Choroidal Vascularity in Non-arteritic Anterior Ischaemic Optic Neuropathy

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ABSTRACT

This study evaluates the peripapillary choroidal vascularity in eyes with non-arteritic anterior ischaemic optic neuropathy (NAION) and compares it with the vascularity of healthy fellow eyes and age-matched subjects. The peripapillary choroidal vascularity index (CVI), a new tool of measurement, was calculated using horizontal swept-source optical coherence tomography scans. CVI was calculated using a previously validated automated algorithm. CVI in NAION and fellow eyes of NAION patients were compared with age-matched eyes of healthy individuals using Kruskal–Wallis test. A total of 20 eyes of 20 patients with acute unilateral NAION with healthy fellow eyes (20 eyes) and 40 eyes of 40 healthy patients were included in the study. The average age of patients with NAION was 56 ± 8 and 55 ± 7 years in age-matched healthy controls. NAION eyes had a significantly lower CVI than age-matched controls in both nasal and temporal areas. NAION nasal CVI was 0.47 ± 0.47 compared to 0.62 ± 0.04 in controls ($p < 0.001$). NAION temporal CVI was 0.45 ± 0.48 compared to 0.58 ± 0.04 in controls ($p < 0.001$). Temporal CVI was 0.45 ± 0.48 in NAION eyes and was significantly lower than counterpart healthy fellow eyes 0.48 ± 0.02 ($p = 0.007$). In conclusion, NAION eyes have significantly reduced vascularity in the peripapillary area. CVI is lower in the nasal and temporal of the optic disc compared to healthy individuals. This may suggest those with smaller CVI are more prone to ischaemia from reduced vascularity resulting in NAION.

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Introduction

Non-arteritic anterior ischaemic optic neuropathy (NAION) is the most common cause of acute optic neuropathy over the age of 50. There are approximately 6000 new cases per year and it afflicts between 2.3 and 10.3 people per 100,000 individuals.^{1,2} This condition is characterized by acute, painless vision loss believed to result from infarction of the optic nerve head (ONH) resulting in optic disc oedema. Optic disc oedema may cause a compartmental syndrome from axonal oedema resulting in further retinal cell death.^{3,4}

However, the exact pathophysiology of this condition is still unclear, and the exact level of vascular compromise has not yet been defined. It is thought to result from a vascular insufficiency in the circulation to the optic disc, most likely at the level of the short posterior ciliary arteries.

Peripapillary choroidal vessels help supply blood to the surface nerve fibre layer and prelaminar part of the ONH.⁵ Disruptions in this choroidal supply have been implicated in NAION.^{4–7} Computation of the choroidal thickness (CT) using optical coherence tomography (OCT) has served as a marker of its vitality and used to study a host of ocular diseases such as central serous chorioretinopathy, age-related macular degeneration, glaucoma, and the study of optic neuropathy and optic disc pathologies.^{6–9}

Previous studies have found variable results regarding peripapillary CT and macular CT in NAION.^{10–15} Some report an increased peripapillary CT, while others report a decrease in NAION eyes.^{10–15} Conflicting results also exist in regards to contralateral eyes and healthy individuals. CT is not a true standard for the vascular supply, since it comprises of the stromal and interstitial layer

along with the blood vessels and capillaries. This makes the above results more difficult to interpret.

Recently, new literature and our prior studies reported that choroidal vascularity index (CVI), is a more robust tool to study the choroid vasculature.^{16–18} Using image binarization techniques the choroidal area can be divided into stromal and luminal areas. CVI is ratio of the luminal area to the total choroid area, providing a more accurate representation of the vascular supply. In order to further elucidate the true choroidal vasculature in NAION, we aim to study the peripapillary CVI in NAION eyes, contralateral normal eyes and compare it to the CVI in the healthy population.

Methods

Study population

This was a cross-sectional, non-interventional study of healthy volunteers and those with NAION from January 2016 to July 2016 at L.V. Prasad Eye Institute, Hyderabad. The study was approved by the Institutional Review Board of the Institute, and all the methods adhered to the tenets of the Declaration of Helsinki.

Patients with a clinical diagnosis of acute NAION, based on history of sudden, unilateral, painless vision loss, presence of disc oedema, a 'disc at risk' in the contralateral eye and presence of associated vascular risk factors were included in the study group. Patients with any other associated retinal/optic disc pathology, bilateral disc oedema were excluded; those patients where other differential diagnoses such as optic neuritis was considered were also excluded from the study. Both males and females were included as healthy volunteers. Inclusion criteria, for healthy volunteers, were best-corrected visual acuity (BCVA) between 20/20 and 20/25, spherical equivalent (SE) between -3 dioptres (D) and $+1.5$ D, no systemic or ocular diseases (other than visually insignificant cataracts). Eyes with poor quality images, scans with invisible choroidal borders throughout, and eyes with any history of any retinal diseases in the study or fellow eye or patients with any systemic diseases were not included. Eyes with SE beyond -3 and $+1.5$ D were excluded. All patients underwent a comprehensive ophthalmology exam including demographic details, BCVA

assessment using Snellen's chart, intraocular pressure assessment using applanation tonometry and fundus examination by a trained neuro-ophthalmologist.

Imaging of the choroid was obtained via swept-source OCT (SS-OCT) scan using DRI-OCT "Triton" (Topcon Corporation, Tokyo, Japan). Triton® is SS-OCT which uses a tuneable laser as a light source to provide a 1050-nm centred wavelength. The device reaches a scanning speed of 100,000 A-scans per second, yielding 8 and 20 μ m axial and transverse resolution in tissue, respectively. Horizontal and vertical cross-sectional high definition, 9 mm long, scans were obtained at the fovea and centre of the optic disc.

Image analysis

As reported previously by our group, choroidal stroma and vessel area analysis involved (1) automated binarization of an OCT B-scan and (2) automated segmentation of the binarized choroid layer using a previously validated algorithm. The automated binarization involved (1) preprocessing, (2) exponential and nonlinear enhancement, and (3) thresholding. OCT images were denoised using the block matching and 3D filtering technique. Thresholding and choroidal segmentation was obtained using a recent method proposed and implemented by previous literature, which reported reproducibility and reliability, for multiple studies.^{17,19,20}

CVI was computed as the vascular area/total area. Measurements over the optic disc were computed over the nasal and temporal quadrants in three groups; eyes with NAION, normal fellow eyes of patients with NAION and healthy control eyes. Age-matching between the groups was done and results were analysed using Kruskal–Wallis test to determine the significance between the populations. A p value of less than 0.05 was considered to be statistically significant.

Results

A total of 20 eyes of 20 patients with unilateral, acute NAION, 20 fellow eyes of these patients and 40 healthy eyes from 40 healthy patients were included in the study. The average age of patients

was 56 ± 8 years in NAION patients and 55 ± 7 years in age-matched healthy controls. Mean duration of symptoms was 14.6 days (range 3–40 days). Average BCVA in NAION eyes was 0.7 ± 0.41 logMAR and BCVA of the fellow eyes was 0.09 ± 0.17 logMAR. CVI was computed in both nasal and temporal quadrants for all eyes. Nasal CVI in eyes with NAION was 0.47 ± 0.47 , temporal CVI was 0.45 ± 0.48 and both were significantly lower compared to 0.62 ± 0.04 and 0.58 ± 0.04 in nasal, and temporal CVI of age-matched healthy subjects respectively

($p < 0.001$). Also noted, temporal CVI was 0.45 ± 0.48 in NAION eyes and was significantly lower than counterpart healthy fellow eyes 0.48 ± 0.02 ($p = 0.007$). Results are summarized in Figure 1 and Figure 2.

Discussion

Understanding peripapillary choroidal vasculature is important in the study of NAION. Through CVI, a more robust tool than CT, for measuring choroidal vascularity we have shown choroidal

Figure 1. Top row panel: OCT scan, Nasal segmentation of OCT scan, binarization and CVI of nasal segmentation, temporal segmentation of OCT scan, binarization and CVI of temporal segmentation all in NAION eye. Middle row panel: OCT scan, nasal segmentation of OCT scan, binarization and CVI of nasal segmentation, temporal segmentation of OCT scan, binarization and CVI of temporal segmentation all in NAION fellow eye. Bottom row panel: OCT scan, nasal segmentation of OCT scan, binarization and CVI of nasal segmentation, temporal segmentation of OCT scan, binarization and CVI of temporal segmentation all in healthy eyes.

Figure 2. Choroidal vascularity index in all eyes.

vascularity is significantly reduced in NAION eyes compared to age-matched healthy controls.

This is in alignment with previous studies that have shown a decrease in CT.^{12,13,15} García-Basterra et al. demonstrated thin peripapillary CT in NAION eyes and fellow eyes compared to their age-matched controls.¹³ These findings are also seen in our study. García-Basterra suggests that thin CT maybe a predisposing factor in developing NAION.¹³ Our results also confirm prior fluorescein angiography, and indocyanine green angiography results that show filling defects in peripapillary circulation in NAION eyes.^{21,22} Augstburger et al. recently demonstrated thinning of the retinal peripapillary choroid in NAION eyes using OCT angiography (OCTA).¹⁵

Other studies have demonstrated peripapillary CT to be thicker in NAION eyes.^{10,11,14,23} Nagia et al. noted that the role of significantly thicker choroid in NAION eyes was unclear and did not have an established cause.²⁴ They hypothesized that patients with thicker peripapillary were disposed to NAION possible secondary to compartment syndrome in the laminar, prelaminar, and retrolaminar optic nerve with resultant ischaemia.²³ This resulting ischaemia makes capillaries prone to swelling and causes local oedema. Jiang notes that this oedema maybe a contributing component to their findings that showed increased peripapillary CT.¹⁴

The choroid comprises of the stromal and interstitial layer along with the blood vessels and capillaries, and CVI is the ratio of the specific vascular area to the total area. None of the above studies isolate the vascular layer from the stromal layer. Hence, in our study, we show that the vascularity independent of the stromal and interstitial layers is thinner in NAION eyes. We show lesser CVI in NAION eyes and the fellow eyes compared to age-matched healthy controls. This may imply those eyes with lesser CVI maybe predisposed to ischaemia and hence to NAION, like García-Basterra suggested that thin CT maybe a predisposing factor in developing NAION.¹³ Transient hypotension in NAION maybe pronounced in those eyes with lesser CVI leading to NAION. Interestingly, there was also significantly lesser CVI in the temporal area of optic disc, which could be due to the watershed supply of vasculature in the temporal quadrant.²⁵ Vasculature affected in NAION has not been well defined, and the pathophysiology is still

being studied. Hence, further studies need to be conducted to determine whether inherently lesser CVI predisposes eyes to NAION, or whether local inflammatory processes in NAION results in vascular compromise leading to lesser CVI.

Some other limitations to study must be noted. The study was not controlled for variables that are subject to diurnal variation. However, the study was normalized since all images were obtained from 9 am to 1 pm. All eyes with NAION were studied in the acute phase of the disease, the retinal nerve fibre oedema maybe a confounding factor in these cases. Further, another limitation was inability to correlate with visual fields. We had data on 12 patients: 10 inferior altitudinal field defects and two superior altitudinal defects) and 8 had generalized field loss. However, there was not enough of a large sample size to draw any conclusions, and will be the next area of interest in further studies. Lastly, while all four quadrants would have been ideal to analyse, imaging precluded from getting vertical scans. We used the temporal and nasal vasculature as a representative of the peripapillary vasculature, and need to analyse all quadrants in future studies.

Overall, using CVI, a novel robust marker of choroidal vascularity, we have shown eyes with NAION have significantly reduced vascularity in the peripapillary area. With present literature and our current understanding of disease this may suggest those with lesser CVI are predisposed to less perfusion resulting in ischaemia and leading to NAION. Changes in choroidal vascularity with visual outcome in NAION can be further explored.

Declaration of interest

There are no competing and/or conflicting interests or acknowledgements.

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