ABSTRACT TITLE **TITLE:** Ophthalmologic correlates of disease severity in Wolfram Syndrome
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ABSTRACT BODY:
Purpose: Wolfram Syndrome (WFS) is a rare, autosomal recessive syndrome that consists of diabetes insipidus, diabetes mellitus, optic nerve atrophy, and sensorineural deafness. Although clinical ophthalmologic manifestations have been reported in advanced WFS, it is unknown when these symptoms emerge and whether retinal imaging provides insight into the pattern of degeneration. To address this issue, we assessed several patients with the disease and determined whether ophthalmic parameters correlate with overall disease severity.

Methods: Eighteen WFS patients, aged 5 to 25, were recruited through the Washington University Wolfram Syndrome International Registry website for comprehensive ophthalmic assessment (visual acuity, assessment of nystagmus, color vision testing, pupillary reflexes, slit-lamp and dilated fundus exams, visual field testing, and retinal tomography imaging) at the Washington University Wolfram Syndrome Research Clinic. Patients were also assessed with the Wolfram Syndrome Unified Rating Scale (WURS), which rates severity of overall WFS symptoms. Correlations were performed to determine how ophthalmic parameters related to overall disease severity.

Results: Visual acuity (VA) in the patients ranged from 20/20 to hand motion with an average VA of 20/60. Clinically apparent optic atrophy was present in 17/18 patients, color vision was abnormal in 17/18 patients, pupils were abnormal in 10/18 patients, cataracts were present in 4/18 patients, and nystagmus was present in 4/18 patients. All of the patients who were able to participate in visual field testing (10/18) had abnormal visual fields. All of the patients, including the patient with no clinically apparent optic atrophy, had thin retinal nerve fiber layers (RNFL) on optical coherence tomography (OCT) imaging of the retina. The average RNFL thickness was nearly 5 standard deviations below normal for a pediatric population. Figures 1 and 2 show the correlation of ophthalmic parameters with disease severity.

Conclusions: Wolfram Syndrome is a rare monogenic disorder with multiple manifestations. Our study provides a detailed ophthalmic phenotype in patients with WFS identifying dramatic abnormalities in color vision and retinal thickness, even at young ages. In addition, we identified measures that may be useful in tracking disease progression. These parameters will be followed longitudinally to determine if they are sensitive to the progression of disease.

Figure 1: Disease Severity vs Nerve Fiber Layer Thickness

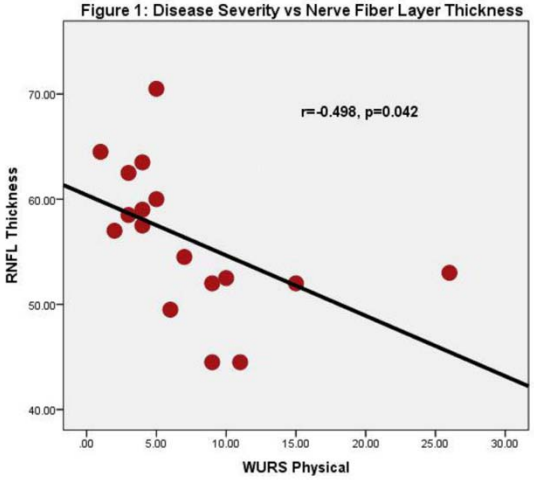
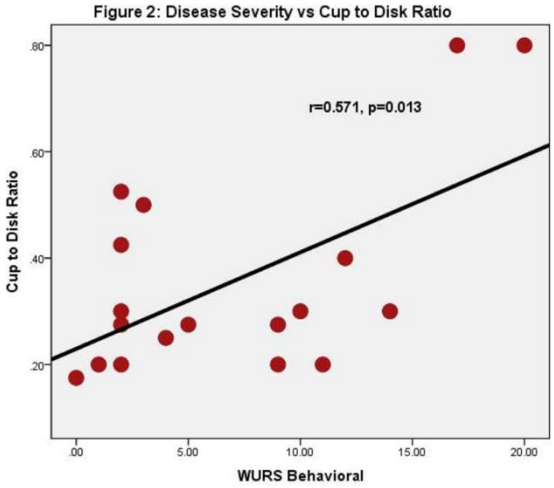


Figure 2: Disease Severity vs Cup to Disk Ratio



Commercial Relationship(s) Disclosure: Smith Ann Chisholm: Commercial Relationship: Code N (No Commercial Relationship)James Hoekel: Commercial Relationship: Code N (No Commercial Relationship)Tamara Hershey: Commercial Relationship: Code N (No Commercial Relationship)Lawrence Tychsen: Commercial Relationship: Code N (No Commercial Relationship)**Grant Support:** Yes**Support Detail:** Jack and J.T. Snow Fund at Washington University, American Diabetes Association, George Decker and Julio V. Santiago Pediatric Diabetes Research Fund, and National Institutes of Health (HD070855; DK016746-39, NCRR 1S10RR022984-01A1, and UL1 RR024992)**Clinical Trial Registration:** No**Other Registry Site:Registration Number:**