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Visual Function and Foveal Avascular Zone Changes in Patients with Diabetic Macular Edema After Intravitreal Injection of Ranibizumab

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Short title*:* Visual Function and Foveal Avascular Zone Changes in Diabetic Macular Edema

ABSTRACT

Purpose: to assess changes in FAZ area in patients with diabetic macular oedema (DME) after intravitreal injection (IVI) of anti-VEGF (Ranibizumab) and its effect on visual function.

Methods: Patients with DME were subjected preoperative to the following ophthalmologic examination: Best corrected visual acuity (BCVA), Contrast sensitivity test, Color vision test, slit lamp examination, fundus examination, ocular tension, FAZ area by Optical Coherence Tomography Angiography (OCTA). Then all patients were injected intravitreally with Anti-VEGF (Ranibizumab) 3 doses with one month interval. Postoperative data was collected regarding the (BCVA), contrast sensitivity test, color vision test, slit lamp examination, fundus examination, ocular tension, FAZ evaluation by OCTA.

Results: The study included 30 eyes with DME, the mean age was 57.4± 6.9 years, 19 (63.33%) were females, and only 11 (36.33%) were males. all visual functions significantly improved after intravitreal (IV) Ranibizumab administration. Also, there was correlation between visual acuity (VA) and FAZ shape, according to FAZ shape pre-operative, all cases had more irregular shape with mean BCVA 0.9746±0.28. while post-operative, 27 (90%) patients had more regular FAZ shape with mean BCVA 0.413±0.162 and only 3 (10%) patients had irregular FAZ shape with mean BCVA 0.852±0.128.

Conclusion: Assessment of the size and shape of FAZ is probably essential for detecting pathological macular alteration and prediction of visual outcomes in DR.

Keywords: Foveal Avascular Zone, Deep Capillary Plexus, Diabetic Macular oedema, OCTA, Superficial Capillary Plexus.

INTRODUCTION

Diabetic retinopathy (DR) has been considered the primary cause of visual impairment among the working population in developed nations. Diabetes mellitus (DM) negatively affects, across various mechanisms, a lot of ocular parts and the visual pathway, but in most cases visual impairment results from DR[1]**.** Visual-threatening adverse events of DR involve diabetic macular oedema (DME), macular ischaemia, vitreous haemorrhage, and tractional retinal detachment. DME is the commonest among them, with a great impact on the patient's life quality[2]**.**

A lot of studies have explained the role of VEGF-A as a mediator of ischaemia-related ocular neovascularization. VEGF-A encourages growth of vascular endothelial cells from arteries, veins, and lymphatics. In addition, VEGF-A stimulates the process of angiogenesis in vivo. Moreover, VEGF administration causes abrupt increases in microvascular permeability in a lot of experimental studies[3]**.**

Intravitreal ranibizumab was the 1st anti-VEGF drug approved by the FDA in the context of DME management[4]**.** It was originally approved for treating neovascular age-related macular degeneration (AMD)[5]**.**

Patients with DME present with a range of visual manifestations according to the foveal affection degree and the chronicity of the oedema. By time, cases experience a gradual progressive vision loss over weeks to months. Several forms

of visual affection could be recorded among the affected cases which include loss of color vision, poor night vision and visual washing-out in sunlight with poor dark-light adaptation[6].

Foveal avascular zone (FAZ) is a distinctive retinal region comprising the highest density of cone photoreceptors and high O2 consumption[7]. As the FAZ of the normal eye typically reveals a circular or elliptical shape, any change from this shape are common in vascular pathologies[8,9], there is a relationship between VA and FAZ circularity, where eyes with poor VA had a more irregular shape of FAZ. The FAZ of DR deviated from the mildly wavy boundaries demonstrated in normal controls, which became evident in severely diseased eyes[10]. FAZ margin defects are primarily owing to capillary loss and vascular remodeling. Additionally, macular oedema could be accompanied by diminished vascular elasticity owing to mechanical stretching that result in block of blood vessels[11].

It has been demonstrated that; there are a limited number of literatures that discussed the role of OCTA in the context of DR[12]. It has been recorded that OCTA of diabetic eyes ranging from no retinopathy to proliferative DR revealed choriocapillaris alterations and/or retinal microvascular changes, which include microaneurysms, enlargement of FAZ, and capillary vasodilation.

Essentially, OCTA allows noninvasive and dye-free imaging of the retinal vasculature offering HR3D images of the various retinal vascular layers individually. OCTA is formerly demonstrated to describe regions of capillary dropout accurately and to image the FAZ without obscuration by dye leaking or macular xanthophyll pigment shadowing in comparison with FA. In addition, it permits quantitative and automated measurements of the retinal vascular density (VD)[13]. So, this study aimed to assess changes in FAZ area in patients with DME after IVI of anti-VEGF (Ranibizumab) and its effect on visual function.

PATIENTS AND METHODS

This prospective interventional study was conducted on 30 eyes of 28 diabetic patients with DME, collected from an outpatient clinic in the Ophthalmic Center, Mansoura University, Dakahlia Governorate, Egypt, from August 2022 to August 2023 after approval from Institutional review board (IRB) (code number MS.22.09.2121), Faculty of Medicine, Mansoura University.

This study included diabetic patients (NPDR) from both genders with DME in need of intra vitreal injection of ranibizumab (with macular thickness >400 micron) confirmed by OCT and FFA, patients aged 55 ± 15 years. But we excluded patients with history of previous IVI injection of anti-VEGF and steroid, with history of focal, grid laser or PRP, with history of pars plana vitrectomy, with media opacity as (corneal opacity, cataract, PCO or vitreous hemorrhage) interfering with imaging, with other retinal diseases as choroidal neovascular membrane, AMD, inflammation and other vascular retinopathies and with ocular trauma.

Method

All cases were subjected to complete history taking including complaint & its duration, History of DM duration, control and medication, past surgical history (ocular trauma or surgery).

Physical examinations included general examination to exclude any systemic diseases. Ophthalmological examination included BCVA using landolt's broken ring chart, for statistical analysis, acuities were expressed in logMAR units, contrast sensitivity test using Pelli-Robson contrast sensitivity chart; The Pelli-Robson test measures contrast sensitivity using a single, large letter size, with contrast varying across groups of letters. Patients read the letters, starting with the highest contrast, and continue until they were unable to read two or three letters in a single group. The individual was allocated a score according to the contrast of the last group in which two or three letters were properly read, colour vision test using Ishihara pseudo isochromatic plates (Ishihara's24 plates) the test was performed at reading distance and the patients were asked to read the numerals which were seen on plates within five s, results analysis as evaluation of the readings of plates 1 to 15 determines the normality or defectiveness of color vision. If 13 or more plates are read normally, the colour vision is considered as normal. If only nine or less than nine plates are read normally, the colour vision is considered as deficient, slit lamp examination to assess media clarity, slit lamp bio microscopy to examine fundus using non-contact Volk lens +78D, measurement of ocular tension using applanation tonometer, and FAZ measuring using OCTA using Swept Source DRI OCT device (Triton, Topcon, Tokyo, Japan) version 2015, OCTA examination was done by selecting

angiography mood from the main menu of the instrument for the macular region centered 3 × 3 mm2.FAZ and perifoveal capillary network was visualized in scans centred on the fovea by performing a 3 × 3 mm2 scan over the macular region; the multiple retinal vascular planes was simplified into two primary layers the superficial and deep capillary plexuses, FAZ was measured, both its size and shape where shape was manually delineated through choosing area from measure(Ruler) then drawing a line along its boundaries, and size popped up and appeared automatically on the screen.

Surgical Technique

Patients with DME were injected intravitreally with Anti-VEGF (Ranibizumab) 3 doses with 1month interval. Before injection the field was sterilized by betadine %5 (two times five minutes apart) followed by instillation of anaesthetic eye drops (Two times three minutes apart). A lid speculum was inserted. IVI of 0.05 ml of a 0.23ml/2.3mg per vial of Ranibizumab via pars plana approach, in the inferotemporal quadrant 4mm posterior to limbus in phakic eyes and 3.5mm posterior to limbus in pseudophakic and aphakic eyes using a 27gauge needle. Flux was prevented by applying soft sponge.

Post-Injection Care and Follow Up

After injection no paracentesis was needed, topical antibiotic eye drops, combined antibiotic steroid eye drops, antiglaucoma eye drops were applied with eye patching. These medications were prescribed for all patients for one week after injection.

Postoperative Assessment

Data was collected regarding the BCVA, contrast sensitivity test, colour vision test, SL examination, fundus examination, ocular tension using applanation tonometer, OCTA using SS-OCT device (Triton, Topcon, Tokyo, Japan) from each case one month after the 3rd IVI of ranibizumab.

Statistical Analysis

The collected data was coded, processed and analysed using SPSS program (Version 24) for windows. The proper statistical tests were used when required. P value less than 0.05 was statistically significant.

RESULTS

The study was conducted in ophthalmic center, Mansoura University, Dakahlia governorate, Egypt, on 30 eyes with DME. Table **(1)** shows that mean age (year) was 57.4± 6.9, 63.33% were females while 36.33% were males. According to Diabetes mellitus, 56.66% were NIDDM and 43.33% were IDDM, according to other systemic diseases 10% had HTN, 3.33% had Cardiac and renal disease. According to past history, 73.33% had no surgery or trauma while 13.33% of them had Lt phaco + PCIOL and 13.33% had Rt phaco + PCIOL. According to ophthalmic history 100% had DR(NPDR) with DME. According to surgical technique, all patients injected with 3 successive monthly IVI of anti-VEGF Ranibizumab, 56.66% in right while 43.33% in left.

Table (1): Demographic data, medical history, past & ophthalmic history and Surgical technique of patients in this study

	Studied patients (n = 30)
Age (year)	
Mean ± SD.	57.4± 6.9
Gender	
Female	19 (63.33%)
Male	11 (36.66%)
Diabetes mellitus	
NIDDM	17 (56.66%)
IDDM	13 (43.33)
other systemic diseases	
NAD	**26 (86.66%)**
HTN	**3 (10%)**
Cardiac + renal	**1 (3.33%)**
Past History	
no surgery or trauma	22 (73.33%)
Lt phaco+PCIOL	4 (13.33%)
Rt phaco+PCIOL	4 (13.33%)
Ophthalmic history	
DR with DME	30 (100%)
Surgical Technique	
3 consecutive monthly IVI of anti VEGF Ranibizumab	30 (100%)
Laterality	
Rt	17 (56.66%)
Lt	13 (43.33%)

phaco: phacoemulsification DR: diabetic retinopathy DME: diabetic macular oedema

Table **(2)** shows that there was a highly statistically significant difference between patients preoperative and postoperative in terms of BCVA and contrast sensitivity test. There was a highly statistically significant difference between patients preoperative and postoperative regarding color vision test, as preoperative 70 % had defect color vision test and 30% had normal vision test. While postoperative, 86.7 % of patients had normal color vision test and only 13.3% had defect color vision test. According to IOP there was no statistically significant difference between pre and postoperative in this study.

Table (2): Comparison of BCVA, Contrast sensitivity test, color vision test, Normal & defect color vision test and IOP (mm\hg) pre and postoperative in this study.

	Preoperative	Postoperative	p. Value
BCVA			
Mean ± SD.	0.97± 0.27	0.456± 0.206	≤0.0001
Contrast sensitivity test			
Mean ± SD.	0.52± 0.159	1.13± 0.37	≤0.0001
Color Vision Test			
2\15	1 (3.33%)	0 (0%)	≤0.001
4\15	1 (3.33%)	0 (0%)	
5\15	1 (3.33%)	1 (3.33%)	
8\15	3 (10%)	0 (0%)	
9\15	4 (13.33%)	1 (3.33%)	
10\15	3 (10%)	0 (0%)	
11\15	7 (23.33%)	1 (3.33%)	
12\15	1 (3.33%)	1 (3.33%)	
13\15	6 (20%)	3 (10%)	
14\15	1 (3.33%)	1 (3.33%)	
15\15	2 (6.66%)	22 (73.33%)	
Normal color vision test			≤0.001
(≥ 13)	9 (30 %)	26 (86.7 %)	
Defect color vision test			
(< 13)	21 (70 %)	4 (13.3 %)	
IOP (mm\hg)			0.8
Mean ± SD.	11.0± 4.93	10.7± 5.1	

Table **(3)** shows that with 78D lens, 93.33% had Diabetic changes: Hge & exudate, DME, 3.33% had CME and 3.33% had NSD, CME, hemorrhage & exudate. According to postoperative fundus exam, condition improved (resolved hemorrhage, exudative cotton wool spots and regained normal foveal reflex) in 86.66%, persistent DME 3.33%, edema subsided but with remnant diabetic changes in 6.67% and anatomically improved, functionally not in 3.33%.

Table (3): Preoperative & Postoperative fundus examination with 78D lens in this study

	Studied Patients (n = 30)
Preoperative Fundus Examination with 78D lens	
Diabetic changes	
Hge & exudate, DME	28 (93.33%)
CME	1 (3.33%)
NSD, CME, hge & exudate	1 (3.33%)
Postoperative Fundus Examination with 78D lens	
Condition Improved	26 (86.66%)
Anatomically Improved, Functionally Not	1 (3.33%)
Persistent DME	1 (3.33%)
Edema Subsided but with remnant diabetic changes	2 (6.67%)

Table **(4)** shows that the mean FAZ area in SCP (µm) before injection was 384.6± 236.5 and increased to 498.25± 258.2 after injection. However, no statistically significant difference was found between pre and postoperative in this study. According to FAZ area in DCP (µm), the mean FAZ area in DCP (µm) before injection was 412.4±268.4 and increased to 493.1±203.2 after injection. However, no statistically significant difference was found between pre and postoperative in this study

Table (4): Comparison of FAZ area in superficial capillary plexus (SCP) and deep capillary plexus (DCP)(µm) pre and postoperative in this study.

OCT Angio	Mean ± SD.	**Median**	**Range**	**IQR**	**p value**
FAZ area in SCP (µm)					
Preoperative	384.6± 236.5	362	976	308	0.08
postoperative	498.25± 258.2	462.5	988	376.5	
FAZ area in DCP (µm)					
Preoperative	412.4±268.4	302	984	398	0.19
Postoperative	493.1±203.2	475.5	912	284.5	
(distorted)	٢(6.67%)				

Table **(5)** shows according to FAZ shape pre-operative, all cases had more irregular shape with mean BCVA 0.9746±0.28 (Fig.1 & Fig. 2).

Table (5): Comparison of pre-operative FAZ shape with BCVA in this study.

BCVA	**Mean ± SD.**	**median**	**Range**	**IQR**
FAZ shape				
Irregular (N=30)	0.9746±0.28	1	0.824	0.398

Table **(6)** shows while post-operative, 27 (90%) patients had more regular FAZ shape with mean BCVA 0.413±0.162 and only 3 (10%) patients had irregular FAZ shape with mean BCVA 0.852±0.128 (Fig.1 & Fig. 2).

Table (6): Comparison of post-operative FAZ shape with BCVA in this study.

BCVA	**Mean ± SD.**	**median**	**Range**	**IQR**	**p.value**
FAZ shape					
Regular (N=27)	**0.413±0.162**	**0.477**	**0.43**	**0.492**	**≤0.001**
Irregular (N=3)	**0.852±0.128**	**0.778**	**0.22**	**0.757**	

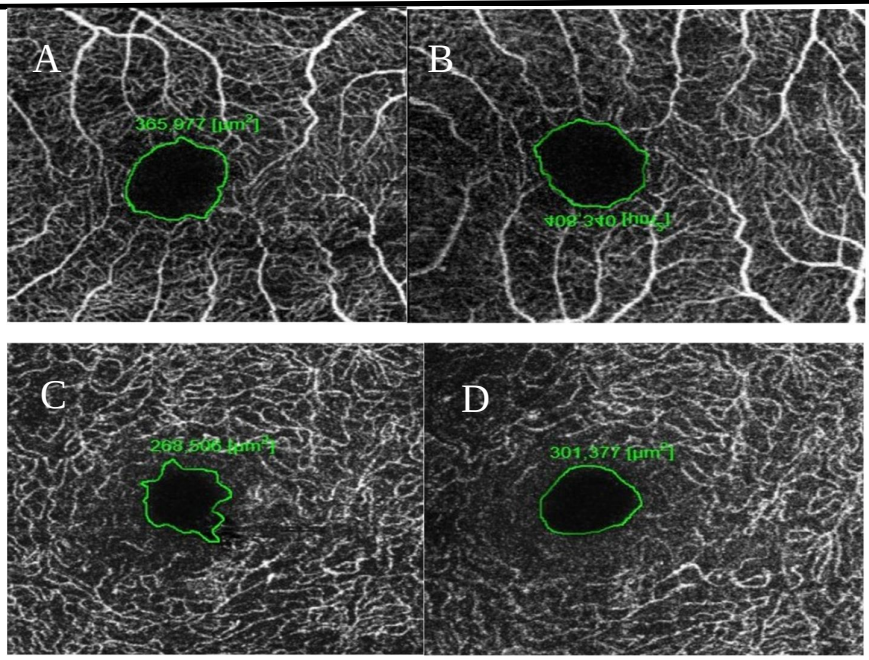

Fig. 1: superficial capillary plexus (SCP) and deep capillary plexus (DCP) with enlined fovea avascular zone (FAZ) images of optical coherence tomography angiography (OCTA). In 55y female diabetic patient with diabetic macular edema (DME) before and after Ranibizumab intra vitreal injections (3 doses with 1month interval). (**A,C**) SCP,DCP before Ranibizumab injections.(**B,D**) SCP,DCP 1 month after Ranibizumab injections(3 doses with 1month interval).showing less irregularity in FAZ shape especially DCP with slight increase in FAZ area.

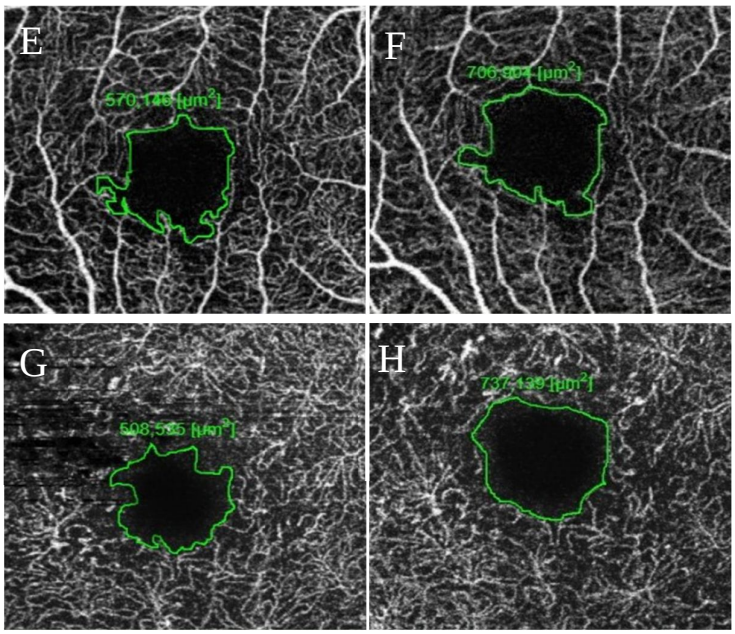

Fig. 2: superficial capillary plexus (SCP) and deep capillary plexus (DCP) with enlined fovea avascular zone (FAZ) images of optical coherence tomography angiography (OCTA). In 45y female diabetic patient with diabetic macular edema (DME) before and after Ranibizumab intra vitreal injections (3 doses with 1month interval). (**E,G**) SCP,DCP before Ranibizumab injections.(**F,H**) SCP,DCP 1 month after Ranibizumab injections(3 doses with 1month interval).showing less irregularity in FAZ shape especially DCP with slight increase in FAZ area.

DISCUSSION

Diabetic retinopathy has been considered a major microvascular complication of DM and is a primary cause of preventable blindness globally[14]. Chronic hyperglycemia has been demonstrated to be accompanied by changes in blood flow, ischaemia, increased VEGF expression, generation of free radicals, endothelial dysfunction, and inflammation, which ultimately ends in visual loss in diabetes-DMI and DME[15]. DME is a complex adverse event accompanied by several factors; the pathogenesis is believed to be owing to disturbed permeability of the blood retinal barrier, with subsequent macular fluid accumulation[16].

The preceding therapeutic standard of DME was laser photocoagulation, but there are various grades of complications, such as lack of an evident increase in both VA and intraocular pressure[17]. In comparison to laser photocoagulation, anti-VEGF therapy could accomplish BCVA and less visual field defect (VFD); the minimal incidence of center comprising macular oedema and vitreous haemorrhage recorded in the anti-VEGF group than laser photocoagulation group[18]. *Nguyen et al (2012)* suggested that anti-VEGF therapy by IVR has to be considered the first therapeutic choice in the context of DME management[19].

Essentially, OCTA is a new, noninvasive diagnostic approach which permits proper visualization of the retinal structure and blood supply. OCTA could reveal and quantify the vascular plexuses, visualize impaired capillary perfusion and neovascularization, and offer data on the dimensions of the FAZ-all achieved without the need for fluorescein dye injection[20]. So, this prospective and interventional study was conducted to assess changes in FAZ area in cases with DME following IVI of anti-VEGF (Ranibizumab) and its effect on visual function.

Our study results have revealed that, the mean age was 57.4± 6.9 years, most of our study participants (63.33%) were females, with only 36.33% were males. Similarly, male/female were 15 (41%) /22 (59%) in DaCosta et al., (2020) study. Diabetic retinopathy could develop in any diabetic patient[21].

Prolonged diabetic duration and poor diabetic control have been considered the main two factors that make patients more susceptible to eye complications[22].

Our study demonstrated that; there was a significant improvement in BCVA after IVI of Ranibizumab. Also, there is a relationship between VA and FAZ circularity, in which more irregularity in FAZ was detected with poorer VA. Before IVI of Ranibizumab, worse BCVA was significantly accompanied by FAZ irregularity and less retinal vascular area in the SCP and the DCP. While, after IVI of Ranibizumab, better BCVA was significantly accompanied by less FAZ irregularity and more retinal vascular area in the in the SCP and the DCP.

This came in the same line with several studies with regard to the correlation between VA and IVI of ranibizumab, although there were certain changes in the rate of IVI of ranibizumab and macular photocoagulation.

Lending credence to the foregoing, Fu et al., (2017) noticed that IVR significantly improved BCVA from baseline, which was owing to the reduction in macular oedema[23]. Also, Nowacka et al., (2016) noticed that IVI of ranibizumab was associated with a significant improvement in VA after three and six months from the initiation of the therapy, which was owing to decreased macular oedema and vascular leaking[24]. In Falcão (2020) meta-analysis of ranibizumab therapy displayed BVCA improvement, with the largest change in BCVA happening throughout the initial year of treatment and continued for three years[25].

In agreement with our results, Endo *et al.,* (2021) found that FAZ margin defects are mostly owing to both capillary dysfunction and vascular remodeling. The FAZ circularity index permits quantification of disturbance of the terminal capillaries in the fovea, which could be a more relevant measure of VA. Additionally, macular oedema could be accompanied by a diminished vascular elasticity owing to mechanical stretching that induce vascular block and could also change FAZ contours. As a result, proper assessment of the size and shape of FAZ is probably essential for the detection of pathologic macular alteration in DR[26].

Balaratnasingam et al., (2016) displayed that the area of the FAZ has a significant correlation with VA in DR following adjusting for ellipsoid zone disturbance. On the other hand, only 38 of the 65 eyes had macular oedema, and the degree of macular oedema wasn't adjusted in the analysis[27]. Hsieh et al., (2019) demonstrated that FAZ-A significantly reduced following ranibizumab therapy, which might have been the result of the non-perfused parafoveal capillary network becoming reperfused following the macular oedema subsided or of the capillary network masked by extensive macular oedema being determined better by OCTA following the macular oedema diminished. On the other hand, FAZ-A and FAZ-CI weren't associated with a significant correlation with VA at baseline or with visual improvement following treatment[28].

Our study demonstrated that contrast sensitivity test significantly improved after IVI of Ranibizumab administration. Similarly, Preti et al., (2014) evaluated the contrast sensitivity measurement after intravitreal Bevacizumab injection and demonstrated significant improvements[29]. In agreement with Turkoglu et al., (2015) study, which found that patients treated with IVR showed small improvements in contrast sensitivity[30].

In our study, there is a statistically significant improvement of color vision test after intravitreal Ranibizumab administration. In line with Turkoglu et al., (2015) study, which found that patients treated with IVR showed small improvements in color vision[30]. Similar to our findings, de Vries et al., (2020) noted that following IVI of anti-VEGF, the IOP was significantly elevated on the injection day, after that, IOP was slightly diminished on the day after injection, and IOP didn't vary significantly from basal value throughout the remaining follow-up measurements[31].

There are different approaches utilized to visualize FAZ that involve intravenous fluorescein angiography, OCTA, and retinal function imager technologies. Since the clinical utilization of OCTA has become more widespread, it has become essential to detect the value of the different parameters measured by the various OCTA software[32,33]. Anti-VEGF medications adjust vasculogenesis in the FAZ and support the optimisation of optical path in the cone dense mosaic of the macula which ultimately results in an improvement of retinal sensitivity[34].

In the current study, as displayed by OCTA both the mean FAZ area in SCP (µm) and in DCP (µm), although it showed relative increase after injection than before injection, it remained non-significant. Our study finding is in collaboration with the assertion of Bromeo et al., (2022) who found that the area, perimeter, and circularity of the FAZ in the SCP and DCP as revealed by OCTA remained statistically unchanged during the initial six months following IVI of anti-VEGF therapy in eyes with DME[35]. In line with our results, Busch et al., (2019) study revealed that retinal vascular area and the FAZ within the nine (3×3) mm2 area didn't significantly vary before and after IVI of aflibercept treatment in cases with DME. It has been demonstrated that, repeated administration of IVI of aflibercept with a mean of 2.6 injections over the course of 8.5 months maintained the retinal perfusion at the macula in cases with DME[36].

Our finding is also contradicted by the assertion of Gill *et al.,* (2017) who observed that FAZ area diminished by time in both observed and managed eyes with DME[37].

As a result, while there are certain studies recording a marked increase in the FAZ area following IVI of anti-VEGF, this outcome wasn't confirmed in different studies. This could be explained by the effect of DME on the FAZ and its interaction with anti-VEGF and macular thickness makes analysis more challenging in these eyes. The FAZ widens as a result of the structural swelling in DME-affected eyes pushing the capillaries in a centrifugal direction[38].

The use of anti-VEGF drugs is hypothesized to be helpful in cases with DMI, but so far, the literature has recorded negative outcomes[39]. There are some factors accompanied by anti-VEGF therapy for DME that could be accompanied by macular perfusion improvement, whereas others might be accompanied by its deteriorating[40].

Factors which may be accompanied by improved retinal perfusion following treatment with anti-VEGF antibodies involve the reversal of leukostasis, that is induced by extensive VEGF secretion in diabetic cases and causes increased capillary obstruction, restoration of the normal retinal structure owing to decreased intraretinal oedema, and suppression of the endothelial hypertrophy which is induced by extensive local

VEGF-A formation and has been demonstrated to be accompanied by capillary lumen obstruction[41].

Factors which can control retinal perfusion deterioration after VEGF suppression involve inducing vasoconstriction of the retinal vasculature, as demonstrated following bevacizumab and ranibizumab injections for DME, maybe owing to the nitric oxide suppression that happens with VEGF suppression and also leading to hypertension in cases of systemic VEGF suppression[42].

Despite the promising outcomes of the current study, the following limitations have to be considered; First, macular oedema could interfere with the signal strength of OCTA measurement. Second, as mentioned formerly, the projection artifact may interfere more with the imaging quality of the deep retinal layer than of the superficial layer. Third, the study has a small number of eyes with different stages of DR. Fourth, the study had a limited observation period of three months which comprises a short follow-up and may have been insufficient to reveal alterations in the FAZ. Finally, we did not determine the effect of other variables which include the degree of diabetic control, severity of DR, and effect of pan retinal photocoagulation on the FAZ parameters. Additional studies with a larger number of eyes, more injections, and a longer follow-up period may be required to confirm the current results. In addition, further studies may be essential to assess the effects of different confounding variables.

CONCLUSION

Our study showed that the FAZ area, in the SCP and DCP as measured by OCTA showed non-significant change during the three months of intravitreal anti-VEGF therapy (Ranibizumab) in eyes with DME. While there were no significant changes in the FAZ, there was significant improvement in visual functions in cases with DME at three months' treatment with intravitreal anti-VEGF (Ranibizumab)**.** Also assessing both the size and shape of FAZ is possibly essential for detection of pathologic change of the macula and prediction of visual outcomes in DR, as eyes with poor VA had a more irregular shape of FAZ while after injections, better VA was significantly associated with less FAZ irregularity in which FAZ regained its regular shape and contour.

Recommendation

According to the finding of the present study we suggest that OCTA (SCP and DCP) markers in a routine clinical sitting may have a promising role in measuring and establishing early progress to anti-VEGF therapy (Ranibizumab).

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Data Availability: The authors declare that all data supporting the findings of this study are available within the article and its supplementary information file.

Competing interests: The authors declare no competing interests.

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Conflict of interest

All authors have no conflicts of interest that are directly relevant to the content of this review.

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