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Retinal Nerve Fiber Layer Thickness Measurements: Uveitis, A Major Confounding Factor

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Objective: To evaluate optical coherence tomography (OCT) retinal nerve fiber layer (RNFL) measurements in patients with active and quiescent uveitis with and without glaucoma and compare results to the published age-adjusted normative data.

Design: Comparative, retrospective pilot study.

Participants: Consecutive patients with uveitis who underwent OCT RNFL measurements between December 2011 and October 2012 were identified: 76 uveitic eyes without glaucoma and 135 uveitic eyes with glaucoma.

Intervention: We conducted OCT of the RNFL.

Main Outcome Measures: Global and sectoral RNFL thickness measurements.

Results: In 19 nonglaucomatous, uveitic eyes with active inflammation, mean global and all sectoral RNFL measurements were greater than the normative 95th percentile. The mean global RNFL OCT measurement was 140.5 microns in such eyes compared with 107.8 microns in the 57 nonglaucomatous, quiescent, uveitic eyes ($P = 0.008$). These measurements were significantly higher than the average of 95.3 microns reported in normal eyes ($P < 0.001$). All mean sectoral measurements except superonasal were significantly higher in active compared with quiescent uveitic eyes ($P = 0.002-0.05$). In glaucomatous eyes with both quiescent and active uveitis, the mean global RNFL measurements on OCT were 92.3 and 95.7 microns, respectively. These measurements were significantly higher than the mean global RNFL thickness (65.3 microns) reported in eyes with the same stage (moderate) of nonuveitic glaucoma.

Conclusions: Uveitis is a major confounding factor in assessing the thickness of the RNFL. A significant thickening of the RNFL was found in patients with active uveitis and a greater RNFL thickness than anticipated in patients with uveitic glaucoma. These data raise concerns about the comparative value of RNFL scans as a method to detect and monitor glaucoma in uveitic eyes. *Ophthalmology 2015;122:511-517 © 2015 by the American Academy of Ophthalmology.*

Glaucoma is a multifactorial optic neuropathy defined by characteristic structural changes of the optic nerve with associated visual field loss.[1] Methods to directly detect optic nerve head damage include clinical observation, serial photography, and, more recently, advanced imaging of the retinal nerve fiber layer (RNFL).[2] Each technique is complementary, but all rely on distinctive, progressive change in the appearance and structure of the optic nerve.

Patients with uveitis are at an increased risk of developing glaucoma,[3] making accurate assessment of the optic nerve head paramount in this population. However, a recent publication from the Multicenter Uveitis Steroid Treatment trial found a relatively high rate of disagreement in intergrader assessment of cup-to-disc ratio based on stereo disc photographs evaluated at the study reading center. The investigators suggest that clinical examinations of optic nerve morphology are particularly limited in uveitic patients because of patient discomfort, media opacity, and time constraints.[4]

Optical coherence tomography (OCT) is used to measure the peripapillary RNFL thickness, which correlates with glaucoma severity in both adult and pediatric populations.[2] The purpose of this pilot study was to evaluate spectral domain (SD) OCT RNFL thickness measurements in patients with uveitis and to compare results with the published, age-adjusted, normative data. The RNFL measurements in eyes with active and quiescent uveitis, as well as in those with and without glaucoma, were also evaluated.

Methods

This study was approved by the Duke University Institutional Review Board and adhered to the tents of the Declaration of Helsinki. A retrospective review of consecutive patients with uveitis evaluated at the Duke Eye Center between December 1, 2011, and October 1, 2012, who also underwent SD OCT RNFL thickness measurements (Spectralis software V.5.1.3.0; Heidelberg Engineering, Dossenheim, Germany), was conducted. These patients were identified by analysis of billing codes in an electronic

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Table 1. Baseline Data and Demographics

Characteristics	Uveitic Glaucoma (n = 135 eyes)	Uveitis, No Glaucoma (n = 76 eyes)
Age (yrs), mean (range)	50.5 (10.8–77.2)	46.0 (11.7–90.7)
Sex n (%)		
Male	31 (23)	12 (16)
Female	104 (77)	64 (84)
Glaucoma surgery,* n (%)	47 (35)	0
Glaucoma meds, mean (range)	0.89 (0–4)	0
BCVA (logMAR), mean (SD)	0.363 (0.569)	0.600 (0.809)
IOP (mmHg), mean (SD)	14.3 (5.1)	15.2 (6.5)
HVF MD mean (SD)	−6.4 (5.0)	0
Active uveitis, n (%)	21 (16)	19 (25)
Stable uveitis, n (%)	114 (84)	57 (75)
Uveitic location, n (%)		
AU	29 (21)	2 (3)
AU+IU	13 (10)	4 (5)
IU	6 (4)	6 (8)
Posterior	10 (7)	13 (17)
Panuveitis	75 (56)	50 (66)
Neuroretinitis	1 (1)	0 (0)
Scleritis	1 (1)	1 (1)
Uveitic etiology, n (%)		
Idiopathic	73 (54)	38 (50)
HLAB27	7 (5)	3 (4)
Sarcoidosis	22 (16)	12 (16)
Multiple sclerosis	4 (3)	2 (3)
ARN	5 (4)	0 (0)
Birdshot	6 (4)	4 (5)
Bartonella	2 (1)	0 (0)
Behçet's	4 (3)	2 (3)
White dot syndrome	2 (1)	8 (11)
VKH	4 (3)	0 (0)
JIA	6	1
Syphilis	0	2
AIR	0	2
Tuberculosis	0	0
MCP	0	2

AIR = autoimmune retinopathy; ARN = acute retinal necrosis; AU = anterior uveitis; BCVA = best corrected visual acuity; HVF = Humphrey visual field; IOP = intraocular pressure (in mmHg); IU = intermediate uveitis; JIA = juvenile idiopathic arthritis; logMAR = logarithm of the minimum angle of resolution; MCP = multifocal choroiditis and panuveitis; MD = mean deviation; SD = standard deviation; VKH = Vogt Koyanagi Harada disease.
*Prior incisional or cyclodestructive glaucoma surgery.

database. We recorded OCT data, including scan quality, and global and sector mean thickness. The medical records of eligible patients were also reviewed and data were collected from the visit that coincided with OCT scan acquisition. Data collected included patient age, gender, uveitis location, uveitis etiology, ocular comorbidities, prior surgeries, current uveitis and glaucoma therapy, Humphrey visual field (HVF) mean deviation (MD) if performed within 6 months of the OCT, logarithm of the minimum angle of resolution visual acuity, intraocular pressure (IOP), and uveitic activity. Eyes were classified as glaucomatous if their IOP was >25 mmHg (Goldmann applanation or Tonopen) along with cup-to-disc asymmetry of >0.2, or with typical glaucomatous disc damage, or associated with a typical glaucomatous visual field loss. Eyes were classified as having "active" uveitis if any of the following were present: documented intraocular inflammation, escalation in immunomodulatory therapy, or a chart comment on increased disease severity by the uveitis specialist (G.J.J.). Quiescent uveitic eyes were defined as those without any documented intraocular inflammation at the current visit. Patients were excluded if OCT scans demonstrated a quality score of <20, if they had eye surgery done in the previous 6 months, or if clinical charts were incomplete. Patients were excluded from HVF analysis if they had documented media opacity such as >2+ nuclear or cortical cataract or dense vitreous haze.

Results

A total of 211 eyes of 110 uveitic patients underwent SD OCT RNFL scans during the study period (Table 1). Of these, 135 eyes of 72 patients had uveitis-associated glaucoma and 76 eyes of 38 uveitic patients had no glaucoma. Twenty-one eyes (16%) and 19 eyes (25%) had active uveitis in the uveitic glaucoma and uveitis without glaucoma groups, respectively.

Uveitic Eyes without Glaucoma

In nonglaucomatous uveitic eyes with quiescent uveitis, the mean global RNFL measurement on OCT was 107.8 microns compared