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Decreased Visual Function Scores on a Low Luminance Questionnaire is Associated with Impaired Dark Adaptation

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Abstract

Purpose: We investigate whether responses on a Low Luminance Questionnaire (LLQ), in patients with a range of AMD severity, are associated with their performance on focal dark adaptation (DA) testing and with choroidal thickness.

Design: Cross-sectional, single-center, observational study.

Participants: One hundred and thirteen participants older than 50 years of age with a range of age-related macular degeneration (AMD) severity.

Methods: Participants answered the LLQ on the same day that they underwent DA testing using a focal dark adaptometer measuring rod intercept time (RIT). We performed univariable and multivariable analyses of the LLQ scores and age, RIT, AMD severity, subfoveal choroidal thickness [SFCT], phakic status, and best-corrected visual acuity.

Main Outcome Measures: The primary outcome of this study was the score on the 32-question LLQ. Each item in the LLQ is designated to one of six subscales describing functional problems in low luminance: driving, emotional distress, mobility, extreme lighting, peripheral vision, and general dim lighting. Scores were computed for each subscale, in addition to a weighted total mean score.

Results: Responses from 113 participants (mean age, 76.2 ± 9.3 years; 58.4% female) and 113 study eyes were analyzed. Univariable analysis demonstrated that lower scores on all LLQ subscales were correlated with prolonged DA testing (longer RIT) and decreased choroidal thickness. All associations were statistically significant except for the association of choroidal thickness and 'peripheral vision'. The strongest association was the LLQ subscale of driving with RIT ($r = -0.97$, $p<0.001$). Multivariable analysis for each of the LLQ subscale outcomes, adjusted

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for age, included RIT, with total LLQ score, ‘driving’, ‘extreme lighting’ and ‘mobility’ also including choroidal thickness. In all multivariable analyses RIT had a stronger association than choroidal thickness.

Conclusion: This cross-sectional analysis demonstrates associations of patient reported functional deficits, as assessed on the Low-Luminance questionnaire, with both reduced dark adaptation and reduced choroidal thickness, in a population of older adults with varying degrees of AMD severity and good visual acuity in at least one eye. These analyses suggest that local functional measurements of DA testing (RIT) and choroidal thickness are associated with patient reported functional deficits.

Age-related macular degeneration (AMD) has been the leading cause of central vision loss in people age 65 or older in developed countries [1, 2]. Decreases in central vision from late AMD is well-established, and even intermediate AMD can display small but statistically significant reductions in central acuity compared with those without AMD[3-5]. Visual function questionnaires document the impact of poor acuity on a person’s daily living and have become a useful patient-reported outcome measure[6-8]. With the exception of trials involving geographic atrophy (GA)[6], clinical trials in AMD have focused on central acuity as the primary outcome measure[9-17].

However, earlier cell changes accompanying AMD have direct links to additional measures of retinal function. Histopathological examination of eyes from patients with AMD has demonstrated preferential loss of rods in the photoreceptor layer of the retina with cones persisting as the last surviving photoreceptors [18-20]. Studies employing multiple approaches to measure rod and cone function have documented preferential reduced rod function in eyes with AMD[2122-25, 23, 26]. A focal dark adaptometer able to focus on areas 0.5 to 3 mm from the fovea, areas thought to have earliest rod loss, has demonstrated impairments in eyes with non-advanced AMD compared to older eyes without AMD even when visual acuity varied little between severity groups[23]. Increasing AMD severity was associated with increased RIT, an outcome of dark adaptation, with eyes having reticular pseudodrusen (RPD) demonstrating the most significant delays[23]. As efforts are underway to identify functional outcomes that would be meaningful in early disease, measures of dark adaptation (DA) has potential to be an informative outcome. To demonstrate the relevance of this outcome measure in clinical trials, there is need for patient-centered validation of dark adaptation.

Recent questionnaires developed for assessing functioning in low luminance or “night vision” have shown differences in patients with AMD[27-31]. The Low Luminance Questionnaire (LLQ) was designed specifically for the purpose of assessing difficulties at night and in low luminance [32]. Other visual function questionnaires, such as National Eye Institute Visual Function Questionnaire (NEI-VFQ) [33], the Visual Function Index (VF-14) [34], the Activities of Daily Vision Scale (ADVS) [35], or others [36-38], are focused primarily on assessing visual difficulty in photopic or mesopic conditions, and have very few questions related to performance on low-luminance tasks. In the development of the LLQ questionnaire, all subscales were significantly associated with impairments in dark adaptation parameters that rely on rod-mediated function but not with cone-mediated parameters [32]. Since the development of the LLQ, and other questionnaires aimed at

assessing function in low luminance [29, 39], few have been able to relate the questionnaire to direct functional testing of dark adaptation in patients.

Thus, the purpose of this study is to investigate whether patient-perceived difficulty in low-luminance, as assessed by their responses on the LLQ, correlate with their performance on DA testing, in patients with a spectrum of AMD disease severity who maintain good visual acuity. Such validation would further support RIT as a clinical measure that reflects patient-relevant visual difficulties in low luminance not captured by conventional photopic high-contrast visual acuity.

METHODS

Study Population

Participants included adults older than 50 years of age both with and without AMD who were recruited from the eye clinic at the National Eye Institute, National Institutes of Health, Bethesda, Maryland, between May 2011 and January 2014. Patients were excluded for (1) advanced AMD in both eyes at baseline visit; (2) any other active ocular or macular disease (i.e., glaucoma, diabetic retinopathy, Stargardt disease); (3) a condition preventing compliance with the study assessment; (4) cataract surgery within 3 months before enrollment; (5) history of vitamin A deficiency; (6) high oral intake of vitamin A palmitate supplement (>10 000 international units per day); and (7) active liver disease or history of liver disease. Study eyes were required to have a best-corrected visual acuity (BCVA) of 20/100 or better.

After examination, eligible participants were separated into groups based on their fundus features. The grading criteria for AMD groups has been previously described [23], but described here in brief. Eligible eyes were screened for the presence of RPD and these eyes were placed into a separate group (RPD group). The remaining eyes were grouped according to increasing order of AMD severity based on the presence of large drusen (>125 mm), advanced AMD, or both. The control group, group 0, consisted of participants without any large drusen or advanced AMD (choroidal neovascularization [CNV] or central geographic atrophy [CGA]) in either eye. Group 1 consisted of participants with large drusen in one eye only and no late AMD in either eye. Group 2 included participants with large drusen in both eyes without any late AMD. Group 3 included participants with large drusen in one eye and late AMD in the other eye (either CGA or CNV). Each participant had only one study eye assigned to undergo the DA testing. In participants without any large drusen, either eye could be designated the study eye. In participants with large drusen in one eye only, the eye with large drusen was the study eye. In participants with large drusen bilaterally, either eye could be the study eye. In participants with advanced AMD in one eye, the nonadvanced eye was the study eye to both to avoid influences of non-central fixation, and also to exclude testing that might reflect poor dark adaptation due to the presence of fluid or blood in the retina rather than the psychophysical measurement of retina function. The study was approved by the Institutional Review Board of the National Institutes of Health, and the tenets of the Declaration of Helsinki were followed. Although not a clinical trial, the study is registered on clinicaltrials.gov (identifier NCT01352975). All participants provided written informed consent after the nature and possible consequences of the study were explained.

The analysis included 113 participants who had LLQ results, DA testing results and subfoveal choroidal thickness (SFCT).

Examination and Imaging

All participants underwent a complete ophthalmic examination, including measurement of BCVA with the Early Treatment Diabetic Retinopathy Study (ETDRS) logMAR visual acuity chart, measurement of intraocular pressure, slit-lamp examination, and dilated fundus examination. Contrast sensitivity was determined for each eye using standard administration of the Pelli-Robson contrast sensitivity chart [40]. Presence of AMD features (drusen, pigmentary change, pigment epithelial detachment, CNV, CGA) and other ocular findings (e.g., phakic status) were documented. Color fundus photographs and FAF images were acquired with the TRC- 50DX retinal camera (Topcon Medical Systems, Tokyo, Japan). Infrared reflectance (IR) and FAF images and spectral-domain (SD) OCT scans were acquired with the Heidelberg Spectralis (Heidelberg Engineering, Heidelberg, Germany). Each set of SD OCT scans consisted of 37 B-scans, each of which comprised 24 averaged scans, obtained within a 30°×15° rectangle centered on the fovea. In addition, enhanced depth imaging OCT scans were acquired for improved visualization of the choroid in a single horizontal scan centered at the fovea obtained over a distance of 30° consisting of 100 averaged scans.

Low Luminance Questionnaire

The Low Luminance Questionnaire (LLQ) is a 32-item questionnaire designed to assess the degree of difficulty experienced by participants at night and in other low light environments [32]. Each item is scored on a scale of 0 to 100, with 0 representing the greatest difficulty and 100 representing the least. Items are assigned to 1 of 6 subscales, namely *Dim Lighting, Driving, Emotional Distress, Extreme Lighting, Mobility,* and *Peripheral Vision.* Item scores are averaged to give one score per subscale. Each subscale is then weighted by number of items and averaged to yield a total mean LLQ score (16). The questionnaire was administered prior to DA testing by a staff member masked to participants' DA testing performance.

Dark Adaptation Testing

Dark adaptation was measured using a prototype of the AdaptDx dark adaptometer (MacuLogix, Hummelstown, PA). Details about the testing procedure have been documented elsewhere [41]. In brief, the patient's pupil was dilated and the participant was asked to focus on a fixation light with the study eye. A photoflash producing an 82% focal bleach centered at 5° on the inferior visual meridian was performed, and threshold measurements were made at the same location with a 1.7° diameter, 500-nm wavelength circular test spot using a 3-down/1-up modified staircase threshold estimate procedure. The initial stimulus intensity was 5 cd/m^2. Threshold measurements were continued until the patient's visual sensitivity recovered to be able to detect a dimmer stimulus intensity of 5×10^{-3} cd/m^2 (a decrease of 3 log units), or until a maximum test duration of 40 minutes was reached, whichever occurred first. The time to this event was defined as the rod-intercept time (RIT). A measurement used in previous DA studies [26], the RIT corresponds to the time to reach a threshold within the second component of rod-mediated DA and is

estimated by linear interpolation of the sensitivity responses. Tests that did not reach this threshold by 40 minutes were reported as “no rod intercept” by the machine and were conservatively defined to have an RIT of 40 minutes. Additionally, participants with data points that reached high sensitivities in a timeframe that was not physiologic were identified by the adaptometer as having “bleaching errors” and these tests were not used in the analysis but repeated.

Subfoveal Choroidal Thickness Measurements

Subfoveal choroidal thickness (SFCT) in study eyes was measured manually on the foveal enhanced depth imaging OCT scans using the caliper tool in Heidelberg Engineering Eye Explorer software (version 1.7.0.0; Heidelberg Engineering, Heidelberg, Germany). The calipers were drawn perpendicularly from the outer surface of the RPE–Bruch’s membrane complex to the inner surface of the chorioscleral interface directly under the center of the fovea. In cases where the choroidal thickness made the chorioscleral interface difficult to visualize, the image brightness and contrast settings were adjusted in Eye Explorer to maximize visibility.

Statistical Analysis

The data was analyzed using nonparametric statistics computed using SAS software version 9.3 (SAS Inc, Cary, NC). Categorical variables were analyzed using chi-square and Fisher exact tests. Continuous variables were analyzed with Wilcoxon and Kruskal-Wallis tests for 2 and more than 2 variables, respectively. Pearson correlation coefficients were calculated for associations between each LLQ subscale and study variable. Analysis of covariance, a method of multivariate analysis allowing for inclusion of continuous and categorical variables, was performed to adjust for age and included the variables that were most significantly associated with LLQ subscales on univariate analysis. Age was included in the model even though the univariable p-value was not statistically significant.

RESULTS

Participant Demographics

The study population was predominantly white, 58% female with a mean age of 73.0±9.2 years with no statistically significant differences between AMD groups except that the reticular pseudodrusen (RPD) group was older than the reference group (79.3 ± 7.7 vs. 72.5 ± 8.4, p=0.04; Table 1).

Ocular characteristics that statistically significantly differed between AMD groups included BCVA (p=0.0021), phakic status (p=0.014), baseline RIT (p<0.0001), and SFCT (p=0.0038) (Table 2). Contrast sensitivity was the only functional characteristic that did not significantly differ between groups (p=0.18).

In the 113 participants, 99 (87.6%) had a study eye BCVA of 20/32 (LogMAR 0.20) or better. The mean visual acuity of the better seeing eye was LogMAR 0.04 (20/22) ± 0.13. The majority of participants (74.3%) had a study eye BCVA that was greater than or equal to

that of the fellow eye, and only 5.3% of participants had their fellow eye as the better-seeing eye by greater than 5 letters. Pseudophakia was present in 32 of the 113 study eyes (28.3%).

As previously reported, there were significant differences in the mean RIT between the AMD groups. Most significant differences in RIT was seen in the RPD group with 80% reaching test ceiling [23]. The mean RIT of Groups 2 and 3 were also significantly longer than Group 0 (Table 2). The range of RIT times for the 113 participants was 6.9 min to reaching the 40 min ceiling (n=18). As previously reported, Group RPD also had significantly thinner SFCT measurements compared to baseline (137.1 ± 62.3 vs. 227.3 ± 120.6) [23].

Association of LLQ subscale scores with Ocular characteristics

We investigated the correlation of performance on the LLQ (total mean LLQ and all subscales) with person and ocular based characteristics including: age and AMD group as well as study eye RIT, BCVA, SFCT, and Contrast sensitivity. Total mean LLQ score was correlated with all considered variables except for age. All LLQ subscale scores and mean LLQ score were correlated with RIT. Age was not significantly correlated with any LLQ scores. A summary of the investigated correlations between continuous and categorical variables are shown in Tables 3-5. AMD group was correlated with total mean LLQ score as well as emotional distress and extreme lighting subscales (Table 3).

Univariable linear regressions were performed between LLQ score categories with various study variables. All LLQ subcategories and total mean LLQ had were significantly associated with RIT (Table 4). The direct measure of focal dark adaptation, RIT, was statistically significantly associated with all LLQ subscales, with the ‘driving’ subscale conferring the largest parameter estimate. All subscales except ‘peripheral vision’ were statistically significantly associated with SFCT. Most LLQ subscales were associated AMD RPD Group and the ‘extreme lighting’ was also associated with AMD Group 2. No other AMD group-LLQ subscale pairing was significantly associated. Four of 6 subscales excluding ‘general dim lighting’ and ‘peripheral vision’ were associated with BCVA. Only the ‘driving’ subscale was associated with age (Table 4).

Multivariable Analysis

An analysis of covariance was performed to assess the relative contributions of variables associated with LLQ scores in univariate analyses. The variables included age, BCVA, RIT, AMD Group, SFCT, contrast sensitivity and phakic status. In the models, RIT had the strongest association with LLQ variables. The strongest associations of RIT and SFCT were with total mean LLQ score and the ‘driving’ and ‘extreme lighting’ subscales (Table 5).

Age-adjusted models for the subscales ‘emotional distress’, ‘general dim lighting’ and ‘peripheral vision’ included RIT but not SFCT. The model for the ‘extreme lighting’ subscale contained RIT, SFCT and contrast sensitivity, while the model for the ‘peripheral vision’ subscale included RIT and phakic status.

DISCUSSION

The strongest association with the LLQ scores was with rod intercept time (RIT). Although we only measured RIT in one specific retinal location, these results suggest that the measurement is associated with overall dysfunction in dark adaptation, as reflected by personally reported functional outcomes on the LLQ, indicating a deficiency that is meaningful to our patient's day-to-day functioning.

Our analysis found that AMD patients' difficulty with night vision and low luminance could not be well described by impairments in visual acuity alone, which is conventionally used as a primary endpoint in treatment trials of AMD [42]. The range of visual acuities in our patients was small with 88% of participants having 20/32 (LogMAR 0.20) visual acuity or better. Though BCVA was statistically significantly associated with several LLQ score categories, these correlations were weaker than that observed for RIT, and any associations between BCVA and LLQ score in our univariate analysis were lost in our multivariate models. This finding is consistent with other studies suggesting that visual difficulty experienced under low luminance may not be adequately explained by impairments in high luminance visual acuity [27-29, 43, 44]. Previous work by Owsley et al [45] suggests that in a population of older adults with a spectrum of AMD the responses on the LLQ were more sensitive to difficulties experienced by participants in every day situations than the NEI VFQ. It would be interesting in future studies to understand how the measure of RIT would correlate with performance on the NEI VFQ in comparison to performance on the LLQ.

In the analysis presented here of LLQ scores, univariate analyses demonstrated correlation with RIT, AMD severity and SFCT. Previous studies have also found that eyes with AMD have lower LLQ scores [32]. However, the multivariate model that best fit the our LLQ data includes RIT and SFCT but not AMD severity. Interpretation of this result is difficult, because the variables RIT, AMD severity and SFCT are correlated. In a previous study of RIT, we reported univariate analyses that demonstrated a statistically significant correlation between RIT and AMD severity (including RPD) and a statistically significant negative correlation between RIT and SFCT and (eyes with thinner choroids exhibited longer dark adaptation times) [23]. The association of RPD with choroidal thinning has also been reported. [5,23,45,46] As eyes with RPD had significantly decreased SFCT in our study, we had previously reanalyzed the relationship between dark adaptation and SFCT removing eyes with RPD and found no significant correlation with SFCT[23]. One proposed mechanism to explain is the role of the choroid in a person's self-reported functioning in the dark is that thinner choroids lead to local decreased retinoid availability [19, 23, 46] with subsequent slowing of rod-mediated DA leading to difficulties with night vision [30]. However, not all studies of dark adaptation have found a correlation with SFCT, especially when only healthy young eyes were included[47]. Because RPD and choroidal thinning are correlated, it is difficult to interpret the importance of choroidal thinning remaining in the final models of LLQ scores, while AMD severity did not.

Older age has also been associated with prolonged dark adaptation. Previous study of visual function in the elderly had found reduced self-reported mobility decreased with measures of visual function including photostress recovery and impact of light on walking [43]. In our

analysis, however, age was not only non-significantly associated with LLQ score in our multivariate model but also non-significantly correlated with most all LLQ scores, except for the 'driving' subscale, in univariate analysis. However, our study included mostly eyes that did not have reduced visual acuity, so the power to look at the association with LLQ scores is limited.

Any significant associations between contrast sensitivity and LLQ score on univariate analysis were lost in multivariate analysis, except for that between contrast sensitivity and 'extreme lighting.' Although the parameter estimate between these two variables may have been relatively large in our multivariate analysis (19.00, p=0.041), it was bound by wide confidence intervals (0.77 – 37.24) and largely driven by two outliers. Removal of these outliers resulted in a non-significant regression between contrast sensitivity and 'extreme lighting' (p=0.242) and it was therefore not included in our final model.

Pseudophakia has been previously found to be associated with LLQ[28], and has been associated with symptoms of glare, especially at night.[48, 49] Univariate analyses demonstrated associations of pseudophakia with almost all LLQ categories, but the variable phakic status was not included in the final multivariate model for any LLQ subscales except 'peripheral vision.' The 'peripheral vision' subscale historically has the poorest test-retest reliability among all 6 subscales, exhibiting a ceiling effect that is likely due to the relative sparing of peripheral vision in AMD as well as having the fewest items in the questionnaire [32]. Furthermore, nonparametric testing showed a fairly small difference in median LLQ scores between pseudophakic and non-pseudophakic patients (96 vs 100, p=0.025).

In conclusion, our analyses suggest that the degree of self-reported night vision symptoms experienced across a range of individuals with varying AMD disease severity, as measured by the LLQ, is significantly associated with rod intercept time, a functional measure of rod-mediated dark adaptation. There was also an important association of reported functional loss with choroidal thinning. This study serves as a cross-validation between DA, a psychophysical measure of rod function, and the LLQ, a psychometric measure of self-reported visual symptoms in low luminance, providing further evidence for considering the use of dark adaptation as a supporting secondary outcome measure for future trials of AMD. Further work is underway to assess associations of change in DA with change in LLQ score over time.

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Table 1.

Baseline Demographics by AMD Group

Characteristic	AMD Group 0	AMD Group 1	AMD Group 2	AMD Group 3	Reticular Pseudodrusen Group	P Value
No.	41	13	30	15	14	
Mean age (SD), yrs.	72.5 (8.4)	70.5 (10.6)	70.8 (9.7)	75.3 (8.4)	79.3 (7.7) *	0.04
Female gender, no. (%)	25 (61.0)	7 (53.8)	15 (50.0)	9 (60.0)	10 (71.4)	0.75
Race, no. (%)						0.39
American Indian / Alaskan Native	0 (0)	0 (0)	0 (0)	1 (6.7)	0 (0)	
Asian	2 (4.9)	0 (0)	2 6.7)	0 (0)	1 (7.1)	
Black	3 (7.3)	0 (0)	0 (0)	1 (6.7)	0 (0)	
White	36 (87.8)	13 (100.0)	28 (93.3)	13 (86.7)	13 (92.9)	

SD = standard deviation

* P < 0.05 for pairwise comparison with AMD Group 0

Table 2.

Baseline Ocular Characteristics by AMD Group

Characteristic	AMD Group 0	AMD Group 1	AMD Group 2	AMD Group 3	Reticular Pseudodrusen Group	P Value
No.	41	13	30	15	14	
Mean LogMar (SD)	0.0050 (0.11)	0.00080 (0.090)	0.080 (0.13)	0.17 (0.20)*	0.11 (0.15)	0.0021
Phakic status, no. (%) pseudophakic	12 (29.3)	3 (23.1)	4 (13.3)	4 (26.7)	9 (64.3)	0.014
Mean Baseline RIT (SD), mins.	12.9 (4.8)	17.1 (10.5)	24.0 (10.8)*	26.6 (9.3)*	39.0 (2.1)*	<0.0001
Mean SFCT (SD), μm	227.3 (120.6)	245.8 (79.4)	231.2 (75.6)	210.9 (97.9)	137.1 (62.3)*	0.0038
Mean Contrast Sensitivity (SD), log score	1.55 (0.16)	1.58 (0.13)	1.47 (0.22)	1.50 (0.14)	1.51 (0.22)	0.18

BCVA = best-corrected visual acuity; SD = standard deviation; SFCT = subfoveal choroidal thickness

*P < 0.05 for pairwise comparison with AMD Group 0

Table 3.

Kruskal-Wallis ANOVA Comparing Median LLQ Scores and Interquartile Ranges between AMD Group

LLQ Score Category	Group 0 (n=41)	Group 1 (n=13)	Group 2 (n=30)	Group 3 (n=15)	Group 4 (n=14)	P Value
Dim Lighting	95 (75 – 100)	87 (75 – 100)	93 (66 – 100)	91 (79 – 95)	81 (58 – 95)	0.45
Driving	80 (55 – 95)	85 (70 – 100)	75 (45 – 95)	80 (33 – 90)	48 (25 – 87)	0.10
Emotional Distress *	100 (93 – 100)	100 (93 – 100)	100 (87 – 100)	100 (81 – 100)	90 (75 – 100)	0.029
Extreme Lighting *	92 (81 – 96)	90 (84 – 100)	77 (59 – 91)	75 (65 – 90)	68 (56 – 90)	0.0036
Mobility	95 (87 – 100)	100 (91 – 100)	91 (83 – 100)	91 (83 – 95)	79 (66 – 95)	0.095
Peripheral Vision	100 (91 – 100)	100 (100 – 100)	100 (83 – 100)	100 (75 – 100)	91 (75 – 100)	0.33
Total Mean LLQ * Score	89 (79 – 97)	90 (87 – 100)	86 (67 – 97)	85 (67 – 93)	74 (55 – 96)	0.053

* P < 0.05 for pairwise comparison with AMD Group 0

Table 4.

Univariate Linear Regression of each LLQ Variable with each Study Variable

LLQ Score Category	Rod-Intercept Time		Subfoveal Choroidal Thickness		Age		Best-Corrected Visual Acuity		Contrast Sensitivity		Phakic Status*		AMD Group+		
	Param Est	P Value	Param Est	P Value	Param Est	P Value	Param Est	P Value	Param Est	P Value	Param Est	P Value	Group #	Param Est	P Value
Driving	−0.97	<.0001	0.09	0.001	−0.66	0.033	0.82	0.041	34.15	0.026	15.1	0.012	1 2 3 4	7.02 −6.53 −9.8 −25.00	0.45 0.36 0.27 0.007
Emotional Distress	−0.48	0.0002	0.04	0.009	−0.19	0.26	0.49	0.021	13.18	0.11	6.7	0.034	1 2 3 4	1.22 −7.17 −5.91 −15.64	0.81 0.057 0.21 0.0015
Extreme Lighting	−0.65	<.0001	0.061	0.0003	−0.29	0.13	0.66	0.006	27.9	0.0028	8.47	0.028	1 2 3 4	2.16 −12.00 −10.61 −15.64	0.70 0.0052 0.048 0.0048
General Dim Lighting	−0.39	0.010	0.038	0.031	0.00017	1.0	0.25	0.31	13.35	0.16	5.60	0.15	1 2 3 4	−3.58 −6.2 −1.87 −9.7	0.55 0.17 0.74 0.093
Mobility	−0.53	0.0003	0.05	0.002	−0.22	0.24	0.48	0.049	17.16	0.067	7.37	0.053	1 2 3 4	2.64 −5.25 −1.92 −14.76	0.64 0.23 0.72 0.0089
Peripheral Vision	−0.34	0.013	0.023	0.15	−0.24	0.17	0.28	0.22	12.16	0.16	9.45	0.0067	1 2 3 4	3.00 −1.2 −2.94 −6.25	0.58 0.77 0.57 0.24
Total Mean LLQ Score	−0.58	<0.0001	0.054	0.0009	−0.26	0.14	0.52	0.024	20.82	0.018	8.63	0.016	1 2 3 4	1.89 −7.18 −5.91 −14.95	0.72 0.078 0.25 0.0049

Param Est = Parameter Estimate

Table 5.

Final Multivariate Regression Model for all LLQ Score Categories

LLQ Score Category	Rod-Intercept Time		Subfoveal Choroidal Thickness		Age		Phakic Status*	
	Parameter Estimate (95% CI)	P Value	Parameter Estimate (95% CI)	P Value	Parameter Estimate (95% CI)	P Value	Parameter Estimate (95% CI)	P Value
Driving	−0.77 (−1.25 – −0.29)	0.0022	0.062 (0.008 – 0.12)	0.027	−0.19 (−0.78 – 0.40)	0.53	—	—
Emotional Distress	−0.49 (−0.74 – −0.23)	0.0003	—	—	0.012 (−0.32–0.34)	0.94	—	—
Extreme Lighting	−0.55 (−0.84 – −0.26)	0.0003	0.044 (0.011 – 0.076)	0.007	0.045 (−0.31 – 0.40)	0.81	—	—
General Dim Lighting	−0.43 (−0.74 – −0.13)	0.0064	—	—	0.18 (−0.21 – 0.56)	0.37	—	—
Mobility	−0.45 (−0.75 – −0.16)	0.0033	0.038 (0.0049 – 0.072)	0.027	0.061 (−0.31 – 0.43)	0.75	—	—
Peripheral Vision	−0.28 (−0.56 – −0.013)	0.043	—	—	0.048 (−0.32 – 0.42)	0.80	8.39 (0.93–15.85)	0.027
Total Mean LLQ Score	−0.49 (−0.77 – −0.22)	0.0006	0.038 (0.007 – 0.069)	0.018	0.033 (−0.31 – 0.37)	0.85	—	—

*pseudophakia is the reference value for phakic status;