THE LITERATURE

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Quantitative Optical Coherence Tomography Angiography of Radial Peripapillary Capillaries in Glaucoma, Glaucoma Suspect, and Normal Eyes

Mammo Z, Heisler M, Balaratnasingam C, et al[1]

ABSTRACT SUMMARY

This cross-sectional, single-institution study used a clinical prototype of speckle variance optical coherence tomography angiography (OCT-A) to quantify and compare the radial peripapillary capillary (RPC) network in glaucomatous eyes, those with suspected glaucoma, and healthy eyes. RPC density was correlated with nerve fiber layer (NFL) thickness and visual field indices (VFI). OCT-A images of 10 eyes from five individuals with unilateral glaucoma, six eyes from three glaucoma suspects, and 16 eyes from nine healthy subjects were included in the study. The investigators used manual tracing techniques to quantify RPC density in OCT-A images. The baseline characteristics of the groups were similar, except for a trend toward increased age among glaucoma subjects that was not statistically significant.

The researchers found that mean RPC density in glaucomatous eyes was significantly lower (0.09 ±0.05) at sites of NFL thinning and disc rim change compared with corresponding regions in the healthy fellow eyes of these patients (0.30 ±0.06, $P < .001$). Mean RPC density in glaucomatous eyes was also significantly lower than in healthy eyes and those of glaucoma suspects (both $P < .001$). RPC density was positively correlated with NFL thickness (slope = 0.001, $P < .001$) and VFI (slope = 0.006, $P < .001$).

DISCUSSION

How might the results of this study influence the monitoring of patients for glaucomatous progression?

This study shows that OCT-A enables the evaluation of a new objective marker of glaucomatous optic neuropathy, namely RPC density. Decreased RPC density appears to correlate well with other structural markers such as disc rim changes and NFL thinning as well as functional deficits based on VFI. The opportunity to monitor an additional structural marker could help eye care providers in assessing glaucomatous progression, but how this information will shape clinical practice remains unknown. Currently, retinal NFL estimates obtained by spectral-domain OCT (SD-OCT) frequently include blood vessels in their measurements, which limits how low the reported NFL can drop.[2] Differentiating between vascular rather than NFL thinning may allow more sensitive monitoring of glaucomatous damage. Manual tracing will have to be replaced with automated analysis, however, before this technology can be efficiently incorporated into routine use.

Do the results of this study expand clinicians' and researchers' understanding of glaucoma's pathophysiology?

OCT-A presents an opportunity to visualize the effects of glaucoma on the RPC. Historically, such visualization has been limited by poor resolution of this fine vasculature by fluorescein angiograms. Previous glaucoma studies using OCT-A have noted decreased "optic disc perfusion," referring to the entire peripapillary circulation, including superficial and deep capillaries as well as large-caliber intraretinal vessels.[3] The study by Mammo and colleagues clarifies that the RPC is preferentially affected by glaucoma, while deeper capillary plexus vessels are preserved. These findings reflect only a point in time, however, and further work must be done to demonstrate the relationship to glaucomatous progression or to establish any causal relationship.

AT A GLANCE

- A cross-sectional, single-institution study using a clinical prototype showed that speckle variance optical coherence tomography angiography enables the evaluation of a new objective marker of glaucomatous optic neuropathy—the radial peripapillary capillary network. The opportunity to monitor an additional structural marker could help eye care providers in assessing glaucomatous progression, but how this information will shape clinical practice remains unknown.
- A prospective, controlled, longitudinal single-center study found that retinal nerve fiber layer thickness measurements obtained with optical coherence tomography and the glaucoma probability score from confocal scanning laser ophthalmoscopy were highly predictive of future conversion on standard automated perimetry.

Can Glaucomatous Visual Field Progression Be Predicted by Structural and Functional Measures?

Schrems WA, Schrems-Hoesl LM, Mardin CY[4]

ABSTRACT SUMMARY

This prospective, controlled, longitudinal single-center study investigated whether retinal nerve fiber layer thickness (RNFLT) measurements obtained by OCT, morphometric parameters of confocal scanning laser ophthalmoscopy (CSLO), and frequency-doubling technique (FDT) perimetry could predict conversion of standard automated perimetry (SAP). The investigators evaluated the conversion of SAP (ie, two consecutive and repeatable abnormal visual field tests) of healthy controls (107 eyes), ocular hypertensives (164 eyes), and patients with early preperimetric glaucoma (169 eyes) over a median follow-up period of 6.9 years. All eyes at baseline had normal SAP results and underwent testing with OCT (Spectralis; Heidelberg Engineering), CSLO (Heidelberg Retina Tomograph; Heidelberg Engineering), optic disc photography, and FDT perimetry.

During the follow-up period, 48 eyes (10.9%) demonstrated visual field conversion. Of these, 40 were in the preperimetric glaucoma group ($P < .001$), and eight were in the ocular hypertension group. At baseline, there was a statistically significant difference in the vertical cup-to-disc ratio (0.5 ±0.23 vs 0.67 ±0.15; $P < .001$), the morphologic glaucoma stage of Jonas (a structured glaucoma staging system; 0.35 ±0.55 vs 1.13 ±0.73; $P < .001$), and pattern standard deviation (1.65 ±0.57 vs 2.27 ±0.76; $P < .001$) between nonconverters and converters. The investigators found that both the measurement of RNFLT by OCT and the glaucoma probability score by CSLO were highly predictive of future visual field conversion while also offering independent predictive information.

DISCUSSION

Which testing methods had the highest positive predictive value of glaucomatous progression?

The highest positive predictive value and positive likelihood ratio was seen with RNFLT nasal outside normal limits at 66.7% and 16.3, respectively. This was followed by Moorfields regression analysis for temporal outside normal limits of 42.1% and 5.9 and an FDT score above five of 33.0% and 3.9. In addition, FDT findings were found at a median of 2.4 years before SAP conversion, with a maximum time of 5.6 years.

A nasal RNFLT outside the normal limits was present in just three of 440 eyes, and it was only observed in eyes that also demonstrated abnormal average RNFLT in at least one other sector. In contrast, temporal-inferior results outside normal limits for RNFLT had a much lower positive likelihood ratio of 7.3, but this was present in 7.8% of the eyes in the study. Furthermore, RNFLT temporal-inferior results outside normal limits demonstrated the highest hazard ratio, with 1.2 (95% confidence interval, 1.1-1.4) per 10-µm loss for OCT. The investigators suggested that temporal-inferior results outside normal limits for RNFLT may play a more important role than the other sectors for clinicians assessing the risk profile of a patient with early glaucoma.

How might the results of this study influence the monitoring of patients for glaucomatous progression?

The investigators found that OCT, CSLO, and FDT provide useful prognostic information for conversion of SAP. In the study, converters had a more advanced stage of glaucoma on the basis of photographic assessment, lower central corneal thickness, and higher pattern standard deviation than nonconverters. Additionally, the researchers improved results by combining structural and functional testing, and they noted that their results were consistent with those of other studies.[5] The investigators found that a combined SD-OCT/FDT score led to an additional yield of +17.8% for predictive sensitivity when compared to SD-OCT score alone (75.6% vs 56.8%) at a specificity of 80%.

A limitation of the study was that it did not exclude patients with glaucoma in the contralateral eye. The researchers concluded that clinicians using optic nerve imaging and FDT perimetry will be able to identify high-risk groups and treat those patients more aggressively for glaucoma before conversion takes place. In contrast, patients with a lower risk of conversion may be observed less frequently. ■

1. Mammo Z, Heisler M, Balaratnasingam C, et al. Quantitative optical coherence tomography angiography of radial peripapillary capillaries in glaucoma, glaucoma suspect, and normal eyes. *Am J Ophthalmol*. 2016;170:41–49.
2. Groth SL, Harrison A, Grajewski AL, Lee MS. Retinal nerve fiber layer thickness using spectral-domain optical coherence tomography in patients with no light perception secondary to optic atrophy. *J Neuroophthalmol*. 2013;33(1):37-39.
3. Jia Y, Wei E, Wang X, et al. Optical coherence tomography angiography of optic disc perfusion in glaucoma. *Ophthalmology*. 2014;121(7):1322-1332.
4. Schrems WA, Schrems-Hoesl LM, Mardin CY, et al. Can glaucomatous visual field progression be predicted by structural and functional measures? *J Glaucoma*. 2017;26(4):373-382.
5. Horn FK, Mardin CY, Bendschneider D, et al. Frequency doubling technique perimetry and spectral domain optical coherence tomography in patients with early glaucoma. *Eye (Lond)*. 2011;25(1):17-29.

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