22**	**0.037***

***:** Statistically significant**, NS:** Non-significant**, SD:** Standard deviation**, t:** Paired t test**, W:** Wilcoxon signed rank test.

Table (6) demonstrated that in the PDR group, pre- and post-operative BCVA, CMT, and FAZ differed statistically significantly (P value < 0.05), but pre- and post-operative SCP fovea VD, SCP para VD, DCP fovea VD, and DCP para fovea VD did not differ statistically significantly (P value >0.05).

Table (6): Pre- and post-operative parameters in PDR Group (n=25)

Variable	Pre-operative	Post-operative	Test of significance	P value
	Mean ±SD	Mean ±SD		
BCVA	**0.82 ±0.47**	**0.67 ±0.21**	**W=3.63**	**<0.001***
CMT (µm)	**408.48 ±100.84**	**338.32 ±86.26**	**t=3.80**	**<0.001***
FAZ (mm)²	**0.24 ±0.10**	**0.30 ±0.14**	**W=3.04**	**0.002***
SCP fovea VD	**27.18 ±9.08**	**28.48 ±11.38**	**W=0.19**	**0.851 (NS)**
SCP Para VD%	**43.80 ±7.78**	**42.56 ±6.70**	**t=0.94**	**0.357 (NS)**
DCP fovea VD%	**39.30 ±7.92**	**45.26 ±4.76**	**t=1.31**	**0.203 (NS)**
DCP Para fovea VD	**45.26 ±4.76**	**44.36 ±4.51**	**t=0.73**	**0.470 (NS)**

***:** Statistically significant**, NS:** Non-significant**, SD:** Standard deviation, **t:** Paired t test**, W:** Wilcoxon signed rank test.

DISCUSSION

DR is a progressive microvascular complication of DM, advancing from NPDR to PDR, with increasing retinal damage and VA loss. Anti-VEGF agents reduce neovascularization and DME, improving retinal integrity and enhancing VA. OCTA provides detailed imaging of FAZ, SCP, and DCP, but more research is needed to link these changes with VA outcomes post-anti-VEGF [11].

The aim of the present study was to assess the utility and to detect changes in OCT findings before and after anti- VEGF injection in NPDR and PDR patients. To achieve this aim, the current study included 39 patients representing 50 eyes with diabetic retinopathy (25 eyes with NPDR and 25 PDR).

Visual acuity differences between NPDR and PDR patients: The present study showed that PDR patients had significantly worse visual acuity as LogMAR BCVA was significantly higher among PDR patients than NPDR patients (NPDR vs. PDR: 0.64 ± 0.13 vs. 0.82 ± 0.47; **p< 0.001)**. In concordance with the present study, recent study included 64 DR patients showed higher values of LogMAR BCVA among PDR patients (0.18 ± 0.16) than NPDR patients (0.04 ± 0.07) with statistically significant difference **(p< 0.001)** [12].

Turkseven *et al.* [13] and **Liu *et al.*** [14] are in agreement with the present study and showed that LogMAR BCVA was significantly higher among PDR than among NPDR patients. In contrast, **Riazi-Esfahani *et al.*** [15] did not find significant differences in LogMAR BCVA between NPDR and PDR patients.

Effect of anti- VEGF on visual acuity among NPDR and PDR patients: The current results demonstrated that anti- VEGF administration resulted in significant improvement of visual acuity in both NPDR and PDR groups **(p< 0.001)** and the percent of change after anti-VEGF was comparable between both groups. However, the mean LogMAR BCVA was still significantly higher among PDR than among NPDR patients after anti- VEGF injection (p< 0.001). In concordance with the present study, **Massengill *et al.*** [16] in recent study included 386 patients and 740 eyes showed that LogMAR BCVA significantly improved in both PDR and NPDR patients after anti- VEGF administration (pre vs. post; 00.27± 0.20 vs. 0.22 ± 0.20; P= 0.04). Also, **Mostafa *et al.*** [17] included 24 diabetic patients with diabetic maculopathy received anti- VEGF. They reported that visual acuity showed significant increase after 1 and 2 months of anti- VEGF **(p< 0.001)**. In contrast with the present study, **Santamaria *et al.*** [18] in previous study included 48 patients (30 NPDR and 18 PDR) did not find significant effect of anti- VEGF on visual acuity.

Central macular thickness differences between NPDR and PDR patients: The current results showed that PDR patients had significantly higher central macular thickness (CMT) than NPDR patients (p= 0.005). In agreement with the present study, **Wang *et al.*** [19] demonstrated presence of significant differences between NPDR and PDR patients as regards CMT which was significantly higher among PDR than among NPDR patients **(p< 0.001)**. In contrast with the present study, **Turkseven *et al.*** [20] could not find significant differences in central macular thickness between PDR and NPDR patients.

Effect of anti- VEGF on CMT among NPDR and PDR patients: The current work demonstrated that anti- VEGF administration resulted in significant improvement of CMT as it was significantly decreased after anti- VEGF in both NPDR and PDR patients **(**p< 0.001; < 0.001) with similar percent of change in both groups. However, CMT was still significantly higher among PDR than among NPDR patients after anti- VEGF injection (p= 0.003). In agreement with the present study, **Massengill *et al.*** [16] demonstrated that CMT was significantly reduced after anti- VEGF in both PDR and NPDR patients (pre vs. post: 308.95 ± 73.10 mm vs. 289.54 ± 62.80 mm; P= 0.02). Similarly, **Mostafa *et al.*** [17] reported significant decline in CMT after 1 and 2 months of Anti- VEGF administration among diabetic maculopathy patients (p < 0.001).

In addition, **Santamaria *et al.*** [18] in another recent study found that CMT was significantly reduced after anti- VEGF among PDR and NPDR patients (p < 0.001). Among 24 NPDR patients, anti- VEGF resulted in significant reduction of CMT from 450 ± 94 mm to 331 ± 69 mm within 3 months (p < 0.001) in previous study by **Dabir *et al.*** [21]**.**

Foveal avascular zone differences between NPDR and PDR patients: The present study did not find significant differences between NPDR and PDR patients as regards foveal avascular zone (FAZ) (p= 0.25). In concordance with the present study, **Alam *et al.*** [22] did not find significant differences in FAZ (superficial and deep) between NPDR and PDR patients despite the higher values of FAZ among PDR patients (p= 0.29). Similarly, previous study included 17 NPDR patients and 23 PDR patients did not find significant differences in area of FAZ between both groups [14]. In disagreement with the present study, **Awad *et al.*** [12] reported significant differences in area and thickness of FAZ between PDR and NPDR patients showing higher area and thickness of FAZ among PDR patients **(p< 0.001)**.

Effect of anti- VEGF on FAZ among NPDR and PDR patients: Injection of anti- VEGF resulted in significant different effect on FAZ between NPDR and PDR as FAZ was significantly increased in PDR patients after anti- VEGF **(p= 0.002),** while in NPDR, FAZ was

reduced after anti- VEGF with insignificant differences as compared to pre- treatment. In agreement with the present study, **Massengill *et al.*** [16] showed that area of FAZ was significantly increased after anti- VEGF among DR patients with diabetic maculopathy (pre vs. post; 0.35 ± 0.09 vs. 0.38 ± 0.11; P= 0.03). In NPDR patients, **Dabir *et al.*** [21] in another study demonstrated that area of FAZ was significantly reduced after anti- VEGF. They assumed that rather than an improvement in macular perfusion, the majority of the FAZ size reduction was caused by a concurrent decrease in capillary displacement as a result of the intraretinal oedema's regression. In contrast with the present study, **Conti *et al.*** [23] did not find significant effect of anti- VEGF on FAZ among both NPDR and PDR patients over 6 months of treatment.

Superficial and deep capillary plexuses differences between NPDR and PDR patients: The current work failed to find significant differences in superficial capillary plexus (SCP) (either foveal or parafoveal) or in deep capillary plexus (DCP) (either foveal or parafoveal) between NPDR and PDR groups. In agreement with the current study, **Alam *et al.*** [22] did not find significant differences between NPDR and PDR OCT findings as regards foveal and parafoveal SCD or DCP. In contrast with the present study, **Wang *et al.*** [19] in a previous study reported that OCT showed vessel density in DCP was significantly lower in PDR patients than NPDR patients **(p< 0.001)**, however in the same line of the present results, they did not find significant differences in SCP between both groups. **Liu *et al.*** [14] demonstrated that OCT of PDR patients showed significant reduction of DCP and overall blood vessels density as compared to NPDR **(p< 0.001)**. Also, in discordance with the present study, **Ashraf *et al.*** [24] showed that vessel densities in SCP and DCP were significantly lower among DPR than among NPDR patients **(p< 0.001)**.

Effect of anti- VEGF on SCP and DCP among NPDR and PDR patients: The present study did not find significant changes in SCP, either foveal or parafoveal, after anti- VEGF injection in both PDR and NPDR patients. However, the degree of change was significantly higher in NPDR patients than PDR patients in parafoveal SCP (p= 0.003) and post-treatment parafoveal SCP was significantly higher among NPDR than PDR patients (p= 0.005). In concordance with the present study, **Massengill *et al.*** [16] did not notice significant changes in vessel densities of SCP after anti- VEGF injection in both NPDR and PDR patients. However, they found that vessel diameters in SCP were significantly reduced after anti-VEGF (p= 0.02). **Santamaria *et al.*** [18] also could not find significant effect of anti- VEGF or significant changes after anti- VEGF in SCP among DR patients. In disagreement with the present study, **Pongsachareonnont *et al.*** [25] in another study included 152 NPDR patients showed that SCP density was significantly increased after anti- VEGF over 2 months.

The present results did not find significant differences regarding the effect of anti- VEGF on foveal DCP between NPDR and PDR patients as it increased in both groups after anti- VEGF with insignificant differences as compared to baseline. However, the effect of anti- VEGF on parafoveal DCP was significantly different between NDPR and PDR. In NPDR patients, parafoveal DCP was significantly increased **(p= 0.037)** while in PDR patients, parafoveal DCP decreased with insignificant differences, thus postoperative parafoveal DCP was significantly higher among NPDR than PDR **(p= 0.003)**. In the same line, **Massengill *et al.*** [16] could not notice significant changes in DCP vessel densities after anti- VEGF in both PDR and NPDR patients. However, they did not examine foveal and parafoveal regions separately. **Mostafa *et al.*** [17] showed that vessel density was significantly reduced among PDR patients who underwent anti- VEGF injection **(p< 0.001)**. Similarly, **Santamaria *et al.*** [18] found that anti- VEGF did not have significant effect on DCP at foveal region, however, DCP was significantly reduced after anti-VEGF at nasal side among PDR patients **(p= 0.001)**. Also, **Wei- Zhang *et al.*** [26] in recent study included 42 NPDR eyes and 47 PDR eyes showed that post-treatment parafoveal DCP density was significantly lower among PDR than NPDR patients. **Santamaria *et al.*** [18] could not demonstrate presence of anti- VEGF on DCP at all regions except nasally, DCP was significantly reduced after 6 months of anti-VEGF **(p= 0.001).** Also, **Sorour *et al.*** [27] failed to find significant changes in DCP after anti-VEGF among NPDR and PDR patients.

LIMITATIONS: The current study had some limitations. The study explored only 1 treatment option of diabetic retinopathy which is anti- VEGF. Also, the study assessed the ranibizumab only. Further studies comparing different anti-VEGF treatments and different treatment modalities is suggested.

CONCLUSION

In eyes with DME, the FAZ size at baseline and the VD of the SCP and DCP of the fovea and parafoveal area showed to be reliable indicators of both morphological and visual improvement following intravitreal ranibizumab injection. The visual prognosis of anti-VEGF treatment in DME may be predicted by OCTA, which provides measures for VD and FAZ size at the macula.

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