

Role of Optical Coherence Tomography Angiography in Diagnosis of Early Glaucoma

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Glaucoma is one of the leading causes of irreversible blindness worldwide. Its estimated prevalence is 111.8 million by 2040.¹ It is a multifactorial disease characterized by loss of retinal ganglion cells (RGC) and retinal nerve fiber layer (RNFL). Optic nerve head (ONH) blood supply varies in different segments. The nerve fiber layer is supplied from the central retinal artery. However, the blood flow of the optic nerve head is from the short posterior ciliary arteries rather than the central retinal artery. These arteries make the incomplete anastomosis around the optic nerve head at the scleral lamina level. This missing anastomotic ring is called the Zinn-Haller arterial ring.²

Some theories such as vascular dysregulation and mechanical trauma have been described in the etiopathogenesis of RGC damage due to glaucoma.² Vascular dysregulation is anchored by the hypothesis that ischemia causes RGC death.³ This theory suggests ischemia of the ONH leads to RGC death. The role of the vasculature and blood flow in the pathophysiology of glaucoma, which is a progressive optic neuropathy, has been extensively investigated.³ Clinical findings such as migraine, Raynaud's syndrome, and nocturnal

hypotension have been described as an evidence of the role of disturbed blood supply in the development of glaucoma.^{4,5}

Various technologies have been explored for the vascular supply of the eye but none of these were appropriate for the optic nerve head.⁶ Recently much work is being done on the optical coherence tomography angiography (OCTA) studies. OCTA is still in evolution and optical coherence tomography (OCT) devices are changing rapidly but the basic principles remain the same.⁶ OCTA has been recently introduced as a noninvasive and reproducible tool to evaluate the vasculature of the retinal layers.⁶ The basic working principle of OCTA is that red blood cells are used as an intrinsic contrast agent to create three dimensional images of microvascular networks.⁶ Functional and structural tests are important for glaucoma diagnosis. However, early diagnosis is critical in glaucoma so OCTA is the new approach in this cause.

In the analysis of OCTA, the parameters which are employed include foveal avascular zone, choriocapillaris, foveal and optic nerve head vessel density (VD) and flow index. VD within the peripapillary retinal nerve fiber layer (pRNFL) is measured from the internal limiting membrane (ILM) to pRNFL posterior boundary.⁷ It is well known that pRNFL is mainly affected in the inferior and superior quadrants in pre-perimetric and early glaucoma.⁷ Wang et al showed that the pRNFL decreased in 77% of the eyes showing early ganglion cell inner plexiform layer (GCIPL) thinning, suggesting that pRNFL analysis may overlook early glaucomatous macular damage.⁸ Zheng et al showed that the supero-temporal and infero-temporal pRNFL and Bruch membrane opening thicknesses below the fifth percentile yielded the best diagnostic performance for glaucoma detection.⁹

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OCTA can be helpful to see the relationship between neuronal and vascular changes in glaucomatous eyes. OCTA-based studies investigated the macular region and found that glaucomatous eyes had a significantly lower superficial vascular complex (SVC) at the macula than healthy eyes. In contrast, no significant difference was found in the intermediate and deep capillary plexuses at the macula. Chung et al showed decreased macular and peripapillary VD in the glaucomatous eyes.¹⁰ The VD parameters were found significantly correlated with other structural and functional parameters. The peripapillary VD differences may be helpful for the diagnosis of glaucoma suspects and healthy eyes.¹⁰ Yarmohammadi et al showed significantly lower VD in glaucoma eyes compared with glaucoma suspects and healthy eyes.¹¹ The studies related to the ocular blood flow in glaucoma are important but difficulty arises as ocular hemodynamics may be different in different populations. Triolo et al evaluated the macular and peripapillary vascular density.¹² They showed that peripapillary VD on average and in the superior and inferior quadrants decreased in the glaucoma group ($p = 0.001$). However, macular VD was not statistically different ($p > 0.05$). A correlation between RNFL thickness and VD was also found at the peripapillary area; but the correlation was not found in all groups.¹²

The Early Manifest Glaucoma trial showed that low perfusion pressure was a risk factor for glaucoma progression.¹³ Perfusion pressure is affected by multiple factors including nocturnal hypotension and Raynaud phenomenon. Various studies have shown their relation with the glaucomatous changes.⁵ As these studies did not consider blood flow at the optic nerve head directly, the relationship between optic nerve perfusion and glaucoma remains incompletely described. Lee et al investigated the relationship between the decreased peripapillary retinal perfusion as examined by OCTA and RNFL defect in eyes with primary open-angle glaucoma (POAG) and a localized RNFL defect.¹⁴ They found that areas of low perfusion on OCTA coincided with the RNFL defect, suggesting that decreased VD is the result of the capillary shut down secondary to RNFL cell death.

A decrease in OCTA parameters could be seen in glaucoma, but the clinical application of this information is still being investigated. There is not enough evidence to use this technology in diagnosing very early stage of glaucoma. However, OCTA studies

still remain the key role to explain the relationship between perfusion and the pathogenesis of glaucoma.

OCTA is a noninvasive technique. OCTA data strongly indicates the value of ocular perfusion in different stages of glaucoma. The combined use of various measurement techniques should be helpful for us. To analyse the diagnostic effects of the perfusion parameters, further studies are necessary.

Conflict of Interest

Authors declared no conflict of interest

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Authors' Designation and Contribution

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