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Comparison of Foveal Avascular Zone Parameters in Diabetic Retinopathy and Normal Retina on Optical Coherence Tomography Angiography Using Automated Software

Summaiya Munim, Faisal Aziz Khan, Muhammad Kashif Hanif, Quratulain Paracha, Beenish Saleem, Sameer Shahid Ameen

Abstract

Objective: To compare Foveal Avascular Zone (FAZ) metrics comprising of FAZ area, perimeter and circularity between individuals afflicted with diabetic retinopathy and those exhibiting healthy, normal retinal profile by using built in algorithm of Optical coherence tomography angiography (OCT-A)

Study Design and Setting: It was an observational study. Conducted at the Ophthalmology Department, PNS Shifa Hospital, Karachi from October 2023 to December 2024.

Methodology: 60 patients participated which included 30 type 2 diabetics with mild to moderate non proliferative diabetic retinopathy (NPDR), without macular involvement and 30 non diabetics age matched normals. FAZ parameters of OCT-Angio Optopol revo nx130 (Area, Circularity and Perimeter) were calculated and compared between two groups using automated built in software. FAZ parameters of mild and moderate NPDR were compared within diabetic group.

Results: Mean age in diabetics was 55.33 ± 6.85 years and in non-diabetics 55.30± 4.94 years. On comparison of FAZ parameters the area and perimeter were statistically significantly enlarged as compared to non-diabetics FAZ parameters ($p < 0.001$). The circularity index was lower among diabetics as compared to non-diabetics ($p < 0.001$). Among the diabetic patients there was a statistically significant enlargement of FAZ area in moderate NPDR versus mild NPDR ($p <0.001$) and difference of FAZ perimeter ($p = 0.07$) and circularity index ($p =0.60$) were statistically insignificant.

Conclusion: Diabetic patients with mild to moderate NPDR having clinically normal appearing maculae show deranged FAZ parameters on OCT-A as compared to age matched normal healthy retinae.

Key Words: Angiography, Diabetic retinopathy, Optical coherence tomography

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INTRODUCTION:

Diabetic retinopathy (DR) has emerged as a leading cause of preventable blindness worldwide. The insidious onset of this microvascular complication, often asymptomatic in its early stages, underscores the necessity of proactive screening, timely diagnosis, and targeted intervention. This complex and multifactorial disorder is characterized by progressive alterations in the retinal microvasculature resulting from chronic hyperglycemia-induced metabolic and hemodynamic disturbances. The evolution of DR encompasses a continuum of changes, ranging from mild non-proliferative stages—marked by microaneurysms, intraretinal hemorrhages, and vascular leakage—to proliferative disease characterized by neovascularization and potentially vision-threatening sequelae.[1] Each stage reflects a progressive disruption of the blood–retinal barrier, pericyte loss, and basement membrane thickening, culminating in ischemia and tissue hypoxia. The resulting microvascular dysfunction and neurodegenerative changes jointly contribute to irreversible visual impairment.

Among the structural and functional alterations in the

diabetic retina, the foveal avascular zone (FAZ) represents a particularly valuable biomarker of retinal perfusion and neurovascular health.[2] The FAZ, centrally located within the macula, is an area devoid of retinal capillaries corresponding to the foveal pit, where cone photoreceptors are most densely concentrated. This specialized avascular region facilitates unhindered light transmission to the photoreceptor layer, enabling optimal visual acuity.[3,4] The precise morphology of the FAZ reflects the balance between vascular supply and metabolic demand within the macula; hence, its integrity is crucial for maintaining high-resolution vision. In the context of DR, the FAZ becomes a focal point for assessing ischemic injury and microvascular compromise. Progressive capillary non-perfusion, vessel rarefaction, and remodeling around the FAZ can lead to measurable enlargement and irregularity of its contour.[1] These morphometric changes have been correlated with disease severity and reduced visual acuity, suggesting their potential as objective, quantifiable indicators of retinal ischemia. Consequently, the assessment of FAZ parameters such as area, perimeter, and circularity has gained prominence in evaluating the extent of microvascular disruption. Earlier investigations have established the clinical significance of FAZ alterations in a variety of retinal diseases, including diabetic retinopathy, retinal vein occlusion, and macular ischemia.[5-7] In diabetic retinopathy, such measurements provide valuable insights into disease progression and therapeutic outcomes.[6]

However, traditional imaging modalities, notably fluorescein angiography (FA) and indocyanine green angiography (ICGA), though long considered the reference standards for assessing retinal perfusion, have inherent limitations.[8] These procedures are invasive, time-consuming, and costly. They require intravenous dye injection, which may elicit allergic reactions or other adverse effects and is contraindicated in certain systemic conditions.[9] Furthermore, their two-dimensional representation of the vasculature restricts detailed layer-by-layer evaluation.

Optical coherence tomography angiography (OCT-A) has revolutionized retinal imaging by offering a rapid, non-invasive alternative for high-resolution, three-dimensional visualization of retinal and choroidal microvasculature. Using motion-contrast imaging based on red blood cell movement, OCT-A generates en face angiograms within seconds, enabling visualization of distinct vascular plexuses from the internal limiting membrane to the choroid.[10] This dye-free technique allows precise and reproducible quantification of microvascular parameters, including the FAZ, using built-in automated software algorithms. The ability of OCT-A to provide depth-resolved imaging and quantitative metrics has markedly enhanced the understanding of DR-related vascular pathology and holds promise for early disease detection.

Despite its potential, the literature remains limited regarding the comparative use of automated OCT-A analysis for FAZ evaluation among diabetic and non-diabetic populations. Most existing studies rely on manual or semi-automated delineation methods, which are susceptible to inter-observer variability and measurement bias. The integration of automated FAZ quantification tools may therefore provide greater accuracy, reproducibility, and clinical utility. Accordingly, the present study aims to conduct a comparative analysis of FAZ parameters specifically area, perimeter, and circularity between patients with diabetic retinopathy and healthy individuals using the automated algorithm incorporated within OCT-A systems. By evaluating these quantitative biomarkers, the study seeks to elucidate the relationship between FAZ morphology and diabetic retinal microvascular alterations, thereby enhancing the role of OCT-A as a non-invasive and objective modality for the early detection and grading of diabetic retinopathy.

METHODOLOGY:

This comparative study was conducted at the Ophthalmology Department, PNS Shifa Hospital, Karachi from 1st October 2023 to 15th December 2024.The study was conducted after obtaining approval from the Institutional Ethics Review Board (ERC-2023/EYE/11). Sample size was calculated by using Open Epi software to compare two proportions with a confidence interval of 95 and power 80. A total of 60 patients participated, which included 30 diabetics with mild to moderate NPDR and 30 non diabetics age matched normal. Written informed consent was taken from all participants. Patients were selected according to conventional sampling technique. Participants with type 2 diabetes and showing mild to moderate NPDR without macular involvement were placed in group one and their age matched normals (non diabetics) were placed in group two. Patients with history of smoking, hypertension, ischemic heart diseases, hyperlipidemics and exhibiting any other maculopathy were excluded from study. Each participant underwent ophthalmic examination, including visual acuity assessment, intra ocular pressure and dilated fundus examination. Subsequently, OCT angiography scans were obtained using spectral domain OCT Optisurg. Optopol (revo nx130). This instrument has an A-scan rate of 130,000 scans/sec with an 840 nm SLED light source and a 50 nm half bandwidth. The acquired OCTA scans were processed using automated software designed for FAZ segmentation and quantification, operated by author. Parameters of FAZ within 3- and 3-mm area of superficial capillary plexus was analyzed. The FAZ parameters that were compared between diabetics and non diabetics were FAZ Area, measured in mm^2 that measures the extent of capillary dropout. FAZ Perimeter, measured in mm which delineates the contour of the FAZ and records the geometric characteristics of the avascular region and FAZ circularity index which is a dimensionless ratio, which measures roundness or irregularity of the FAZ shape and vascular remodeling.

The SPSS version 27 was used to analyze the data. Descriptive statistics were calculated for age. Frequency and percentages were calculated for gender and stages of diabetic retinopathy. Shapiro- Wilk normality test was applied for age, area, perimeter and circularity index of FAZ and all the data was found to be normally distributed for both the groups. Student- t test was selected to compare FAZ parameters among diabetic and non diabetic groups and among patients with mild and moderate NPDR. A p-value < 0.05 was considered to be statistically significant.

RESULTS:

The age ranged from 42-70 years. Mean age in diabetic patients group was 55.33 ±6.85 years and in non diabetic patients group was 55.30± 4.94 years. There was no statistical significant difference in the mean age of both groups. Therefore both groups depicted age matching (p= 0.983). Male to female ratio was 1:1. Among the 30 diabetic patients group 15 (25%) had mild NPDR and 15 (25%) had moderate NPDR. On comparison of FAZ parameters among diabetics and non diabetics there was a statistically significant difference of parameters as shown in Table 1. Among the diabetic patients there was a statistically significant difference of FAZ area between mild and moderate NPDR and difference of FAZ perimeter and circularity was statistically insignificant as shown in Table 2.

DISCUSSION:

In a healthy retina, the FAZ is small, well-defined, and symmetrical, reflecting the physiological avascularity of the central fovea, which optimizes light transmission and visual acuity. In DR, however, progressive microvascular damage and capillary non-perfusion lead to characteristic FAZ enlargement, irregularity, and loss of circular symmetry.[11] These changes occur secondary to ischemic insults and microvascular remodeling, which disrupt the integrity of the retinal capillary network. OCTA has emerged as a robust, non-invasive tool for detailed visualization of these microvascular changes, enabling precise quantitative evaluation of the FAZ and other vascular parameters. One of the hallmark features of DR identified through OCT-A is FAZ enlargement. Multiple studies have consistently demonstrated a significant increase in FAZ area among diabetic patients compared to healthy controls.[12] This enlargement is primarily attributed to progressive loss of retinal capillaries due to ischemia, which lead to an expansion of the avascular region surrounding the foveal pit. In contrast, the FAZ in normal individuals remains compact and circular, delineated by a continuous ring of capillaries that preserve retinal perfusion and metabolic homeostasis. The ability to detect and quantify even subtle FAZ changes using OCT-A provides a valuable opportunity for early identification of microvascular compromise and delaying progression of diabetic retinopathy,[13] potentially facilitating timely interventions such as strict glycemic control, lipid regulation, and management of systemic comorbidities that may slow or prevent disease progression.

Table-1: Comparison of foveal avascular zone parameters among diabetics and non diabetics. (n=60)

Foveal avascular zone	Diabetic (n=30)	Non diabetic (n=30)	*p*-value
Area (mm^2)	0.44 ± 0.69	0.20 ± 0.05	<0.001
Perimeter (mm)	3.91 ± 0.72	2.26 ± 0.35	<0.001
Circularity	0.37± 0.06	0.78 ± 0.07	<0.001

Table-2: Comparison of foveal avascular zone parameters between mild NPDR and moderate NPDR. (n=30)

Foveal avascular zone	Moderate NPDR (n=15)	Mild NPDR (n=15)	*p*-value
Area (mm^2)	0.39 ± 0.02	0.50 ± 0.04	<0.001
Perimeter (mm)	4.15 ± 0.77	3.68 ± 0.61	0.07
Circularity	0.36 ± 0.07	0.38 ± 0.06	0.60

FAZ in diabetic retinopathy has been well documented using FFA and is still considered to be the traditional gold standard for assessing retinal vasculature and identifying ischemic zones, its invasive nature limits its routine use, particularly in serial monitoring.[14] FFA requires intravenous dye injection, which carries potential risks of allergic reaction, nausea, and contraindication in renal dysfunction.[9] In contrast, OCTA offers a safe, rapid, and reproducible alternative, providing high-resolution en face images of the retinal vascular plexuses without the need for dye administration. Furthermore, OCTA enables the segmentation of vascular layers, allowing independent assessment of superficial and deep capillary plexuses. These capabilities make OCT-A particularly valuable for studying the early and subclinical stages of DR, where FFA might still appear unremarkable. Several studies[15-16] have utilized OCT-A to assess FAZ parameters in DR; however, they relied on manual delineation analysis and techniques, which are susceptible to inter-observer variability and human error. Our study overcomes these limitations by employing automated, built-in software algorithms for FAZ quantification, thereby minimizing measurement bias and improving reproducibility. The automated approach enhances the reliability of results, offering standardized quantitative metrics that can be consistently applied across clinical and research settings.

FAZ area can serve as an early indicator of diabetic retinopathy even before clinical signs appear.[17] Our findings indicate a significant enlargement of the FAZ area among diabetic patients compared with non-diabetic controls. The mean FAZ area in diabetic participants was 0.44 mm^2, nearly double that of non-diabetics 0.20 mm^2. This difference aligns with previous studies reporting similar trends. Pamulapati et al. observed a marked increase in FAZ area in diabetic eyes relative to controls, suggesting that the extent of FAZ

enlargement correlates with disease severity.[11] Similarly, Courtie and Aitchison[18,2] reported that FAZ expansion was a consistent finding in eyes with DR, even in the absence of clinically evident macular edema. These findings support the concept that FAZ metrics may serve as sensitive markers of early retinal ischemia before overt structural changes become apparent. The pathophysiological basis for FAZ enlargement lies in the selective vulnerability of retinal capillaries to chronic hyperglycemia. Prolonged exposure to elevated glucose levels induces pericyte apoptosis, endothelial cell dysfunction, and thickening of the capillary basement membrane. This process leads to microaneurysm formation and eventual capillary dropout, resulting in localized areas of non-perfusion and enlargement of the avascular foveal zone. The FAZ area, therefore, serves as a direct reflection of the cumulative ischemic burden within the macula.[12] Although many prior studies have established FAZ enlargement as a diagnostic and prognostic marker, few have explored its relationship to specific stages of NPDR. Our study specifically focused on comparing mild and moderate NPDR with age-matched controls to determine whether FAZ alterations vary across disease stages. In our study we specifically compared FAZ parameters in mild to moderate stage of NPDR with age matched normal so as to further specify the association of stages of DR with FAZ and we observed that FAZ area enlargement was evident even in mild NPDR, with progressive expansion in moderate stages, highlighting its potential as a biomarker for early disease detection and grading.

The FAZ circularity index, a geometric descriptor reflecting shape regularity, provides complementary insight into FAZ morphology. In healthy individuals, the FAZ is typically round or slightly oval, with high circularity indices indicative of structural integrity. As the retinal microvasculature becomes compromised, the FAZ loses its symmetry and becomes increasingly irregular or lobulated. The circularity index thus decreases with advancing ischemia and disease progression. Shiihara et al.[15] reported an average circularity index of 0.76 in normal eyes, consistent with the regular, compact FAZ morphology of healthy subjects. Krawitz et al.[16] demonstrated an increase in acircularity index values among patients with NPDR 1.57 compared with controls 1.32, signifying shape distortion secondary to vascular dropout. Their study, however, relied on manual tracing techniques, which are operator-dependent. Another study conducted by NM Bates also depicted significant difference in FAZ circularity between diabetics and nondiabetics.[19] On the contrary, the circularity index was similar among patients with NPDR (0.63) and diabetics without DR (0.63) but difference was noted between NPDR (0.63) when compared to non-diabetic controls (0.69) according to Kim et.al.[20] The difference of circularity index among diabetics and non-diabetics of our study are in agreement with these studies however our study was advantageous over them as we compared circularity index between mild NPDR and moderate NPDR although the difference was statistically insignificant. The circularity index's diagnostic value lies in its ability to detect early geometric distortion even before substantial FAZ area enlargement occurs. This metric could serve as an adjunctive parameter for monitoring microvascular integrity, with potential implications for predicting visual outcomes and disease progression.

The FAZ perimeter, representing the total boundary length of the avascular zone, is an important indicator of retinal vascular remodeling. It is another assessment tool for FAZ which is increased in diabetics as a result of capillary alteration and shows significant differences between diabetic retinopathy and and normal retinas. An increased perimeter suggests irregular capillary margins and localized vessel loss. Conrath et al.[21] first reported significant increases in FAZ perimeter among diabetic patients using fluorescein angiography In our study FAZ perimeter in non-diabetics was recorded to be 2.26 mm which is comparable to a result of 2.20 mm shown by Claudia P in his study, [22] while in our study the diabetic FAZ perimeter was found to be 3.91mm which is an enlarged FAZ. This substantial difference underscores the degree of capillary alteration in DR. Our finding is consistent with another study conducted by Hogg RE et al. who declared FAZ perimeter and circularity being impacted most significantly in DM [23] although they manually measured the perimeter and we used built in software which gave us consistent values that were not affected by inter-observer variability and more authentic for interpretation. This difference of FAZ between diabetic and non-diabetic retinas is the result of increase in FAZ parameters in diabetic patients, as a result loss of retinal capillaries due to ischaemia. [12]

Taken together, our results reaffirm that FAZ parameters area, circularity, and perimeter are significantly altered in diabetic retinopathy and can serve as sensitive biomarkers for early microvascular compromise. These findings support previous research suggesting that irregular FAZ morphology may precede visible structural lesions, thus serving as an early warning sign of subclinical DR.[3] Early identification of such subtle vascular changes could prompt stricter metabolic control and closer ophthalmic monitoring, potentially delaying disease progression.

Previous studies have demonstrated a correlation between FAZ parameters and visual acuity. Duffy et al.[24] reported that increased FAZ area was significantly associated with decreased best-corrected visual acuity (BCVA), emphasizing the functional impact of foveal ischemia. Tang et al.[25] further established that decreased circularity corresponded with reduced BCVA, suggesting that FAZ shape irregularity may be more predictive of visual dysfunction than area alone. Although our study did not include direct visual acuity correlations, the structural alterations observed in FAZ parameters are consistent with these findings and reinforce

the clinical importance of early detection.

The enlargement and irregularity of the FAZ reflect cumulative microvascular damage that compromises oxygen and nutrient delivery to the central retina, leading to photoreceptor dysfunction and vision loss. Future studies incorporating both structural and functional assessments would be valuable in elucidating the exact relationship between FAZ metrics and visual performance in different stages of DR. The use of automated OCT-A software for FAZ analysis presents several clinical advantages. First, it allows for standardized, objective, and reproducible measurements, reducing observer bias. Second, automated segmentation enables rapid data acquisition, making it feasible for routine clinical screening. Third, longitudinal monitoring of FAZ metrics could facilitate early identification of disease progression, even before visible fundus changes. From a research perspective, automated OCT-A quantification allows large-scale data analysis with high precision, enabling robust statistical comparisons and facilitating machine learning–based predictive modeling in diabetic retinopathy.

Limitations: This study has several limitations. First, the sample size was relatively small, which may limit the generalizability of our findings. A larger cohort would enhance statistical power and allow for more comprehensive subgroup analyses, particularly regarding different stages of DR. Second, the study was conducted at a single center, potentially introducing selection bias related to population characteristics and imaging equipment. Multi-center studies with diverse populations would improve external validity. Although automated software minimizes human error, segmentation artifacts and signal attenuation may still influence measurements, especially in eyes with poor fixation or media opacity. Our study did not evaluate functional correlations such as best-corrected visual acuity, contrast sensitivity, or electrophysiological parameters, which could provide valuable insights into the relationship between structural FAZ changes and visual performance.

Future research should aim to include larger, multi-centric cohorts with longitudinal follow-up to explore the predictive value of FAZ metrics for progression to diabetic macular edema or proliferative stages. Integration of OCT-A with other imaging modalities—such as adaptive optics or wide-field angiography—could further elucidate the full extent of microvascular alterations. Additionally, machine learning–based analyses of OCT-A data may enable automated risk prediction and personalized disease monitoring.

CONCLUSION

In our study automated software was used to asses FAZ perimeters which plays a key role in enhancing the objectivity and reproducibility of FAZ measurements. This analysis of OCTA images provided a precise measurement of FAZ area, perimeter, and circularity, with the software detecting subtle differences that were often overlooked by manual measurements. This automated approach ensured high inter- and intra-observer agreement, making it a reliable tool for clinical applications. Therefore we conclude that in patients who have various stages of NPDR but clinically normal appearing maculae show deranged FAZ parameters as compared to age matched normal healthy retinae offering us precise, reproducible and recordable measures. These results underscore the diagnostic potential of automated FAZ quantification as a sensitive, non-invasive biomarker for early detection and grading of diabetic retinopathy. The ability to detect subtle vascular changes before the onset of clinical retinopathy may facilitate early intervention and improved patient outcomes

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Summaiya Munim study design, drafting the manuscript Data acquisition, data analysis, data interpretation.
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