Characterization of Wedge-Shaped Defects in Prelaminar Tissue in Eyes With Primary Open Angle Glaucoma

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Characterization of Wedge-Shaped Defects in Prelaminar Tissue in Eyes with Primary Open Angle Glaucoma

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Abstract (375 Words)

Purpose: To identify the functional and clinical significance of prelaminar wedge defects (PLWDs) detected by swept source optical coherence tomography (SS-OCT) in patients with primary open angle glaucoma (POAG).

Methods: This is a prospective, cross-sectional study of patients with POAG and PLWDs, patients with POAG and no PLWDs, and age-matched healthy control subjects. Imaging was performed with SS-OCT (Topcon DRI Swept Source OCT) and spectral-domain OCT. POAG patients with severe glaucoma indicated by Humphrey Visual Field Mean Deviation <-12 dB or history of penetrating glaucoma surgery, and eyes with significant non-glaucomatous optic nerve abnormalities were excluded. PLWDs were defined as lesions where the curve and smooth delineation of the cup contour is lost and a triangular (wedge-shaped) defect can be outlined in the prelaminar layer (Figure 1) and were identified on radial and 5-line cross scans by two observers masked to diagnosis. Two-sided t-test, analysis of variance with Bonferroni correction, and multivariate logistic regression analysis adjusting for systemic and ocular characteristics were performed.

Results: 16 POAG patients with PLWDs, 24 POAG patients without PLWDs, and 23 control patients were enrolled in the study. PLWDs were found in 40.0% of POAG patients vs. 8.7% of control subjects (p=0.018). Of the POAG patients with PLWDs, 9 (56.3%) had subsequent imaging, all of which showed persistent PLWDs. POAG patients with and without PLWDs had similar HVF MD (-5.8 ± 5.0 dB vs. -4.8 ± 4.9 dB, p= 0.55). Paracentral loss on HVF was present in 56.3% of POAG with PLWDs and 33.3% of POAG without PLWDs (p= 0.20). POAG patients with PLWDs had more frequent history of disc hemorrhage (DH) than POAG patients without PLWDs (p=0.04). In the multivariate analysis, POAG patients with PLWD were younger in age (p=0.03) and had increased odds of having a history of DH (odds ratio= 14.1, p=0.02) compared to POAG patients without PLWD after adjusting for gender (p=0.37), VF MD (p=0.20) and maximum IOP (p=0.14).

Conclusion: Wedge-shaped defects in the prelaminar tissue are found more frequently in eyes with POAG than control subjects. These defects are associated with younger age and a history of DH. These structural changes may represent a distinct pattern of damage in glaucoma and may potentially represent an optic nerve phenotype associated with a distinct POAG subset.
Section 1: Introduction

Glaucoma is the second leading cause of blindness in the world and is a heterogeneous group of diseases that result in the gradual and progressive loss of retinal ganglion cells and axons, and classically manifests as optic nerve head excavation on fundoscopic examination. These structural features are secondary to changes in both the prelaminar tissue and the lamina cribrosa connective tissue. Various studies have described the quantitative changes, particularly alterations in thickness, that occur in the peripapillary retinal nerve fiber layer (RNFL) and prelaminar tissue of patients with glaucoma. The prelaminar component, composed of both neuronal and connective tissue, is therefore a relevant and important structure in the pathophysiology of glaucoma.

Thorough examination of the prelaminar tissue has been restricted by limited visualization with conventional imaging. The advent of the next generation of ophthalmologic imaging devices has allowed for high resolution imaging and improved characterization of the optic nerve head (ONH). Compared to conventional spectral-domain imaging, swept-source OCT (SS-OCT) has longer central wavelengths of 1050 nm and higher scanning speeds of 100,000 A-scans per second\(^1\). These characteristics allow for deeper tissue penetration, less shadowing artifacts from overlying blood vessels in the ONH, and denser and larger scanning patterns for a given acquisition time. More importantly, with a sweeping laser source of varying wavelengths, the device can simultaneously image both superficial and deep tissue in high resolution\(^1\). In a previous study, SS-OCT facilitated the identification of morphologic changes in the prelaminar tissue (holes and wedge-shaped defects) and lamina cribrosa defects; prelaminar wedge defects were found to be more common in eyes with primary open angle glaucoma (POAG) compared to eyes with chronic angle closure glaucoma or control eyes\(^2\).

However, changes in the prelaminar tissue of the optic nerve head in POAG patients have not been fully characterized. Knowledge of the clinical significance of PLWDs could enhance our understanding of distinct glaucoma phenotypes and potential differences in disease pathogenesis of. In this study, we aim to further elucidate the distinct demographic, ophthalmic and functional characteristics that may be correlated with prelaminar wedge defects in POAG, in an attempt to delineate the clinical relevance of this observed structural feature.

Section 2: Student Role

A novel imaging device, SS-OCT, was utilized to image the eyes of POAG patients and healthy control patients. Radial and 5-line cross SS-OCT images were then reviewed under the supervision of a faculty
member from Harvard Medical School (LQS) for structural alterations of the prelaminar and laminar tissue, with a primary focus on the presence and location of prelaminar wedge defects and laminar defects. The corresponding patients’ Humphrey Visual Field examinations within the closest date to SS-OCT imaging were interpreted, particularly for the presence of paracentral loss, according to previously published guidelines. Images of the optic disc were assessed for the presence and location of DHs. Data collection was performed for recruited patients, including acquiring demographic information, ocular history information, and quantitative measurements of the optic nerve head and retinal nerve fiber layer. In collaboration with computational biologists, statistical data analyses including t-test, ANOVA, and multivariate regression model were conducted. Interpretation of the results were presented in a poster format at the American Glaucoma Society Annual Meeting. Abstract and manuscript writing is currently being completed.

Section 3: Methods

This was a prospective, cross-sectional study. Approved by the Institutional Review Board of Massachusetts Eye and Ear (MEE). Informed written consent was given by all participants. The study is in accordance with HIPAA regulations.

Description of the Study Population

Adult subjects with ages between 40 to 90 of Caucasian and African American ethnicities were recruited at the MEE for a prospective observational study involving SS-OCT and SD-OCT imaging of the optic nerve head. All subjects had best corrected visual acuity of 20/50 or better in both eyes. Most of them were part of prior published studies by our group comparing SS-OCT and EDI-OCT in measuring quantitative ONH parameters, characterizing chronic angle closure glaucoma, and assessing quantitative ONH parameters associated with paracentral loss in POAG.

Primary Open Angle Glaucoma Definition

Primary open angle glaucoma patients were recruited from the Glaucoma Service of the MEE. Patients had a clinical diagnosis of POAG by a glaucoma specialist consisting of open angles on gonioscopy, glaucomatous optic disc damage (confirmed by peripapillary retinal nerve fiber layer thickness profile by SD-OCT) with corresponding reproducible functional loss on reliable Humphrey visual field (HVF) testing, defined as fixation loss <33%, false positive <20%, and false negative <20%. Exclusion criteria are as follows: HVF mean deviation (MD) worse than -12dB in either eye, history of previous penetrating glaucoma surgeries, such as trabeculectomies and glaucoma drainage devices, and significant non-
glaucomatous optic nerve and retina pathology associated with functional loss. In addition, eyes with optic disc torsion of more than 15 degrees, tilt ratio >1.3 and significant peripapillary atrophy were also excluded from the study.

Control Definition
Control subjects were recruited from the Comprehensive Eye Service of the MEE. Controls were age matched to POAG patients by decade. Patients had maximum IOP of 21 mmHg or lower, and no evidence of glaucomatous optic disc damage. Patients with a family history of glaucoma and significant retinal disease(s) were excluded.

Image Acquisition
Swept-source OCT (Deep Range Imaging (DRI) OCT-1, Topcon, Tokyo, Japan) was utilized to image both eyes of each subject. Twelve high resolution radial scans and ten 5-line cross scans, with an average of 32 frames per image, were used to evaluate for prelaminar tissue and laminar tissue defects. The retinal nerve fiber layer thickness was quantified using spectral-domain OCT (Spectralis, Heidelberg Engineering GmbH, Heidelberg, Germany).

Qualitative Image Analysis
The prelaminar tissue and lamina cribrosa imaged on radial and 5-line cross scans from SS-OCT were reviewed by two observers (CAC, LQS) masked to patient diagnosis. The prelaminar tissue was evaluated for wedge defects defined as a lesion where the curved and smooth delineation of the cup contour is lost and a triangular (wedge-shaped) defect can be outlined in the prelaminar layer, which may or may not reach the anterior surface of the LC (Figure 1). The images adjacent to the prelaminar wedge defect were closely examined for the potential of artifact, most commonly due to the presence of vasculature. Individuals with questionable prelaminar wedge defects were excluded. Images of patients with subsequent SS-OCT studies were evaluated for new PLWDs and persistence of previously identified PLWDs. The lamina cribrosa was evaluated for defects defined as discontinuities of the anterior LC surface, which may or may not extend to the posterior LC surface. All available disc photos were evaluated for the presence and location (superior vs. inferior) of hemorrhages.
Quantitative Image Analysis

Measurements of the prelaminar tissue and lamina cribrosa were performed independently by two observers masked to diagnosis utilizing customized Image J plugins by previously described protocols. In brief, the minimum rim width at Bruch’s membrane opening (BMO-MRW) was measured as the minimum distance between internal limiting membrane and Bruch’s membrane opening. Horizontal lamina cribrosa depth was measured from the anterior surface of the lamina cribrosa to a reference line connecting the two termination points of Bruch’s membrane on a scan centered on the ONH.

Statistical Analysis

Statistical data analysis was conducted in collaboration with computational biologists. Only one eye per patient was included in the study, if both eyes met the inclusion criteria then the right eye was selected. A two-sided t-test was performed for continuous variables between two groups and analysis of variance (ANOVA) for continuous variables between three groups. Bonferroni correction was applied for multiple comparisons to correct for alpha error. Fischer’s exact test was utilized for categorical variables. A multivariate logistic regression model comparing POAG eyes with and without PLWD, after adjusting for systemic and ocular characteristics, was performed. POAG patients without PLWDs served as a reference. Variables included age, gender, HVF MD, maximum intraocular pressure (IOP), and history of DH. Statistical significance was considered at a p-value <0.05.

Section 4: Results

Sixty-three subjects (40 POAG patients and 23 controls) were included in this study. PLWDs were found in 40.0% of POAG patients (n=16) versus 8.7% of control subjects (n= 2, p=0.018). Of the POAG patients with PLWD, nine (56.3%) had subsequent imaging, all demonstrating persistent PLWDs and no additional new PLWDs. Laminar defects were present in 43.8% of patients with POAG with PLWDs and none of the POAG patients without PLWDs (p=24) and controls (p=23).

Baseline Systemic and Ocular Characteristics

The mean age was 63.0 ± 9.9 years for POAG patients with PLWD, 69.0 ± 7.3 years for POAG patients without PLWD, and 66.3 ± 7.0 years for controls patients and most subjects were Caucasian (93% overall) (Table 1). Gender distribution was 37.5% male in POAG patients with PLWD, 58.3% in patients without PLWD, and 39.1% in control patients (Table 1). Control subjects had worse best corrected visual acuity than POAG patients with PLWDs (0.13 LogMAR ± 0.11 vs. 0.03 LogMAR ± 0.06, p<0.001) and
without PLWDs (0.13 LogMAR ± 0.11 vs. 0.05 LogMAR ± 0.08, p=0.004) (Table 1, Table 3a). The mean IOP on the day of imaging was 13.8 mmHg ± 2.8 for POAG with PLWD, 13.9 mmHg ± 2.7 for POAG without PLWD, and 14.6 mmHg ± 2.3 in controls, and were similar between all groups (Table 1). The known untreated maximum IOP was similar among the two POAG groups, but lower in control subjects (17.0 ± 3.0 mmHg) compared to POAG without PLWD (21.4 ± 5.2 mmHg, p<0.001) (Table, Table 3a). The POAG patients with and without PLWDs had similar HVF MD (-5.8 ± 5.0 dB vs. -4.8 ± 4.9 dB, p=0.55) (Table 1, Table 3a). Paracentral loss, defined as a cluster of 3 or more contiguous points with retinal sensitivity depression of -5dB on HVF pattern deviation plot (Figure 1), was present in 56.3% of POAG patients with PLWDs and 33.3% of POAG patients without PLWDs (p=0.20) (Table 1, Table 3a).

The POAG patients with PLWDs had more frequent history of DH compared to POAG patients without PLWDs (37.5% vs. 8.3%, p=0.04) (Table 1, Table 3a). The location of DHs (superior vs. inferior) and PLWDs were compared and found to be concordant in 83.3% of cases for patients with POAG and PLWD.

On multivariate analysis, POAG patients with PLWDs were associated with younger age and increased odds of having a history of DH compared to POAG patients without PLWDs (odds ratio 0.89 and p=0.029, odds ratio=14.08 and p=0.021, respectively) after adjusting for gender (p=0.38), VF MD (p=0.20) and maximum IOP (p=0.14) (Table 1, Table 3b).

Quantitative Characteristics

POAG patients with and without PLWDs had similar mean global BMO-MRW (198.3 μm ± 38.2 vs. 220.4 μm ± 54.7, p=0.14), minimum BMO-MRW (92.6 ± 46.5 vs. 117.7 ± 48.3, p=0.11), average RNFL (75.8 ± 13.7 vs. 79.0 ± 20.8, p=0.56), and thinnest RNFL (54.5 ± 12.2 vs. 50.5 ± 13.7, p=0.35) (Table 3). Control subjects had larger global BMO-MRW (332.0 ± 66.2) and normalized global BMO-MRW (337.7 ± 67.4) than POAG patients with PLWD and without PLWD (p<0.001 for all) (Tables 1 and 3a), larger minimum BMO-MRW (210.7 ± 49.7) than POAG patients with PLWD and without PLWD (p<0.001 for both), thicker average RNFL (96.4 ± 11.0) than POAG patients with PLWD (p<0.001) and without PLWD (p=0.002), and thicker thinnest RNFL (63.9 ± 12.5) than POAG patients with PLWD (p=0.04) and without PLWD (p=0.004) (Tables 2 and 3a).
Section 5: Discussion, Limitations, Conclusions, and Suggestions for Future Work

In this prospective, cross-sectional study we utilized swept-source optical coherence tomography to identify wedge-shaped defects in the prelaminar tissue of the optic nerve in patients with primary open angle glaucoma. SS-OCT allowed for high-resolution imaging of the prelaminar and laminar tissue of the ONH that was not previously able to be visualized via fundoscopic examination and conventional ONH imaging. PLWDs were frequently detected with SS-OCT (16 out of 40 POAG patients, and 2 out of 23 control patients). In the POAG patients these defects were found to be associated with younger age and history of DH. Furthermore, in POAG patients with PLWD and DH, the PLWD location coincided with the DH in 83.3% of cases (5 out of 6). Of the POAG patients with PLWD, nine out of sixteen (56.3%) had subsequent imaging all demonstrating persistent PLWDs suggesting that this is not a transient change.

Our findings suggest that these structural changes may represent a distinct pattern of damage in glaucoma and may potentially represent an optic nerve phenotype associated with a distinct POAG subset. The defects association with DHs may point towards a vascular etiology. In contrast to the transient nature of DHs, prelaminar wedge defects persist and can possibly serve as an additional important marker in the surveillance of glaucoma patients if clinical observation is supplemented with high resolution imaging. Previous histology and imaging studies have also reported wedge shaped defects on the prelaminar tissue extending into the lamina cribrosa, but the associated patient characteristics and functional significance was not investigated. Further research is needed to more comprehensively understand the ophthalmic characteristics associated with prelaminar wedge defects, and its implications on disease progression and functionality.

Glaucoma is a heterogeneous group of progressive diseases that ultimately result in optic nerve head tissue damage via varying pathophysiologic processes. Distinct structural changes of the optic nerve, and the underlying mechanisms, are not fully characterized and require further investigation as they may help in further identifying different subsets of glaucoma. Changes to the prelaminar tissue of the optic nerve head have been observed in patients with glaucoma and is therefore a relevant structure in the pathophysiology of the disease.

There are several limitations in this research project. First, the sensitivity for detecting prelaminar wedge defects may be limited by the number of cross-sectional images made available by the SS-OCT.
imaging device. This could be addressed by changing the SS-OCT imaging protocol to provide denser cross-sectional cuts. Second, the prelaminar wedge defects were found in two control subjects, suggesting that it is not a specific finding. Also, there were a few ambiguous cases which alludes to the subjective nature of image interpretation. However, we had two observers masked to diagnosis to correct for subjectivity. In addition, the study has a relatively small number of patients and could benefit from confirmation of the results by a larger study. However, despite our small sample size we were able to identify significant differences. Also, the demographics are not universally representative as most patients were Caucasian. Lastly, the cross-sectional nature of this study does not allow for the evaluation of cause and effect relationships.

In conclusion, the advent of SS-OCT imaging technology facilitates the detection of structural damage of the optic nerve and allowed for identification of wedged-shaped defects in the prelaminar tissue of POAG patients. Our results show that the PLWDs are associated with younger age and a history of DH. In addition, the PLWDs were generally found to be in the same location as the DHs. Our findings suggest that these structural changes may represent a distinct pattern of damage in glaucoma and may potentially represent an optic nerve phenotype associated with a distinct POAG subset.

Section 6: Acknowledgements

Imaging technicians and study coordinators at MEE. Dr. Lucy Shen for her mentorship and guidance throughout the research study.

Funding and Support: Glaucoma Center of Excellence and Miller Research Fund at MEE, Eleanor and Miles Shore Fellowship, Harvard Medical School (LQS)

Disclosures: Dr. Lucy Shen is a consultant for Genentech and received research support from Topcon.
References


Tables and Figures

Figure 1. Optic Nerve Imaging and HVF

Figure 1. Patient Image
a. SS-OCT radial image demonstrating a prelaminar wedge defect delineated by a red dashed line present in the inferior-nasal region of the optic nerve. b. Optic disc photograph demonstrating a prominent inferior disc hemorrhage. c. Humphrey visual field defects noted on pattern deviation, most prominently in the paracentral area.
Table 1. BASELINE CHARACTERISTICS

<table>
<thead>
<tr>
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<th>POAG with PLWD</th>
<th>POAG without PLWD</th>
<th>Control Group</th>
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<tr>
<td>Subjects (n)</td>
<td>16</td>
<td>24</td>
<td>23</td>
</tr>
<tr>
<td>Gender, Male (%)</td>
<td>37.5</td>
<td>58.3</td>
<td>39.1</td>
</tr>
<tr>
<td>Age (years)</td>
<td>63.0 ± 9.9</td>
<td>69.0 ± 7.3</td>
<td>66.3 ± 7.0</td>
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<tr>
<td>Ethnicity, Caucasian (%)</td>
<td>100.0</td>
<td>82.6</td>
<td>90.5</td>
</tr>
<tr>
<td>BCVA (LogMAR)</td>
<td>0.03 ± 0.06</td>
<td>0.05 ± 0.08</td>
<td>0.13 ± 0.11</td>
</tr>
<tr>
<td>Visual Field MD (dB)</td>
<td>-5.8 ± 5.0</td>
<td>-4.8 ± 4.9</td>
<td>NA</td>
</tr>
<tr>
<td>Visual Field PSD (dB)</td>
<td>6.6 ± 4.5</td>
<td>4.3 ± 3.7</td>
<td>NA</td>
</tr>
<tr>
<td>IOP, Current (mmHg)</td>
<td>13.8 ± 2.8</td>
<td>13.9 ± 2.7</td>
<td>14.6 ± 2.3</td>
</tr>
<tr>
<td>IOP, Maximum (mmHg)</td>
<td>18.6 ± 3.5</td>
<td>21.4 ± 5.2</td>
<td>17.0 ± 3.0</td>
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<tr>
<td>History of DH (%)</td>
<td>37.5</td>
<td>8.3</td>
<td>NA</td>
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<tr>
<td>HVF Paracentral Loss (%)</td>
<td>56.3</td>
<td>33.3</td>
<td>NA</td>
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</table>

Data expressed as mean ± standard deviation unless otherwise specified.

Abbreviations: POAG, primary open angle glaucoma; PLWD, prelaminar wedge defect; BCVA, best corrected visual acuity; LogMAR, logarithm of the minimal angle of resolution; IOP, intraocular pressure; DH, disc hemorrhage; HVF, Humphrey Visual Field

Table 2. QUANTITATIVE CHARACTERISTICS

<table>
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<th>POAG with PLWD</th>
<th>POAG without PLWD</th>
<th>Control Group</th>
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<tr>
<td>Horizontal LCD</td>
<td>453.6 ± 92.1</td>
<td>434.9 ± 103.5</td>
<td>419.0 ± 103.9</td>
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<tr>
<td>Global BMO-MRW (µm)</td>
<td>198.3 ± 38.2</td>
<td>220.4 ± 54.7</td>
<td>332.0 ± 66.2</td>
</tr>
<tr>
<td>Normalized Global BMO-MRW (µm)</td>
<td>201.7 ± 38.9</td>
<td>224.1 ± 55.6</td>
<td>337.7 ± 67.4</td>
</tr>
<tr>
<td>Minimum BMO-MRW (µm)</td>
<td>92.6 ± 46.5</td>
<td>117.7 ± 48.3</td>
<td>210.7 ± 49.7</td>
</tr>
<tr>
<td>Average RNFL (µm)</td>
<td>75.8 ± 13.7</td>
<td>79.0 ± 20.8</td>
<td>96.4 ± 11.0</td>
</tr>
<tr>
<td>Thinnest RNFL (µm)</td>
<td>54.5 ± 12.2</td>
<td>50.5 ± 13.7</td>
<td>63.9 ± 12.5</td>
</tr>
</tbody>
</table>

Swept source OCT scans were used to measure horizontal LCD, global BMO-MRW, normalized global BMO-MRW, and minimum BMO-MRW, while spectral domain OCT scans were used to measure average and thinnest RNFL. Abbreviations: LCD, Lamina Cribrosa Depth; BMO, Bruch’s membrane opening; MRW, minimum rim width; RNFL, retinal nerve fiber layer; DH, disc hemorrhage; MD, mean deviation; PSD, pattern standard deviation.
### Table 3. STATISTICAL ANALYSES

**A. Comparison of POAG with PLWD, POAG without PLWD and Controls**

<table>
<thead>
<tr>
<th>Variable</th>
<th>POAG PLWD vs POAG</th>
<th>POAG PLWD vs Control</th>
<th>POAG no PLWD vs Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCVA (LogMAR)</td>
<td>0.34</td>
<td>&lt;0.001</td>
<td>0.004</td>
</tr>
<tr>
<td>Visual Field MD (dB)</td>
<td>0.55</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Visual Field PSD (dB)</td>
<td>0.10</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>IOP, Day of Imaging (mmHg)</td>
<td>0.89</td>
<td>0.52</td>
<td>0.52</td>
</tr>
<tr>
<td>IOP, Maximum (mmHg)</td>
<td>0.15</td>
<td>0.26</td>
<td>0.002</td>
</tr>
<tr>
<td>History of DH (%)</td>
<td>0.04</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Paracentral Loss on HVF (%)</td>
<td>0.20</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Global BMO-MRW (µm)</td>
<td>0.14</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Minimum BMO-MRW (µm)</td>
<td>0.11</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Average RNFL (µm)</td>
<td>0.56</td>
<td>&lt;0.001</td>
<td>0.002</td>
</tr>
<tr>
<td>Thinnest RNFL (µm)</td>
<td>0.35</td>
<td>0.04</td>
<td>0.004</td>
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</tbody>
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Statistical analysis performed with one-way Analysis of Variance and Bonferroni correction was applied for multiple comparisons when data were available from all three groups; p<0.05 was considered statistically significant.

**B. Multivariate Analysis Comparing POAG Subjects**

<table>
<thead>
<tr>
<th>Variables</th>
<th>POAG PLWD vs POAG no PLWD</th>
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<tbody>
<tr>
<td>Age</td>
<td>Odds Ratio [ 95% CI]</td>
</tr>
<tr>
<td>Gender</td>
<td>0.89, [0.80, 0.99]</td>
</tr>
<tr>
<td>VF-MD</td>
<td>0.47, [0.09, 2.46]</td>
</tr>
<tr>
<td>Max-IOP</td>
<td>0.88, [0.72, 1.07]</td>
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<tr>
<td>History of DH</td>
<td>0.83, [0.66, 1.06]</td>
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</table>

<table>
<thead>
<tr>
<th>Variables</th>
<th>Odds Ratio [ 95% CI]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>14.08, [1.50, 132.30]</td>
<td>0.021</td>
</tr>
</tbody>
</table>

*B. Logistic regression model used to analyze POAG with PLWD vs. POAG without PLWD. POAG without PLWD served as reference. Abbreviations: CI, confidence interval; MD, mean deviation; DH, disc hemorrhage.*