

Foveal Avascular Zone Morphology in Glaucoma: A Systematic Review of Oct Angiography Findings

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ABSTRACT

Introduction: Globally, glaucoma ranks as the foremost contributor to permanent blindness. Optical coherence tomography angiography (OCT-A) enables direct assessment of the foveal avascular zone (FAZ). Measurements of FAZ morphology provide reproducible and objective metrics, functioning similarly to laboratory-based biomarkers. OCT-A offers measurable and consistent evaluations of FAZ morphology specifically area, perimeter, and circularity that can serve as imaging biomarkers, akin to laboratory test results. Standardization of these parameters may enable integration into laboratory information systems and AI-driven diagnostic tools.

Objective: This review was conducted to systematically examine evidence on FAZ alterations in glaucoma as detected by OCT-A.

Evidence Review: A systematic search of PubMed, ScienceDirect, and Google Scholar identified studies from January 2015 to July 2025. Eligible articles included original research on FAZ in glaucoma assessed by OCT-A. Reviews, case reports, editorials, and non-English papers were excluded. Study selection and reporting followed PRISMA guidelines.

Results: Eighteen studies were included. The majority demonstrated that glaucoma patients, especially those with moderate-to-severe disease or central field impairment, had larger FAZ areas, increased perimeters, and reduced circularity compared with controls. These vascular changes were significantly correlated with thinning of the retinal nerve fiber layer and ganglion cell–inner plexiform layer, alongside decreased central field sensitivity. Some variability was noted across glaucoma subtypes and disease stages. Surgical interventions such as trabeculectomy were reported to partially reverse FAZ enlargement.

Conclusions: FAZ enlargement and loss of circularity represent consistent vascular biomarkers of glaucomatous damage. The OCT-A assessment of FAZ may enhance the monitoring of disease progression and treatment efficacy, requiring validation in larger longitudinal studies.

KEYWORDS: Glaucoma, Optical Coherence Tomography Angiography, Foveal Avascular Zone, Diagnostic Technology, Laboratory Medicine, Biomarkers, Medical Laboratory Science..

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INTRODUCTION

Glaucoma encompasses a spectrum of optic neuropathies characterized by progressive degeneration of retinal ganglion cells and their axons, culminating in structural optic nerve head changes and permanent visual field loss. The disease is clinically distinguished by peripheral field defects, separating it from other causes of blindness. Glaucoma is generally classified into primary open-angle, primary angle-closure, and secondary types.¹

Globally, an estimated 60 million individuals are affected, making glaucomatous optic neuropathy a leading cause of irreversible vision loss. In the United States, it is the second most common cause of blindness, disproportionately affecting the elderly. Open-angle glaucoma is particularly prevalent in individuals of African ancestry, who are at markedly higher risk of blindness compared with other populations. Angle-closure glaucoma is more frequently observed in women and in Asian populations, linked to anterior segment anatomical predispositions.²

A thorough ophthalmic evaluation—including tonometry, gonioscopy, visual field assessment, ophthalmoscopy, and OCT-based imaging—remains essential for diagnosis and management. OCT-A introduces an advanced non-invasive technique for high-resolution imaging of retinal and choroidal microvasculature.³ Beyond visualization, OCT-A provides measurable outputs such

as FAZ area, perimeter, and circularity, which can be interpreted in a manner similar to quantitative laboratory indices. This supports a paradigm shift from solely clinical assessment toward multimodal, biomarker-based diagnosis.⁴

While early research focused on larger vessels, the advent of OCT-A has enabled detailed analysis of the microcirculation. In 2012, a study demonstrated the capability of OCT-A to image optic nerve vasculature, and subsequently, Liu et al reported characteristic peripapillary vascular changes in glaucoma. Given its ability to detect flow in minute capillaries, OCT-A is a powerful tool to complement standard structural and functional tests.⁵

The FAZ, a capillary-free foveal region particularly vulnerable to ischemia, has emerged as a focus in glaucoma research. Enlargement of the FAZ is a recognized indicator in ischemic retinal conditions such as diabetic retinopathy and retinal vein occlusion, and accumulating evidence suggests its relevance in glaucomatous pathology as well.^{6,7} This review aims to systematically explore the OCT-A findings related to FAZ morphology in glaucoma patients and to synthesize their clinical implications.

MATERIAL AND METHODS

Literature Search Strategy

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement.^{[1][2]}

Literature Search Strategy

A comprehensive literature search was performed in the PubMed, ScienceDirect, and Google Scholar electronic databases for articles published in the last ten years. The search strategy employed the following keywords and their combinations: "glaucoma," "Foveal Avascular Zone," and "Optical Coherence Tomography Angiography." The reference lists of selected articles were also manually screened for additional relevant studies.

Study Selection and Eligibility Criteria

Inclusion criteria were: (1) original research studies; (2) investigation of FAZ morphology using OCT-A in patients with any type of glaucoma; (3) published in the English language; and (4) available in full-text format. Exclusion criteria included: (1) review articles, editorials, letters, or case reports; (2) studies not involving glaucoma patients; (3) animal or in-vitro studies; and (4) non-English publications.

Data Extraction and Quality Assessment

Initial screening of titles and abstracts was performed, followed by a full-text review of potentially eligible articles to determine final inclusion. Data from the selected studies were extracted into a structured table, including author, year, study design, sample characteristics, key results, and specific FAZ findings. The methodological quality of the included studies was appraised using the Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence. The study selection process is detailed in the PRISMA flow diagram (Figure 1).

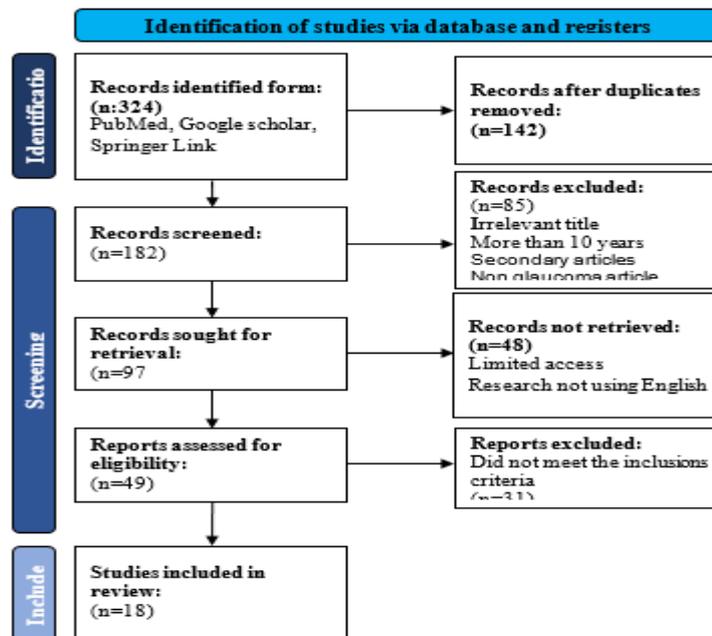


Figure 1: PRISMA diagram in systematic review search.

RESULTS

The initial search approach identified 324 articles. Following the removal of duplicates and the assessment of titles and abstracts, 45 papers were selected for in-depth analysis. This systematic review comprised 18 studies following the application of the inclusion and exclusion criteria. Table 1 encapsulates the principal findings and attributes of this investigation.

Table 1: Summary of Included Studies on FAZ Morphology in Glaucoma

No	Author (Year)	Evidence / Method	Sample	Key Outcomes	Reported FAZ Alterations
1	Zivkovic M. et al. (2017)	Level 4, Cross-sectional case-control	NTG patients (n=21)	Vertical ($t=5.58$, $p<0.001$), horizontal ($t=3.59$, $p<0.001$), maximum diameter ($t=5.94$, $p<0.001$), and FAZ area ($t=5.76$, $p<0.001$) all significantly larger vs. controls. Vessel density significantly reduced ($t=-5.80$, $p<0.001$).	FAZ dimensions expanded with concurrent reduction in vascular density.
2	Choi J. et al. (2017)	Level 4, Case-control	POAG patients (n=52)	Macular vessel density markedly lower in glaucoma vs. controls: superficial ($p=0.013$), deep ($p<0.001$), full retina ($p=0.002$). FAZ perimeter increased, circularity decreased ($p<0.001$). FAZ circularity index correlated with RNFL ($p=0.007$) and GCIPL thinning ($p=0.009$).	Larger FAZ perimeter and reduced circularity. Circularity index significantly related to RNFL and GCIPL loss; visual field indices (MD, PSD) confirmed.
3	Kwon J. et al. (2017)	Level 4, Retrospective	OAG patients (n=78)	Eyes with central VF defects (CVFD) showed greater FAZ area, lower circularity, and thinner macular GCIPL compared to peripheral VF defects. Larger hemi-FAZ observed in hemimacula corresponding to CVFD ($p<0.05$).	FAZ expansion and reduced circularity associated with CVFD severity and regional GCIPL thinning.
4	Zloto O. et al. (2022)	Level 4, Cross-sectional	POAG (n=45), XFG (n=30)	No significant differences in FAZ dimensions among groups. Circularity not correlated with IOP, MD, CMT, GC, or RNFL thickness.	No vascular or morphologic FAZ differences among POAG, XFG, and controls.
5	Igarashi R. et al. (2020)	Level 4, Retrospective	POAG patients (n=52)	FAZ area inversely correlated with RNFL ($r=-0.54$), GCIPL ($r=-0.58$), and GCC thickness ($r=-0.61$) (all $p<0.001$). Also negatively associated with foveal threshold, mean sensitivity, and MD on 10-2 VF ($p<0.001$).	Enlarged FAZ linked with neuroretinal thinning and poorer visual field indices.
6	Kwon J. et al. (2018)	Level 4, Retrospective cross-sectional	OAG patients (n=126)	FAZ parameters (area, perimeter, circularity) correlated with vessel density in foveal, parafoveal, and peripapillary regions (all $p<0.001$). Also related to mGCIPL thickness and central VF mean sensitivity.	Increased FAZ size, elongated perimeter, and reduced circularity corresponded with reduced vascular density and structural thinning.
7	Li F. et al. (2021)	Level 4, Prospective	POAG or OHT (n=238 eyes from 119 patients)	Larger baseline FAZ area associated with subsequent RNFL and GCIPL thinning ($p<0.05$), but not with VF metrics (MD, PSD).	FAZ enlargement anticipated future structural decline, serving as an early biomarker.
8	Philip S. et al. (2019)	Level 4, Cross-sectional observational	POAG (n=28), XFG (n=26)	No significant difference in FAZ metrics between groups.	No FAZ alterations noted between POAG and XFG.
9	Cheng K.K.W. et al. (2021)	Level 4, Prospective observational	NTG patients (n=70 eyes from 35 patients)	FAZ size and MSFD not related to disease severity. FAZ unchanged between better and worse eyes; MSFD reduced in NTG with systemic hypertension.	No FAZ modification detected; systemic hypertension reduced MSFD.
10	Liu K. et al. (2020)	Level 4, Case-control	APAC (n=33), PACG (n=33)	FAZ size and perimeter showed no differences across groups. FAZ circulation (flow index and vessel density) reduced, lowest in APAC.	Circulatory parameters reduced across angle-closure spectrum, especially APAC; no FAZ size changes.

No	Author (Year)	Evidence / Method	Sample	Key Outcomes	Reported FAZ Alterations
11	Kocatürk T. et al. (2021)	Level 4, Cross-sectional comparative	XFG patients (n=54)	Eyes with exfoliative glaucoma exhibited significantly reduced macular vessel density (VD) and perfusion density (PD) in both foveal and parafoveal regions ($p<0.05$). FAZ area and perimeter also smaller than controls. ROC analysis showed clear diagnostic separation.	Reduced FAZ size and vascular parameters in XFG; findings suggest diagnostic potential.
12	Wu J.H. et al. (2023)	Level 4, Cross-sectional	POAG (n=64)	Moderate-to-advanced POAG eyes demonstrated significantly larger FAZ area and perimeter compared with early-stage cases. These changes correlated with poorer BCVA ($p<0.05$).	Enlarged FAZ dimensions in advanced glaucoma correlated with decline in central visual acuity.
13	Yoon J. et al. (2023)	Level 4, Retrospective	OAG patients (n=131)	Progressive eyes showed faster FD300 reduction and mGCIPLT thinning compared to stable group. They also had larger FAZ area, reduced pericentral perfusion, and thinner mGCIPLT.	FAZ enlargement with reduced pericentral perfusion and thinning of mGCIPLT in progressive glaucoma.
14	Kromer R. et al. (2018)	Level 4, Prospective observational	POAG (n=30)	No significant FAZ area difference vs. controls ($p=0.703$). FAZ size inversely correlated with central flow density ($r=-0.465$, $p=0.004$).	FAZ size not different from controls, but inversely related to flow density.
15	Güngör D. et al. (2022)	Level 4, Prospective observational	POAG patients (n=20)	Following trabeculectomy, significant reductions in FAZ area ($p=0.026$) and perimeter ($p=0.049$) observed, alongside increased foveal vessel density ($p=0.005$).	Post-surgery, FAZ dimensions decreased and vascular density improved, reflecting restored microcirculation.
16	Ch'ng T.W. et al. (2020)	Level 3, Prospective observational, 12-month follow-up	OAG eyes undergoing surgery (n=40)	FAZ area, perimeter, and acircularity index increased at 1 month post-op ($p<0.05$), returning to baseline by 12 months. Macular vessel density increased from month 3. Changes independent of IOP reduction.	Transient postoperative FAZ enlargement and irregularity resolved within 12 months, suggesting inflammatory microvascular response.
17	Shoji T. et al. (2022)	Level 3, Prospective observational cohort	POAG patients (n=54; non-surgical eyes as control)	In surgical eyes, both IOP and FAZ area significantly decreased post-trabeculectomy ($p<0.001$). No changes in fellow non-operated eyes. FAZ reduction correlated with baseline FAZ, foveal sensitivity, and IOP decrease.	Significant postoperative FAZ shrinkage linked to IOP reduction and sensitivity improvement.
18	Nishida T. et al. (2024)	Level 3, Longitudinal cohort, 4-year follow-up	115 eyes (POAG and suspects), 81 patients	Eyes with FAZ progression showed faster GCC thinning ($-1.5 \mu\text{m}/\text{year}$ vs $-0.8 \mu\text{m}/\text{year}$; $p=0.026$) and more rapid VF MD decline ($-0.5 \text{ dB}/\text{year}$ vs $-0.2 \text{ dB}/\text{year}$; $p=0.017$). FAZ progression associated with IOP fluctuation (OR 1.54) and range (OR 1.20 per mmHg).	Progressive FAZ enlargement correlated with both structural deterioration (GCC thinning) and functional decline (VF MD), though not with macular vessel density.

Note: intraocular pressure (IOP), normal-tension glaucoma (NTG), primary open-angle glaucoma (POAG), visual field (VF), acute primary angle closure (APAC), primary angle-closure glaucoma (PACG), ocular hypertension (OHT), mean deviation (MD), mean ganglion cell-inner plexiform layer thickness (mGCIPL), ganglion cell-inner plexiform layer (GCIPL), central macular thickness (CMT), ganglion cell (GC), retinal nerve fiber layer (RNFL), retinal ganglion cell (RGC), receiver operating characteristic (ROC), odds ratio (OR), vessel density (VD), Whole-image VD (wiVD), acircularity index (AI).

DISCUSSION

This systematic review synthesizes evidence on FAZ morphological changes in glaucoma detected by OCT-A. The findings from the 18 included studies indicate that the FAZ is a clinically relevant structure in glaucoma pathophysiology, with alterations in its area, perimeter, and circularity correlating with disease presence and severity.

Meta-Analytical Commentary and Synthesis of Findings

A qualitative synthesis of the evidence reveals several consistent trends. The most robust finding across studies is the enlargement of the FAZ area in glaucoma patients compared to controls.⁸ This was reported in studies of normal-tension glaucoma (NTG) and

primary open-angle glaucoma (POAG).⁹ This enlargement appears to be more pronounced in eyes with more advanced disease and those with central visual field (CVF) defects, suggesting it is a marker of significant macular damage.¹⁰⁻¹⁷

Alterations in FAZ shape, specifically an increased perimeter and decreased circularity, were also frequently reported. A lower circularity index suggests a more irregular or distorted FAZ, which Choi et al. found was significantly correlated with RNFL and GCIPL thinning.⁷ This indicates that as neuroretina tissue is lost, the supporting capillary network may remodel, leading to a less uniform FAZ boundary. A laboratory medicine perspective highlights how OCT-A complements traditional in vitro biomarkers. While biochemical assays—such as inflammatory cytokines and oxidative stress markers—and genetic testing provide molecular insights, OCT-A contributes quantitative, in vivo measures of vascular remodeling. Its reproducible FAZ metrics can be integrated into laboratory information systems, interpreted with AI, and standardized much like parameters in hematology or clinical chemistry. By combining OCT-A with biochemical and molecular diagnostics, glaucoma assessment could evolve into a comprehensive, laboratory-based profile that supports precision medicine.^{7, 8, 11}

However, there is heterogeneity in the findings. Some studies did not observe significant differences in FAZ parameters.^{9, 14, 15} Zloto et al. found no significant changes in POAG or exfoliation glaucoma (XFG) compared to controls, and Liu et al. reported no morphological FAZ changes in angle-closure glaucoma despite reduced blood flow.^{9, 15} These discrepancies may be attributable to differences in patient populations (e.g., disease severity, glaucoma subtype) or variations in OCT-A imaging and segmentation algorithms. For example, the study by Kocatürk et al. uniquely found a *decrease* in FAZ area and perimeter in XFG, a finding that warrants further investigation.

Correlation with Structural and Functional Damage

A strong theme emerging from this review is the link between FAZ morphology and established markers of glaucomatous damage.

Structural Correlation: The structural correlation is underscored by inverse relationships between FAZ dimensions and retinal layer thicknesses, suggesting that microvascular remodeling may precede neuroretinal degeneration. Functionally, FAZ enlargement aligns with worsening visual field mean deviation and diminished foveal sensitivity. Longitudinal studies strengthen the view that FAZ changes can predict progression.¹⁸

Functional Correlation: The link between FAZ changes and central visual function is also well-supported. Studies using 10-2 visual fields found that a larger FAZ area was correlated with worse mean deviation (MD) and reduced foveal sensitivity.^{8, 10} Nishida et al.'s longitudinal data further strengthened this by showing that eyes with progressive FAZ enlargement had a significantly faster rate of MD decline.¹⁹ This topographical correlation underscores the clinical relevance of FAZ metrics, as central vision loss is a primary driver of disability in advanced glaucoma.²⁰

Impact of IOP-Lowering Treatment

The dynamic nature of FAZ morphology is highlighted by studies examining the effects of surgical intervention. Three prospective studies reported that successful trabeculectomy led to a significant reduction in FAZ area.^{21, 22} This postoperative change was correlated with the magnitude of IOP reduction and improvements in macular perfusion, suggesting that relieving pressure may restore some microcirculatory function.^{20, 22} In contrast, Ch'ng et al. observed a transient *increase* in FAZ area and irregularity one month after surgery, which they attributed to postoperative inflammation, with parameters returning to baseline by 12 months.²¹ Together, these findings indicate that the FAZ is not a static structure but can be modulated by both IOP and inflammatory processes.²³

Limitations

This review is subject to several limitations. First, the included studies are predominantly cross-sectional and observational, which limits causal inference. Second, there was significant heterogeneity in study populations, OCT-A devices, and analytical software, which complicates direct comparisons and precludes a formal quantitative meta-analysis. Third, most studies were conducted at single centers with relatively small sample sizes.

CONCLUSION

This systematic review highlights foveal avascular zone (FAZ) morphology as a promising biomarker in glaucoma. Enlarged FAZ area and reduced circularity consistently correlate with retinal nerve fiber layer and ganglion cell thinning, central visual field loss, and decreased foveal sensitivity. Longitudinal evidence suggests FAZ alterations may precede neuroretinal degeneration and predict functional decline, with partial reversibility after intraocular pressure reduction. Variability across studies underscores the need for standardized OCT-A protocols. Integration of FAZ metrics with biochemical, molecular, and genetic assays could establish OCT-A as a laboratory diagnostic tool, supporting precision medicine in glaucoma diagnosis and monitoring.

ARTICLE INFORMATION

Conflict of Interest Disclosures: The authors declare no competing interests. (Note: This is a template statement. Authors must provide their specific disclosures).

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Ethical Approval: As a systematic review of previously published studies, formal ethical approval was not required. The authors confirm that all studies included in this review obtained appropriate ethical clearance and patient consent as per their original publication.

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