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REVIEW ARTICLE

Optical coherence tomography-angiography: A new diagnostic and follow-up tool for glaucoma

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Abstract

Glaucoma is an optic neuropathy and is one of the leading causes of irreversible vision loss worldwide. There are studies on the role of vascular dysfunction in the pathogenesis of glaucoma. Evaluation of intraocular blood flow will be useful in elucidating the pathogenesis. Various techniques are available for the diagnosis and follow-up of patients with glaucoma. Optical coherence tomography angiography (OCTA) has emerged as a new technology to detect the vascular effects of the glaucoma. Optical coherence tomography angiography (OCTA) is a new technology and many publications have been made in the field of glaucoma. In this article, we aimed to review the studies conducted on the role of OCTA technology in glaucoma and to draw attention to how OCTA can be helpful for diagnosis of glaucoma and follow-up of patients with glaucoma. Whole literature through by PubMed for the keywords of optical coherence tomography angiography and glaucoma were scanned. This review included articles up to February 2021. Only English languages articles were included. Optical coherence tomography angiography provides a rapid and noninvasive quantitative assessment of the microcirculation of the retina, optic nerve, and choroid. Optical coherence tomography angiography uses the action of red blood cells as an intrinsic contrast agent. It has high reproducibility. Optical coherence tomography angiography studies have shown that microcirculation in the superficial optic nerve, peripapillary retina and the macula are reduced in glaucoma patients. Optical coherence tomography angiography parameters in the peripapillary region are thought to be better biomarkers in advanced glaucoma than OCT parameters. Recent literature shows that OCTA has the potential to provide useful information in the diagnosis and follow-up of patients with glaucoma.

Keywords: *Glaucoma, optical coherence tomography angiography, optic nerve.*

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Introduction

Glaucoma is an important cause of irreversible vision loss worldwide. Increased intraocular pressure (IOP) and impaired ocular blood flow are two important factors contributing to the development and progression of glaucoma [1]. These changes in ocular perfusion pressure caused by the difference in mean arterial pressure and intraocular pressure were thought to cause glaucomatous optic neuropathy due to ischemic damage by causing ischemia in the optic nerve [2]. In the Early Manifest Glaucoma study, it was stated that low ocular perfusion pressure is a risk factor in the progression of glaucoma [3]. Barbados Eye study and Los Angeles Latino eye study also showed a relationship between low ocular perfusion pressure and the prevalence of glaucoma [4,5]. Fluorescein angiography (FA) and ICG angiography studies have shown changes in blood flow in glaucoma. However, these investigations allow the flow to be evaluated more qualitatively than quantitatively. Color doppler USG is problematic in terms of resolution. Laser flowmetry has been evaluated as a limited application due to reproducibility and difficulty in clinical application. Doppler OCT studies also lacked sensitivity in measuring blood flow. Early diagnosis is important in glaucoma. Thus, functional and structural tests are crucial in the diagnosis and follow-up of glaucoma [6-8].

In this brief review article, we aimed to review information about the role of Optical Coherence Tomography-Angiography (OCTA) in the glaucoma management. We collected English written literature conducting OCTA studies on glaucoma and summarized the place of OCTA in eyes with glaucoma.

Optical Coherence Tomography-Angiography

Optical coherence tomography angiography has emerged as a non-invasive, quantitative, fast and new technology for evaluating ocular vascularity. It is based on optical coherence tomography (OCT) [6,7]. Non-invasive imaging and evaluation of the microcirculation in the optic nerve head and peripapillary retina is possible by using OCTA [8,9]. Parameters used in OCTA analysis include foveal avascular region, choriocapillaris, foveal and optic nerve head vessel density (VD) and flow index. Optical coherence tomography angiography is noninvasive as no contrast material is required. Its advantages are its high resolution and high repeatability compared to other modalities. Projection artefact and motion artefact are its disadvantages. It cannot directly measure blood flow rate either, its images are static [6,10]. Especially two parameters used frequently in the literature are vessel density (VD) and flow index (FI). These measurements are used to represent perfusion

OCTA in Glaucoma

OCTA of papillary and peripapillary area in Glaucoma

Studies have shown that optic nerve head and peripapillary retina show a decrease in VD and flow indexes in eyes with primary open-angle glaucoma (POAG) [8,11,12]. It is known that the peripapillary retinal nerve fibre layer (pRNFL) is mainly affected in the lower and upper quadrants in perimetric and early glaucoma. OCTA can help show the relationship between vascular and neuronal changes in glaucomatous eyes [13].

It was Jia et al. who published the first report on the optic nerve head (ONH) in OCTA [14]. Liu et al. showed that the density of peripapillary vessels in eyes with glaucoma was decreased in eyes with glaucoma compared to normal eyes [12]. Subsequently, several studies presented differences in ONH and microcirculation of the peripapillary region between glaucoma, glaucoma suspects and normal patients. Eyes with glaucoma with higher pre-treatment IOP values showed the largest difference in the optic disc compared with normal eyes, but no difference was found in the macular or peripapillary areas. This has been explained by the decrease in vascular density in the optic disc due to vascular compression in glaucoma associated with pre-treatment IOP values [15,16]. One potential reason for the lower discriminatory power of the optic disc from OCTA parameters can be explained as the significant heterogeneity in optic disc morphology. Vascular crowding of the large vessels in the optic disc also makes it difficult to specifically examine microvascularity. The pathophysiology of glaucomatous damage in the optic disc and the peripapillary areas is different, and it can explain the difference in the impairment of parameters of OCTA between two areas [17].

OCTA and RNFL Relationship in Glaucoma

There are studies with different evaluations about the correlation of structural changes in OCTA and glaucoma. Chen et al. reported that although there was no difference in RNFL thickness, glaucoma patients had significantly lower peripapillary vessel density

compared to normal subjects [18]. Some studies have shown a strong correlation between RNFL and OCTA parameters [19,20]. Pradhan et al. reported that the decrease in vascular density and RNFL thinning differed in different peripapillary sectors in eyes with POAG compared to normal eyes [21]. Macular and peripapillary VD have been shown to decrease in eyes with glaucoma [22]. Peripapillary VD differences may be helpful in diagnosis. Other studies have shown that there is no correlation between OCTA parameters and structural changes.

A strong correlation have been reported between peripapillary vessel density of the inferotemporal and superotemporal sectors and visual field loss [23,24].

OCTA of Macular Area in Glaucoma

In a study evaluating the diagnostic accuracy of macular scans in control and mild glaucoma eyes, it was shown that the vascular density in the outer field has a higher diagnostic performance compared to the inner field vascular density [25]. The superotemporal and inferotemporal macula have been found to the most susceptible macular areas to glaucoma. These areas are mostly located within the 6x6 mm area but outside the central 3x3 mm area [26,27]. 6 × 6 mm macular scans may, therefore, give rise to higher diagnostic accuracy. In one study, the internal macular vessel density gradually decreased, while the internal macular thickness did not change during a follow-up period of 13.1 months [28]. In another study, a correlation was found between RNFL thickness in the peripapillary area and VD; however, the correlation was not found in all groups [13]. The inner macular thickness is suggested to be better indicator than the inner macular vessel density in the detection of glaucoma disease [29]. The differences between studies may be due to differences in the area chosen for measurements of inner vessel density and inner retinal thickness [30]. Decreases in OCTA VD may occur before the structural and functional deterioration in glaucoma suspects. This situation suggested that OCTA may be helpful in early diagnosis and follow-up of glaucoma [31]. The percentage reduction in macular vessel density in early glaucoma eyes was lower than the percentage reduction in macular ganglion cells thickness, whereas this ratio was similar in preperimetric eyes [32]. Rapid reduction in macular vessel density has been associated with severe glaucoma [33].

It has been suggested that glaucoma is associated with decreased vascular density in the macular region; however, the precise role of this parameter in the diagnosis and progression of glaucoma is unclear [34].

OCTA in Different Types and Stages of Glaucoma

Hou et al. reported significantly higher intraocular vascular density asymmetry in those with glaucoma suspicion compared to normal eyes [35]. Yarmohammadi et al. showed that the mean parafoveally vessel density in the eyes of patients with preperimetric POAG was significantly different from that of normal eyes [36]. Lee et al. found that low perfusion peripapillary retinal areas in OCTA coincided with the RNFL defect. Optical coherence tomography angiography can provide us with information about ocular perfusion at different stages of eyes with glaucoma [37]. A significantly higher peripapillary vessel density has been found in eyes with normotensive glaucoma (NTG) compared to eyes with POAG, but no significant difference has been found in structural and functional parameters [38]. The patients with POAG have been found to have lower peripapillary vascular density compared to normal eyes [39]. No significant difference in peripapillary OCTA parameters in terms of blood flow index and vessel density has been found between NTG and POAG [40]. A significant decrease in peripapillary VD has been found in eyes with primary angle-closure glaucoma (PACG) [41]. The vascular density in both parafoveal and peripapillary regions has been shown to be significantly lower in PACG eyes than in normal eyes. They showed that poorly controlled PACG eyes had lower vascular density in the peripapillary area than well-controlled PACG eyes. Optic nerve head and peripapillary vascular changes correlated well with disease and severity of glaucoma, and this may be an important indicator of disease progression [42]. Rao et al, found a reduction in VD in PACG but did not find this change in angle-closure without glaucoma [43]. The circumpapillary VD in the eyes with angle-closure was significantly lower after acute angle-closure [44]. A significantly reduced peripapillary VD has also been reported in eyes with pseudoexfoliative glaucoma [45].

When the studies were evaluated, it was thought that OCTA parameters in the peripapillary region were better biomarkers compared to OCT parameters in advanced glaucoma. The peripapillary small vessel density was also found to be associated with the severity of glaucomatous visual field damage in eyes with advanced POAG [46].

Association of OCTA with Visual Field in Glaucoma

Optical coherence tomography angiography parameters (VD, FI) have been shown to have a moderate and high correlation with visual field parameters [11,14,47,48]. When peripapillary vascular density of POAG patients with visual field defect in one eye and normal visual field in the other eye are compared with each other and with normal eyes, the mean peripapillary vascular density was found to be higher in unaffected eyes of patients with POAG than in other affected eyes. However, no significant difference was found from normal eyes [36]. The correlation between the visual field mean deviation (MD) and OCTA parameters has been found to be stronger than the correlation between visual field MD and OCT parameters. Therefore, vascular loss as a OCTA finding has been suggested as a better biomarker than structural changes for worse visual function in eyes with glaucoma [9].

OCTA in Follow-Up of Glaucoma

In one study, it was stated that deep VD values measured by OCTA may indicate the risk of impaired visual function in patients with glaucoma [49]. There are also studies showing the improvement in VD measurements with the decrease in IOP after the treatment [50]. Although OCTA provides us with various evidence on the vascular pathogenesis of glaucoma, the clinical application of this information is still under investigation. The contradictions between studies present uncertainties in establishing the causal link.

OCTA in Myopic Patients with Glaucoma Suspicion

In a OCTA study evaluating myopic and normal eyes with and without POAG, the relationships between peripapillary vessel density and mean visual field sensitivity in POAG with and without high myopia was investigated [51]. It has been suggested that peripapillary vascular density may be useful in monitoring disease progression in high myopic eyes with glaucoma [52]. In another study, it was shown that the macular VD in the deep capillary plexus decreased significantly faster in highly myopic glaucomatous eyes than those without high myopia. It has been stated that these findings may be important in risk assessment of myopic POAG patients [53]. In the evaluation of glaucoma in highly myopic eyes, a multimodal approach with papillary anatomic and circumpapillary microperimetric assessments has been proposed for to be important [54]. As studies on myopic glaucoma increase, OCTA may be an important tool in the follow-up of myopic glaucoma.

OCTA of Choriocapillaris in Glaucoma

Kwon et al. observed parafoveal visual field defects in 96% of eyes with choroidal microvascular dropout (CMvD) and only 39% of eyes without CMvD, suggesting that this may provide a clinical overview of the spatial location of damage in glaucomatous eyes. Recent studies support that blood flow disruption can also occur in the deep layers of the retina and choroid, in addition to the superficial layers [55]. A higher frequency of choroidal microvascular dropout (CMvD) in eyes with glaucoma with parapapillary gamma zone has been reported to be associated with glaucoma progression or central visual field defects [56]. Eyes with choroidal microvascular dropout (CMvD) have been shown to be closely associated with the nocturnal diastolic blood pressure drop. Accordingly, the modulation of nighttime DBP decreases can be achieved by 24-hour ambulatory blood pressure monitoring of CMvD patients. Thus, it has been suggested that glaucoma progression can be prevented or slowed down [57].

OCTA and Diurnal Variation

Mansouri et al. found that diurnal IOP variations had no significant effect on peripapillary and macular vessel density in eyes with glaucoma [58]. In another study, daily changes in IOP, mean ocular perfusion pressure (MOPP) and retinal vessel density (RVD) were significantly higher in POAG eyes compared to healthy eyes. Compared to the study of Mansouri et al., in this study RVD measurement, blood pressure and MOPP evaluation were performed in the evening. According to these findings, they suggested that daily RVD changes may indicate the hemodynamic variation of POAG [59].

Conclusion

Current OCTA studies show that microcirculation is reduced in various stages of glaucoma. Optical coherence tomography angiography has come into our practice as a new objective approach to diagnosis and follow-up in glaucoma. It may be advantageous in certain types of glaucoma such as myopic glaucoma, or detection of progression of the advanced glaucoma. It seems that OCTA will take place in the management of glaucoma as an adjunctive tool in the future. However, there is no evidence that it is superior to standard structural and functional investigations in ability to

detect the glaucomatous disease. Whether impaired microcirculation in glaucomatous eyes induces neuronal damage or already glaucomatous damaged tissue with reduced consumption induces impaired microcirculation remains to be clarified. In conclusion, although there is insufficient evidence to use this technology in the very early diagnosis of glaucoma, further OCTA studies will help explain the relationship between perusion and glaucoma pathogenesis. It will be beneficial to use various functional and structural tests together in the diagnosis and follow-up of glaucoma.

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Conflict of interest
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