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Original Research Article

Correlation between optical coherence tomography angiography measured vessel density and retinal nerve fiber layer thickness in moderate primary open angle glaucoma cases and normal controls

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ABSTRACT

Purpose: Aim of this study was to establish a correlation between findings obtained from Optical Coherence Tomography Angiography (OCT-A) and Retinal Nerve Fiber Layer (RNFL) thickness measurements in a series of moderate Primary Open Angle Glaucoma (POAG) cases and normal controls.
Materials and Methods: In this observational cross-sectional study a total of 100 eyes were included, comprising 50 eyes with glaucoma and 50 control eyes without glaucoma. All participants underwent comprehensive anterior and posterior segment evaluations, intraocular pressure (IOP) measurement using Goldmann applanation tonometer, gonioscopy, visual field testing, and OCT imaging, which included OCT-A. The OCT-A imaging was performed using the RTvue XR Avanti by Optovue. Two types of analysis were conducted: a comparative analysis between the normal and glaucomatous groups using an unpaired t-test to assess differences in RNFL thickness and vessel density values, and a correlation analysis within each group to examine the strength of correlation between RNFL loss and reduction in vascular density.
Results: The results showed a significant reduction in vessel density index in all quadrants of glaucomatous eyes compared to normal eyes. Moreover, this reduced vessel density was found to be significantly correlated with the reduction in RNFL thickness in glaucoma patients. Specifically, the uperior and inferior quadrants exhibited the strongest correlation with each other.
Conclusion: The severity of vascular compromise demonstrated a significant correlation with the extent of retinal nerve fiber loss in patients with glaucoma. OCT-A can serve as a valuable adjunct in the diagnosis of glaucoma and monitoring its progression.

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1. Introduction

Glaucoma, a prevalent eye disease, is a leading cause of irreversible blindness globally. Early diagnosis plays a crucial role in addressing this condition as glaucomatous changes are irreversible but preventable. Elevated intraocular pressure (IOP) is a major determinant in the progression of glaucomatous neuropathy. Although the loss of the retinal nerve fiber layer (RNFL) is a well-known occurrence in the natural history of the disease, it may also manifest in the absence of raised IOP. Currently, optical coherence tomography (OCT) is employed to quantify RNFL loss, aiding in monitoring glaucoma progression. However, the role of vascular perfusion in the progression of glaucoma has been well-documented in the literature. Ocular hypoperfusion has been associated with glaucomatous progression in eyes with normal IOP levels. Furthermore, systemic diseases like hypertension and diabetes can contribute to the disease's progression due to vascular dysregulation.[1]

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Optical Coherence Tomography Angiography (OCTA) is an innovative imaging modality that enables non- invasive visualization of the retinal and choroidal vasculature without the use of a contrast agent. By employing serial A scans to observe erythrocyte mobility within blood vessels, OCTA provides a 3- D mapping of the retinal and choroidal circulatory systems. Its diagnostic capabilities have been demonstrated in various macular diseases, including diabetic maculopathy, retinal vascular disorders, and age-related macular degeneration (ARMD).

The principle behind OCTA is the use of the Split Spectrum Decorrelation Angiography (SSADA) algorithm. This algorithm capitalizes on the mobility of erythrocytes and moving blood within the vascular columns, leading to variations of reflectivity over successive scans. The resultant high decorrelation between different time frames and images allows the elimination of sequential decorrelated frames and immobile outliers, resulting in improved resolution and image clarity by eliminating tissue motion artifacts.

In the context of this study, we aim to investigate the segmental vascular density of the optic nerve head and compare it with morphological indices of RNFL thickness and ganglion cell count.[2–5] By doing so, we seek to explore potential correlations between OCTA-measured vessel density and the structural parameters of the RNFL in a series of moderate primary open-angle glaucoma cases and normal controls.

The objective of this research is to provide insights into the relationship between retinal vascular perfusion and glaucoma progression. Understanding this association may enhance early detection and management strategies for glaucoma, offering promising prospects for preserving visual function and preventing irreversible vision loss. Consequently, this study contributes to the growing body of knowledge in the field of glaucoma research and further validates the clinical utility of OCTA in ocular disease assessment.

2. Materials and Methods

2.1. Study design

This study is an observational cross-sectional investigation conducted at Uma Eye Clinic between February 2019 and October 2020.

2.2. Participants

A total of 100 patients were included in the study after obtaining institutional ethical clearance. The sample consisted of two groups: (i) primary open angle glaucoma suspects or known cases (n = 50) and (ii) control subjects without glaucoma (n = 50). The inclusion criteria were age greater than 35 years, visual acuity correctable to 6/12, and clear ocular media. Exclusion criteria comprised angle closure glaucoma, pre-existing retinal pathologies, age below 35 years, media opacities that hindered testing, axial myopia exceeding -5, and a history of trauma or inflammation.

2.3. Data collection

Informed consent was obtained from all participants in either English or the regional language. The evaluation included full anterior and posterior segment examinations, intraocular pressure (IOP) measurement using Goldmann applanation tonometry, gonioscopy, visual field testing, and OCT imaging with angiography.

2.4. OCTA imaging

OCTA imaging was performed using RTvue XR Avanti by Optovue, acquiring 70,000 A-scans per second with a tissue resolution of 5μm axially and a beam width of 15μm. The split spectrum decorrelation algorithm enabled blood flow detection within retinal vascular columns. Vessel density and flow were analyzed separately in four layers of the retina complex: (1) Ganglion cell layer (superficial plexus), (2) Network of blood vessels between inner plexiform and outer plexiform layers, (3) Layer of photoreceptors, and (4) 30-micron offshoot for vasculature of the choroid.

2.5. Outcome measures

The OCTA results for the optic nerve head were recorded as perfusion of the whole disc, inside disc, and peripapillary disc, encompassing superior, inferior, nasal, and temporal vessel densities. RNFL thickness measurements for the Peripapillary zone were recorded in the superior, inferior, nasal, and temporal quadrants. The GCC analysis provided average GCC, superior GCC, and inferior GCC values.

2.6. Statistical analysis

Data from the various parameters were compiled and analyzed. The Mann-Whitney U test was employed for comparison analysis between glaucoma and control groups. The Spearman's rank correlation test was used to establish correlations between vessel density and RNFL values within each group. Visual fields were also correlated with vessel density values (whole disc vessel density) in both groups. The significance level was set at $p < 0.05$.

3. Results

In this study, a total of 100 eyes were included, with 50 eyes diagnosed with moderate primary open-angle glaucoma (POAG) and 50 eyes serving as normal controls. The mean age of the participants was 52.45 years, with the majority falling within the 61-70 age range. Among the participants, 55% were females and 45% were males. All patient eyes demonstrated a best-corrected visual acuity equal to or better than 6/12. The average intraocular pressure (IOP) for glaucomatous patients was 18.93 mmHg, while for normal controls, it was 15.57 mmHg.

The optical coherence tomography (OCT) analysis of the retinal nerve fiber layer (RNFL) thickness was conducted and compared between glaucomatous and control subjects.[6] The RNFL thickness was measured in four quadrants: Superior, Inferior, Nasal, and Temporal.

The mean RNFL thickness in the Superior quadrant for glaucomatous patients was 84.77 μm, whereas for normal patients, it was 131.25 μm, resulting in a mean difference of 46.48 μm. In the Inferior quadrant, glaucomatous patients had a mean RNFL thickness of 72.85 μm, while normal patients had 142.31 μm, showing a mean difference of 69.46 μm. The Nasal quadrant revealed a mean RNFL thickness of 69.54 μm for glaucomatous patients and97.38 μm for normal patients, with a mean difference of 27.83333 μm. In the Temporal quadrant, glaucomatous patients had a mean RNFL thickness of 59.88 μm, and normal patients had 73.71 μm, resulting in a mean difference of 13.83333 μm. All four quadrants showed statistically significant differences with p-values < 0.001.

The ganglion cell count was also compared between normal and glaucomatous subjects. The average ganglion cell count in glaucomatous subjects was 77.42 cells, while in normal subjects, it was 93.94 cells, resulting in a mean difference of 16.52 cells. In the superior portion of the optic disc, glaucomatous patients had an average ganglion cell count of 82.60 cells, and normal subjects had 93.56 cells, with a mean difference of 10.96 cells. In the inferior portion of the optic disc, glaucomatous patients had an average ganglion cell count of 72.33 cells, and normal subjects had 94.42 cells, with a mean difference of 22.09 cells. The Visual Field Index (VFI) was found to be 88.50 for glaucomatous patients and 99.48 for normal subjects, showing a mean difference of 10.98. All ganglion cell counts and the VFI showed significant differences with p-values < 0.001.

The OCT angiography (OCT-A) findings in this study demonstrated a significant reduction in vascular density in glaucomatous patients compared to normal controls. The mean vessel density (MVD) in glaucoma patients was 43.95, while in normal subjects, it was 51.55, resulting in mean difference of 7.60 with a p-value < 0.001.

When analyng the individual quadrants of the optic nerve head's perfusion as detected by OCT-A, there was a marked reduction in vascular flow index in all quadrants of the optic nerve head in glaucomatous patients compared to normal controls.[7] The Superior vessel density in glaucoma patients was 41.40, while in normal subjects, it was 53.81, with a mean difference of 12.41. In the Inferior quadrant, the vessel density was 37.08 for glaucomatous patients and 55.13 for normal subjects, showing a mean difference of 18.05. The Nasal vessel density in glaucoma patients was 41.10, and in normal subjects, it was 48.00, resulting in a mean difference of 6.90. Finally, the Temporal vessel density was 44.25 in glaucomatous patients and 51.71 in normal subjects, showing a mean difference of -7.46. All quadrants demonstrated statistically significant differences with p-values < 0.001.

In healthy subjects, the temporal vessel density showed a moderate correlation with a value of 0.392 and a p-value of < 0.006. This finding can be attributed to the anatomical retinotopic arrangement of the nerve fiber layers, as the temporal aspect of the optic disc receives the papillomacular bundle.

In summary, this study revealed that glaucomatous eyes exhibited significant reductions in RNFL thickness and ganglion cell count, as well as decreased vascular density compared to normal controls. These findings support the use of OCT and OCT-A as valuable tools in detecting and monitoring glaucoma.

4. Discussion

Glaucoma is a progressive optic neuropathy characterized by ganglion cell loss and retinal nerve fiber layer (RNFL) thinning. Early detection of glaucoma is crucial, as substantial RNFL loss can occur before the appearance of visual field defects and clinically detectable changes, such as increased cup-disc ratio and neuroretinal rim thinning. In this study, we investigated the correlation between vessel density measured through Optical Coherence Tomography Angiography (OCT-A) and RNFL thickness in moderate primary open-angle glaucoma cases and normal controls.

The mean age of the glaucomatous patients in our study was 52.45 years, consistent with previous reports stating that the disease typically manifests in older age groups. Additionally, our findings corroborate with Kreft et al.[4] who suggested that late detection of glaucoma in patients above 40 years of age is associated with a worse prognosis. Moreover, we observed that visual acuity remained relatively good in the early-mid stages of glaucoma despite significant RNFL loss, underscoring the importance of early diagnosis.

In the context of normal-tension glaucoma (NTG), its pathology is thought to differ from ocular hypertension, with vascular insufficiency playing a primary role.[8] While there is some controversy surrounding whether NTG is a distinct entity or merely glaucoma that develops independently of intraocular pressure (IOP), our study did not find any sex predilection in NTG.[9]

IOP, long considered a major risk factor for glaucoma, may not necessarily predict the severity of glaucomatous damage. The mean IOP in our glaucomatous patients was 18.93 mmHg, while normal controls had a mean IOP of 15.57 mmHg. This emphasizes the need for alternative markers to gauge glaucomatous damage accurately.

Table 1: Comparison of RNFL thickness between patients with glaucoma and healthy subjects

	Variables	Patientswith Gluacoma	Normal subjects	P value*
RNFL thickness	RFNL Superior	84.77±27.10	131.25±24.97	<0.001
	RFNL Inferior	72.85±20.28	142.31±21.90	<0.001
	RFNL Nasal	69.54±45.79	97.38±21.38	<0.001
	RFNL Temporal	59.88±14.01	73.71±12.67	<0.001

Table 2: Comparison between GCC and visual field index in glaucoma and normal patients

	Variables	Patients with Gluacoma	Normal subjects	P Value *
GCC	GCC analysis with Avg	77.42±7.71	93.94±7.13	<0.001
	GCC patients Superior	82.60±8.75	93.56±10.07	<0.001

Table 3: Comparison of vessel density between patients with glaucoma and healthy subjects

	Variables	Patients with Gluacoma	Normal subjects	P Value *
Vessel Density	Whole disc vessel density	43.95±5.78	51.55±5.49	<0.001
	Inside disc vessel density	41.40±2.51	53.81±8.72	<0.001

Table 4: Comparison of peripapillary vessel density between patients with glaucoma and healthy subjects

	Variables	Patients with Gluacoma	Normal subjects	P value*
Peripapillary vessel density	PVD Superior	41.40±11.29	53.81±9.95	<0.001
	PVD Inferior	37.08±3.67	55.13±3.61	<0.001
	PVD Nasal	41.10±7.34	48.00±13.77	<0.001
	PVD Temporal	44.25± 4.19	51.71±4.26	<0.001

Central corneal thickness (CCT) is another crucial parameter in glaucoma assessment. Thinner CCT is associated with a higher risk of glaucoma progression, independent of IOP. It is now widely accepted that CCT, as a standalone factor, serves as a risk indicator for glaucoma.

Our study successfully utilized OCT to detect and quantify RNFL thinning, even before characteristic visual field loss appeared, consistent with previous research.[10] OCT-A took this a step further by analyzing the vascular density in the retina, enabling a correlation between RNFL loss and vascular changes.[11] Dagny Zhu et al.'s work on NTG also highlighted a strong correlation between disc flow index and cup-to-disc ratio, indicating poorer perfusion in discs with larger cups and more severe damage.[12] Reduced vascular supply and hemodynamic dysregulation pose significant risks in glaucoma, particularly in NTG cases.[8] Monitoring such patients with 24-hour blood pressure monitoring and carotid Doppler studies for evidence of vascular insufficiency is prudent. Studies involving OCT-A have shown its reliability in analyzing foveal vasculature and detecting macular flow hypoperfusion in various conditions, such as diabetes mellitus and retinal vein occlusion.[13]

Our study's main finding demonstrates that vessel density in glaucomatous patients is significantly reduced compared to normal controls, both when measuring the entire disc's vessel density and when measuring each quadrant of the optic disc separately. This association was not observed in healthy subjects. Furthermore, vessel density reduction on OCT-A reaches a base level at a more advanced disease stage than the structural changes detected by OCT, offering the potential to monitor progression in advanced glaucomatous damage.

Correlating the vascular supply with RNFL thickness, we observed strong correlations between the superior and inferior quadrants of the optic nerve head. This can be attributed to the anatomic retinotopic arrangement of the nerve fiber layers, with the temporal aspect of the disc receiving the papillomacular bundle.

In conclusion, our study provides valuable insights into the correlation between OCT- A measured vessel density and RNFL thickness in moderate primary open-angle glaucoma cases and normal controls. Early detection of glaucoma remains vital, and OCT-A holds promise as a valuable tool for identifying vascular changes associated with RNFL loss. Further research in larger populations and longitudinal studies will help solidify its role in monitoring glaucomatous progression.

5. Conclusion

In conclusion, our study highlights the valuable insights that Optical Coherence Tomography (OCT) and Optical Coherence Tomography Angiography (OCTA) provide in the early diagnosis and monitoring of glaucoma suspects. By enabling visualization of structural changes in the retinal nerve fiber, OCT aids in the early detection of glaucoma even before clinical manifestations become apparent.

We acknowledge that our study has some limitations, such as the relatively small sample size and the inclusion of only moderate glaucoma cases. Future research with larger, diverse populations and longitudinal designs should be conducted to further validate the potential of OCTA in glaucoma management.

In conclusion, our study underscores the clinical significance of combining OCT and OCTA measurements to enhance the diagnostic capabilities and monitoring of primary open angle glaucoma. The integration of these imaging modalities has the potential to revolutionize glaucoma management by offering a more comprehensive understanding of the disease's progression and optimizing patient outcomes. As we move towards personalized medicine, OCTA holds great promise in contributing to a more targeted and effective approach in the care of glaucoma patients.

6. Source of Funding

None.

7. Conflict of Interest

None.

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