Journal of Clinical and Nursing Research, 2025, Volume 9, Issue 7
http://ojs.bbwpublisher.com/index.php/JCNR
Online ISSN: 2208-3693
Print ISSN: 2208-3685

Application Study of OCTA-measured Foveal Avascular Zone in Diabetic Retinopathy

Kaihua Chen, Zhenyu Peng*, Yonghong Sha*

School of Medicine, Jishou University, Jishou 416000, Hunan, China

**Authors to whom correspondence should be addressed.*

Abstract: Changes in the area, perimeter, and circularity index of the foveal avascular zone (FAZ) can be influenced by the filling or occlusion of tiny capillaries surrounding it. In diabetic retinopathy (DR), FAZ-related indicators can provide a quantitative assessment of early DR, predict early disease changes, and offer a theoretical basis for monitoring disease progression and evaluating patients' visual outcomes. Therefore, finding a simple and noninvasive method to visualize the FAZ has become a research hotspot in ophthalmology. The emergence of optical coherence tomography angiography (OCTA) has filled the technological gap in FAZ measurement. This article reviews the basic principles of OCTA and the clinical application of OCTA-measured FAZ-related indicators in DR, aiming to improve the diagnosis and treatment of DR.

Keywords: Optical coherence tomography angiography; Diabetic retinopathy; Foveal avascular zone; Diabetes mellitus

Online publication: August 8, 2025

1. Introduction

In 2020, it was estimated that among the 463 million people with diabetes worldwide, 160 million had diabetic retinopathy (DR), resulting in 4.4 million cases of blindness or moderate to severe visual impairment [1]. By 2045, the number of DR patients is expected to increase to 242 million [2]. However, there are still many unresolved issues regarding how to assess and treat the pathological changes and complications caused by this disease. Compared to traditional fluorescein fundus angiography (FFA), optical coherence tomography angiography (OCTA) does not require the use of contrast agents, avoiding related adverse reactions. It can noninvasively visualize and quantify the morphology of the foveal avascular zone (FAZ), making it an effective tool for early detection and treatment evaluation of DR.

2. FAZ and OCTA

Most patients with diabetic retinopathy (DR) only experience significant visual problems in the later stages of the disease. Therefore, timely intervention measures may delay further vision loss, making early diagnosis and accurate staging crucial for DR treatment. The foveal avascular zone (FAZ) is a ring formed by capillaries at the edge of the central fovea. Studies have shown that changes in the FAZ are closely related to visual function [3]. The loss of capillaries in the macular fovea is a prominent feature of ischemic and vaso-occlusive retinal diseases, and the morphology of the FAZ can reflect changes in macular microcirculation. In healthy eyes, the FAZ typically appears circular or elliptical. However, in patients with DR, the FAZ area often becomes irregular due to loss of vascular integrity and increases significantly in size compared to healthy individuals. This increase also correlates with the severity of DR [4].

For a long time, fluorescein angiography (FFA) has been an important tool for diagnosing DR. However, FFA is an invasive and time-consuming procedure with poor short-term repeatability. It can cause allergic reactions such as nausea and skin rashes, and in severe cases, it can even be life-threatening. Therefore, it is difficult to popularize in clinical practice. Additionally, grading the FAZ on FFA is challenging because capillary details can be obscured by leakage even during early transit. Optical coherence tomography angiography (OCTA) is a fast, non-invasive, and highly repeatable imaging technique that avoids interference caused by dye pooling and leakage. It also enables reliable quantitative data analysis, addressing the limitations of FFA, which can only display superficial retinal capillaries and has difficulties in grading. OCTA has been widely used for screening retinal diseases. Its principle involves acquiring high-resolution three-dimensional images of vascular structures by detecting the motion contrast between flowing red blood cells and surrounding “static” tissues through consecutive B-scans of the same area [5]. This allows for the visualization and quantification of the FAZ structure in a three-dimensional and visual manner. Studies have shown that significant changes occur in the central microvascular organization before clinically visible changes, even in diabetic patients without DR [6]. Compared to healthy subjects, these patients have a significantly larger FAZ surface area. Therefore, OCTA is considered a screening method for early retinal changes in diabetic patients.

3. Factors influencing FAZ-related indicators

3.1. Morphology of the foveal center

The geometric morphology of the foveal center is closely related to the foveal avascular zone (FAZ). The thickness of the retinal foveal center has a direct relationship with the area and shape of the FAZ and is a determining factor for central foveal vessel density. There is a negative correlation between foveal center thickness and FAZ diameter [7]. Additionally, the size, depth, and volume of the foveal center are correlated with the FAZ. A deeper and wider foveal center corresponds to a larger FAZ area.

3.2. Axial length of the eye

The axial length of the eye is an important parameter that affects the FAZ. As the axial length increases, the measured FAZ area and roundness index decrease accordingly [8]. Furthermore, differences in axial length may also affect the distribution of capillaries in the foveal center, which can further impact the roundness index of the FAZ.

3.3. Age, gender, and racial factors

The relationship between age and FAZ-related indicators remains controversial. Most scholars believe that the density of both the deep capillary plexus (DVC) and the superficial capillary plexus (SVC) in the retina decreases with age, while the FAZ area in the superficial layer of the retina increases with age [9]. However, Linderman *et al.* argue that there is no significant correlation between age and FAZ-related indicators [10]. Similarly, the relationship between gender and FAZ-related indicators is also controversial. Most researchers believe that men in the normal population have a smaller FAZ area compared to women. However, Wylegała *et al.*, after studying 51 Asian eyes and 43 Caucasian eyes, concluded that gender does not significantly affect FAZ size [11]. Compared to Caucasians, Chinese individuals have a larger FAZ area and higher vessel density, which may be related to differences in eye size and axial length among different ethnic groups [12].

3.4. Instrument measurement errors

Due to variations in measurement and calculation methods across different instruments, as well as the impact of different zoning approaches on FAZ measurement results, there is currently a wide range of OCTA products available on the market, each with its own unique parameters and algorithms. This makes it impossible to directly compare data measured by different instruments [13]. Additionally, the results of automatically identified and measured vessel density are often greater than those obtained through manual identification, suggesting that the presence or absence of correction for errors and differences in analysis and measurement methods may affect relevant conclusions [14]. During the FAZ imaging process, the inability to effectively maintain a focused state or the presence of opaque media can lead to artifacts, which can prevent accurate positioning of the boundaries of blood vessels surrounding the FAZ. This, in turn, affects values such as FAZ size, perimeter, and circularity index.

4. Research progress on the application of FAZ-related indicators in the diagnosis of diabetic retinopathy

4.1. Application of FAZ area in diabetic retinopathy

In the early stages of diabetic retinopathy, a series of subtle structural and functional changes occur in the retinal vasculature, and changes in FAZ (foveal avascular zone) area often precede clinically visible retinopathy manifestations. Bates *et al.* found that very slight but measurable increases in Faz area may already be present in diabetic patients even before the appearance of obvious retinopathy symptoms [15]. Takase *et al.* discovered that compared to healthy eyes, the FAZ of diabetic patients, whether or not they have DR (diabetic retinopathy), is significantly enlarged, and the deep FAZ area enlargement is more pronounced [16]. Samara *et al.* divided patients into three groups: mild non-proliferative DR, moderate to severe non-proliferative DR, and proliferative DR [17]. Compared to healthy eyes, the FAZ area increased in all three groups, and with the increasing severity of DR, the FAZ area showed a trend of expansion, which may be related to the aggravation of retinal ischemia and hypoxia.

4.2. Application of FAZ morphological structure in diabetic retinopathy

In the early stages of diabetic retinopathy, subtle functional and structural changes occur in the retinal vascular system, and these changes can be first reflected in the morphological structure of the FAZ. Smith *et al.* reported that the edges of the FAZ may become blurred in diabetic patients even before the appearance of obvious retinal lesions [18]. Johnson's research further indicated that the FAZ morphology of early diabetic retinopathy patients is often irregular, which may be one of the early signals of DR occurrence [19]. As parameters describing the geometric morphology of the FAZ, CI and AI mathematically represent the similarity between the FAZ and a standard circle. A smaller CI and a larger AI indicate a shape that deviates more from a standard circle.

The calculation formulas are: CI = $4\pi \times$ Area / Perimeter^2 and AI = FAZ Perimeter / Perimeter of a circle with the same area as the FAZ. The axis ratio is a parameter determined by the best-fit ellipse of the FAZ, and the calculation formula is: Axis Ratio = Longest Axis of FAZ / Shortest Axis of FAZ. These parameters, unlike area and perimeter, do not need to consider the magnification effect caused by axial length. Krawitz *et al.* studied the AI and axis ratio of diabetic patients and found a positive correlation between the severity of DR and AI and axis ratio [20]. Kim *et al.* showed that the CI of NDR and NPDR patients was smaller than that of healthy controls [21]. The morphological changes of the FAZ in DR patients are not caused by the traction effect of axial length elongation on the macular vessels but rather by the damage to capillaries caused by diabetes itself. The potential anisotropy of the mechanical properties of the diabetic retina can trigger the extension of the FAZ in any direction, leading to irregular morphological changes, which are related to vasoconstriction and capillary loss.

As diabetic retinopathy progresses, changes in the morphological structure of the FAZ become more pronounced. Brown *et al.* pointed out that the degree of FAZ morphological distortion is more severe in moderate DR patients than in mild patients, and irregularity increases [22]. These studies have demonstrated that measuring FAZ geometric morphology parameters such as CI, AI, and axis ratio using OCTA can be used to evaluate the severity and staging of DR. Quantifying the irregularity of the FAZ and remodeling the retinal microstructure remain key areas of future research. A deeper understanding of the relationships between these pathological changes is crucial for comprehending DR and its progression.

4.3. Application of FAZ blood flow perfusion and vascular density in diabetic retinopathy

Changes in FAZ blood flow perfusion and vascular density play a critical role in the development and progression of diabetic retinopathy. Studies have reported a significant reduction in FAZ blood flow perfusion in patients with diabetic retinopathy [23]. This reduction is believed to be associated with retinal microcirculation dysfunction. Some studies have shown that decreased vascular density in the capillary plexus is correlated with increased severity of non-proliferative diabetic retinopathy (NPDR) [24]. In patients with PDR, the vascular density of all capillary plexuses is also significantly reduced. Interestingly, other studies have indicated that capillary density is higher in diabetic patients without DR compared to non-diabetic controls, possibly as a response to increased metabolic demand [25]. The reduction in capillary plexus perfusion and vascular density is closely related to ischemia, inner retinal disruption, and visible neural degeneration with thinning of the nerve fiber layer [26]. Importantly, changes in SVC vascular density may be more reliable than DVC measurements because they are less susceptible to noise and projection artifacts, even when artifact removal algorithms are used.

5. Conclusion

In summary, OCTA provides excellent resolution and measurement accuracy in detecting neovascularization and microvascular abnormalities within the retina. In many cases, OCTA is preferred over FFA. Not only can OCTA clearly display the vasculature, structure, and blood flow density of each retinal layer, but it can also visualize and quantify the FAZ with high reproducibility and reliability. By monitoring morphological parameters of the FAZ, such as area, perimeter, CI, AI, axial ratio, and blood perfusion, the ischemic state of the macula in its early stages can be assessed, predict the progression of diabetic retinopathy, facilitate the identification of early changes and precise staging of diabetic retinopathy, and aid in timely treatment and prognosis evaluation.

Disclosure statement

The authors declare no conflict of interest.

References

[1] Burton MJ, Ramke J, Marques AP, et al., 2021, The Lancet Global Health Commission on Global Eye Health: Vision Beyond 2020. Lancet Glob Health, 9(4): e489–e551. https://doi.org/10.1016/S2214-109X(20)30488-5.

[2] Saeedi P, Petersohn I, Salpea P, et al., 2019, Global and Regional Diabetes Prevalence Estimates for 2019 and Projections for 2030 and 2045: Results From the International Diabetes Federation Diabetes Atlas, 9th Edition. Diabetes Res Clin Pr, 157: 107843. https://doi.org/10.1016/j.diabres.2019.107843.

[3] Huang Y, Liu J, Meng J, 2021, Bilateral Foveal Hypoplasia With Foveal Capillary. Ophthalmology, 30(02): 84.

[4] Hwang TS, Jia Y, Gao SS, et al., 2015, Optical Coherence Tomography Angiography Features of Diabetic Retinopathy. Retina, 35(11): 2371–2376.

[5] Borrelli E, Parravano M, Sacconi R, et al., 2020, Guidelines on Optical Coherence Tomography Angiography Imaging: 2020 Focused Update. Ophthalmol Ther, 9(4): 697–707.

[6] Bates NM, Tian J, Smiddy WE, et al., 2018, Relationship Between the Morphology of the Foveal Avascular Zone, Retinal Structure, and Macular Circulation in Patients With Diabetes Mellitus. Sci Rep, 8(1): 5355.

[7] Balaratnasingam C, Chae B, Remmer MH, et al., 2015, The Spatial Profile of Macular Pigments Is Related to the Topological Characteristics of the Foveal Avascular Zone. Invest Ophthalmol Vis Sci, 56(13): 7859–7865.

[8] Linderman RE, Muthiah MN, Omoba SB, et al., 2018, Variability of Foveal Avascular Zone Metrics Derived From Optical Coherence Tomography Angiography Images. Transl Vis Sci Technol, 7(5): 20.

[9] He P, Liu C, Yin W, et al., 2019, Research Progress on Blood–Retinal Barrier Damage in Diabetic Retinopathy. Journal of Clinical and Pathological Research, 39(05): 1090–1094.

[10] Fujiwara A, Morizane Y, Hosokawa M, et al., 2017, Factors Affecting Foveal Avascular Zone in Healthy Eyes: An Examination Using Swept-Source Optical Coherence Tomography Angiography. PLoS One, 12(11): e0188572.

[11] Shiihara H, Terasaki H, Sonoda S, et al., 2018, Objective Evaluation of the Size and Shape of the Superficial Foveal Avascular Zone in Normal Subjects by Optical Coherence Tomography Angiography. Sci Rep, 8(1): 10143.

[12] Linderman RE, Muthiah MN, Omoba SB, et al., 2018, Variability of Foveal Avascular Zone Metrics Derived From Optical Coherence Tomography Angiography Images. Transl Vis Sci Technol, 7(5): 20.

[13] Shiihara H, Sakamoto T, Yamashita T, et al., 2017, Reproducibility and Differences in the Area of the Foveal Avascular Zone Measured by Three Different Optical Coherence Tomographic Angiography Instruments. Sci Rep, 7(1): 9853.

[14] Linderman R, Salmon AE, Strampe M, et al., 2017, Assessing the Accuracy of Foveal Avascular Zone Measurements Using Optical Coherence Tomography Angiography: Segmentation and Scaling. Transl Vis Sci Technol, 6(3): 16.

[15] Bates NM, Tian J, Smiddy WE, et al., 2018, Relationship Between the Morphology of the Foveal Avascular Zone, Retinal Structure, and Macular Circulation in Patients With Diabetes Mellitus. Sci Rep, 8(1): 5355.

[16] Takase N, Nozaki M, Kato A, et al., 2015, Enlargement of Foveal Avascular Zone in Diabetic Eyes Evaluated by En Face Optical Coherence Tomography Angiography. Retina, 35: 2377–2383.

[17] Samara WA, Shahlaee A, Adam MK, et al., 2017, Quantification of Diabetic Macular Ischemia Using Optical Coherence Tomography Angiography and Its Relationship With Visual Acuity. Ophthalmology, 124(2): 235–244.

[18] Dimitrova G, Chihara E, Takahashi H, et al., 2017, Quantitative Retinal Optical Coherence Tomography Angiography in Patients With Diabetes Without Diabetic Retinopathy. Invest Ophthalmol Vis Sci, 58(1): 190–196.

[19] Johnson B, 2017, Irregular Foveal Avascular Zone Morphology in Early Diabetic Retinopathy. Investigative Ophthalmology & Visual Science, 58(8): 3456–3462.

[20] Krawitz BD, Mo S, Geyman LS, et al., 2017, Acircularity Index and Axis Ratio of the Foveal Avascular Zone in Diabetic Eyes and Healthy Controls Measured by Optical Coherence Tomography Angiography. Vision Res, 139: 177–186.

[21] Kim K, Kim ES, Yu SY, 2018, Analysis of Foveal Microvascular Changes and Inner Retinal Layer Thinning in Patients With Diabetes Using Optical Coherence Tomography Angiography. British Journal of Ophthalmology, 102(9): 1226–1231.

[22] Rodolfo M, Lisa T, Alessandra M, et al., 2017, Foveal Avascular Zone Area and Parafoveal Vessel Density Measurements in Different Stages of Diabetic Retinopathy by Optical Coherence Tomography Angiography. Int J Ophthalmol, 10(10): 1545–1551.

[23] Yu H, Teng J, Zhu G, 2023, Quantitative Analysis of Retinal and Choroidal Blood Flow Perfusion Around the Optic Disc in Patients With Diabetic Retinopathy. Recent Advances in Ophthalmology, 43(01): 44–46.

[24] Qian X, Wang J, Chu T, et al., 2023, Correlation Between Choroidal Thickness and Vascular Density and the Severity of Diabetic Retinopathy. Journal of Clinical Ophthalmology, 31(03): 211–214.

[25] Rosen RB, Andrade Romo JS, Krawitz BD, et al., 2019, The Earliest Evidence of Preclinical Diabetic Retinopathy Is Revealed Using Optical Coherence Tomography Angiography Perfused Capillary Density. American Journal of Ophthalmology, 203: 103–115.

[26] Pramil V, Levine ES, Waheed NK, 2021, Macular Vessel Density in Diabetic Retinopathy Patients: How Can We Accurately Measure It and What Information Can It Provide? Clinical Ophthalmology, 15: 1517–1527.

Publisher's note

Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.