Changes in the Quality of Life of People with Keratoconus

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Abstract

Purpose—The Collaborative Longitudinal Evaluation of Keratoconus Study (CLEK) has previously shown that people with keratoconus report significantly impaired vision-related quality of life (V-QoL) as measured on the National Eye Institute Visual Function Questionnaire (NEI-VFQ), similar to people who have severe macular degeneration. In this report we evaluate changes that occurred in V-QoL over 7 years of follow-up.

Design—Prospective cohort study of 1166 participants followed for 7 years.

Methods—We estimated change in quality of life by projecting the slope of a minimum of three reports on 11 scales of the NEI-VFQ. Correlation with clinical indicators was evaluated, and differences were assessed between those who had clinically significant changes in clinical factors and those who did not. Logistic regression was used to assess factors associated with a decline in 10 points or more in a scale score over 7 years.

Results—All scales showed modest decline except Ocular Pain and Mental Health. Baseline factors were not associated with longitudinal change in NEI-VFQ scores. A 10-letter decline in high-contrast binocular visual acuity and a 3.00 D increase in corneal curvature were associated with significantly larger declines in V-QoL. In multivariate analysis, these factors also were found to be associated with a 10-point decline in NEI-VFQ scale scores.

Conclusions—Keratoconus is associated with significantly impaired V-QoL that continues to decline over time. For a substantial plurality these declines are significant.

Keywords

keratoconus; quality of life; NEI Visual Function Questionnaire; NEI-VFQ CLEK Study

Introduction

Keratoconus is a relatively rare disease resulting in reduced vision, irregular astigmatism and corneal scarring.[1] It is most commonly seen in younger people[2, 3] with the average age of patient-reported onset ranging from 9.2 years to 28.0 years.[1, 2, 4] This is a significant contrast to other eye diseases that affect vision, such as glaucoma and macular degeneration, both of which have a much later age of onset.[5, 6]

Although typically thought of as a disease with modest impact on visual function and quality of life, keratoconus may be more devastating than was previously thought because its impact is on people who are considerably active and in their primary income-earning years. It is, therefore, thought that this might explain a number of characteristics that have been observed in people with keratoconus including increased anxiety and reactivity to stressful situations.[7]

An alternative to assessing keratoconus with clinical indicators is to use quality of life questionnaires such as the National Eye Institute Visual Function Questionnaire (NEI-VFQ) which was developed to assess vision-related quality of life (V-QoL) for a broad spectrum of ocular conditions, such as diabetic retinopathy, glaucoma, and macular degeneration.[8–10] Among people with keratoconus, self-reported vision-specific quality of life on the NEI-VFQ was similar to that reported in the Age-Related Eye Disease Study (AREDS) by much older people with categories 3 and 4 macular degeneration.[11]

The previous CLEK report indicated associations between vision-specific quality of life and clinical characteristics of keratoconus, but the cross-sectional nature of the data does not permit the assessment of changes in quality of life nor the identification of potential causes for those changes. Longitudinal analyses must be performed to establish such linkages, and to date, we are aware of only one longitudinal study of quality of life as reported by the NEI-VFQ,[12] and this particular study was conducted with individuals who were diagnosed with macular degeneration. Consequently, it should be noted that no such studies have been performed of people with keratoconus using any instrument. In this report we provide the first longitudinal examination of changes in vision-specific quality of life of people with keratoconus and evaluate the clinical factors associated with those changes.

Methods

The Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study is a multicenter, observational study designed to assess the natural history of keratoconus. Details of the CLEK Study and its enrollment criteria have been presented elsewhere.[2] We enrolled 1209 patients and completed 8 years of follow-up. The institutional review board of each participating clinic approved the CLEK protocol, and all subjects signed informed consent documents before enrollment.

All CLEK patients completed an annual examination to assess visual acuity and ocular health. Vision-related quality of life was measured with a self-administered questionnaire, the NEI-VFQ.[10] This was additionally completed by the participant at each follow-up visit but was not administered at baseline (i.e., the enrollment visit). The process by which the NEI-VFQ was administered to CLEK participants and our baseline findings have been reported elsewhere. [11] As with the baseline paper, we rely on the enrollment visit for "baseline" clinical measures, and the first visit at which the NEI-VFQ was administered (i.e, the first follow-up visit) for "baseline" NEI-VFQ scores.

In this study, the change in V-QoL was characterized by the slope of a line fitted between three or more annual measures of an NEI-VFQ scale. The unadjusted slope of the trend in scores was calculated for each NEI-VFQ scale by ordinary least squares regression techniques. Because the NEI-VFQ was not administered at the CLEK baseline visit (the survey was not available in the period of 1995 to 1996), slope calculation considered only follow-up visits 1 to 8. Data from all CLEK examination visits were included up to the last visit a patient completed or the last visit before penetrating keratoplasty (PK) in either eye. Patients who underwent PK in either eye at the time of CLEK enrollment or at year 1 were excluded, and data after PK during the study was censored (Less than ten eyes of CLEK participants underwent epikeratophakia, therefore, in constructing our sample we treated epikeratophakia in the same manner as PK. No CLEK patients underwent deep lamellar keratoplasty during the study period).

To be included in the dataset, a participant must have completed at least three CLEK examination visits that included completion of the NEI-VFQ. The annual slope of each NEI-VFQ scale was extrapolated to the projected change over time by multiplying the slope per year by seven which is the number of years of data collection. To ensure that outlying observations did not result in an overestimation of the change in scale scores, we compared the mean of the difference between the year 1 and year 7 observations to the subset of patients meeting inclusion criteria and for whom we had observations in both years 1 and 7. This analysis yielded extremely modest differences between the difference score and the slope.

In these analyses we did not consider the General Health scale because it was not considered to be relevant to reporting V-QoL.

To identify clinical factors associated with significant changes in V-QoL, we considered a decrease of 10 points or more over 7 years (i.e., a patient having a slope coefficient less than –1.42 points on an NEI-VFQ scale) as representing a large decline. We are aware of no empirical report concerning the size of a clinically significant change on the NEI-VFQ, but other authors have suggested that half of a standard deviation represents a minimal clinically important difference on a variety of other quality of life instruments.[13] In our previous report one-half of a standard deviation on the NEI-VFQ for people with keratoconus is 5.8 to 11.5 points, with a median of 9.0 to 9.5 points.[11] Thus for simplicity, we chose a 10-point change as representing a clinically meaningful change in a scale score.

We assessed the association between clinical variables and a 10-point decline in V-QoL by multivariate logistic regression.[14] For analysis, we first considered variables identified as having been associated with differences in baseline NEI-VFQ scores along with longitudinal factors.[11] Baseline factors considered were age, high-contrast binocular entrance visual acuity, corneal curvature (measured by steep keratometry and calculated as the average of right and left eyes), contact lens wear, and presence of a corneal scar at baseline. Longitudinal factors examined were changes in high-contrast binocular entrance visual acuity, corneal curvature (steep keratometry, average measure of right and left eyes), and incidence of corneal scarring.

The methods used to calculate the slopes for visual acuity and corneal curvature in CLEK patients have been described elsewhere.[15, 16]

Logistic regression models were constructed for each scale with a 10-point decline on the NEI-VFQ scale as the outcome variable. To ensure comparability of clinical variables between scales, we identified a common set of covariates to be used in the models. Demographic and clinical covariates to be included in the final model were identified through a process that began by including all candidate variables in the initial model. The model was then evaluated and variables were eliminated one at a time, beginning with the variable with the largest p value. All variables with a value of $p < .10$ were included in the model for each scale, and the variable performance was evaluated in the logistic models. The intercorrelation of these variables was examined for evidence of multicolinearity. The models were then reevaluated and the most parsimonious set of covariates was identified. Any variable with a value of $p < .05$ in the model for at least one scale was retained, as were those known or theorized to have a relation with quality of life of people with keratoconus. The fit of the final models was evaluated, with a nonsignificant χ^2 value on the Hosmer-Lemeshow test considered to indicate a good fit.[14]

To ease interpretation of results, clinical variables were dichotomized at clinically meaningful breakpoints: baseline binocular entrance visual acuity worse than 20/40, baseline corneal curvature ≥ 52 D, a decline of 10 letters or more in visual acuity, and a 3.00 D increase in corneal curvature. When these clinical measures were treated as the independent variable, the dichotomized variable was included in the model. When the clinical measure was treated as a covariate in the multivariate model (i.e., it was not the independent variable of interest), the continuous measure of the variable was used.

All analyses were performed with SAS Release 9.1 (SAS Institute, Cary, NC).

Results

Of the 1209 CLEK patients, 925 (76%) met the criteria for inclusion in these analyses. The demographic characteristics of these patients are provided in Table 1, and the clinical characteristics are detailed in Table 2.

The unadjusted mean slopes (Table 2) show that, on average, patients with keratoconus perceive a decline in V-QoL on all scales except Ocular Pain and Mental Health. Extrapolating the annual slope to the 7-year follow-up period of CLEK indicates that the average decline on most scales was modest, ranging from 0.21 points (for Distance Activities) to 3.85 points (Dependency). The increases in Ocular Pain and Mental Health were similarly modest (1.61 points for Ocular Pain and 3.36 points for Mental Health).

Table 3 details the means of the unadjusted regression coefficients (slopes) stratified by key clinical factors. A decline in visual acuity and an increase in corneal curvature and incident scar were associated with a decline in V-QoL on all scales. Significant differences in changes of scale scores were associated with a decline of more than 10 letters on visual acuity for all scales except Ocular Pain. A 3.00 D increase in corneal curvature was associated with a significant difference on all scales except Ocular Pain, Social Function, and Color Vision. An incident corneal scar was associated with a significant difference on all scales except Near Activities, Social Function, and Peripheral Vision.

Univariate analyses found that key factors associated with changes in V-QoL were race (characterized as white and non-white), education, baseline NEI-VFQ scale score, change in visual acuity, and change in corneal curvature. Although baseline visual acuity and corneal curvature were not found to be significantly associated with the outcome, these covariates were included in the multivariate model to ensure its completeness.

Table 5 details the adjusted odds ratios associated with a CLEK patient experiencing a 10-point decline in the NEI-VFQ scale score over the 7 years of the CLEK Study. The proportion of patients perceiving such a decline ranged from 13% (Color Vision) to 24% (Peripheral Vision). Baseline corneal curvature was associated with a 10-point decline in General Vision, Ocular Pain, and Dependency. Decrease in high-contrast binocular entrance visual acuity of more than 10 letters was associated a 10-point change on all scales except Ocular Pain and Driving. An increase in corneal curvature greater than 3.00 D was associated with a 10-point decline on all scales except General Vision, Social Function, and Color Vision.

Discussion

Over 7 years, CLEK participants, on average, reported a decline in their V-QoL as measured by most NEI-VFQ scales. On scales for which a decline was seen, the decline was modest (see Table 2), ranging from less than 1 point over 7 years (General Vision) to almost 2 points (Near Activities). The exceptions to this were Dependency, which declined considerably, and Mental Health and Ocular Pain, which improved. In both cases, we suspect that these were examples of changes in extreme attitudes of participants. As previously noted, we found in our baseline report that the average Mental Health score of CLEK participants with normal visual acuity was comparable to people with advanced blinding disease.[11] Adaptation to their disease could possibly occur over time, resulting in reduced anxiety. This may explain the otherwise counterintuitive finding of a positive slope on the Mental Health scale in this cohort. Of note, although the mean Mental Health score increased, almost 17% of participants had a slope coefficient that, when extrapolated over 7 years, resulted in a 10-point decline in their scale score (see Table 4). In contrast, at baseline the Dependency scale score was the highest. Not surprisingly, this scale exhibits the most severe response to disease progression because this scale had the greatest opportunity to decline.

In our cross-sectional study, we found that the clinical indicators with the strongest association with lower V-QoL at baseline were visual acuity worse than 20/40 and corneal curvature ≥52 D. These baseline measures were not found to be significantly associated with changes in V-QoL on any scale except Dependency, for which a baseline corneal curvature of ≥52 D was associated with a decline in the scale score (see Table 3). On the other hand, a 10-point change in visual acuity was found to be significantly associated with declines in all NEI-VFQ scale scores, except Ocular Pain. A 3.00 D or greater increase in curvature was associated with a decline in all scales except Ocular Pain, Social Function, and Color Vision. For the clinician, this may indicate that positive clinical measures at a single visit are not indicative of a good prognosis for a patient's quality of life. It is the change in these clinical measures over time has the strongest influence on the patient's attitude toward his or her disease and perception of its impact on visual function.

This relation was found to be robust in multivariate analyses in which we adjusted for race, education, baseline VFQ scale score, and clinical factors (see Table 4). We found that a substantial minority of CLEK participants had a decline in V-QoL that, when extrapolated over 8 years, was ≥10 points. In the multivariate analysis, a decrease in binocular high-contrast visual acuity of more than 10 letters was associated with increased probability of a 10-point decline in scale scores on all scales except Ocular Pain and Driving, whereas an increase in corneal curvature greater than 3.00 D was associated with increased risk of a 10-point decline on all scales except General Vision, Social Function, and Color Vision. The significance of these findings becomes more apparent considering that the CLEK Study recently reported that over 7 years 19% of participants had a 10-letter loss in high-contrast, best-corrected visual acuity[15] and that 25% of participants had a 3.00 D increase in first definite apical clearance lens.[16] Clearly, a substantial plurality of people with keratoconus are at risk of substantial declines in their already low-perceived V-QoL.

The AREDS investigators previously reported the responsiveness of the NEI-VFQ to changes in clinical status (i.e., loss of 15 letters and/or change in lens opacity) of elderly people with chronic disease.[12] They found that the NEI-VFQ was responsive to changes in visual acuity on most scales but less responsive to changes in lens opacity. In our study of younger adults with keratoconus we found that the NEI-VFQ was responsive to less-severe changes in clinical status. When considered alongside the results reported by the AREDS investigators, our findings provide compelling evidence of the responsiveness of the NEI-VFQ to clinically significant change in visual acuity for study participants across a range of ages and types of ocular disease.

We also report that the NEI-VFQ is responsive to clinically significant changes in corneal curvature in people with keratoconus. This is of particular interest given that corneal curvature (or keratoconus) was not considered a clinical factor by the team that designed the NEI-VFQ. [9] In univariate analysis (see Table 3) we found that change in corneal curvature was significantly associated with change on all scales except Ocular Pain, Social Function, and Color Vision. We also found that people with the 3.00 D increase in corneal curvature were at significantly increased risk of a 10-point decline in V-QoL on all scales except General Vision, Social Function, and Color Vision. Importantly, change in curvature was associated with substantially increased risk of a large decline on the ocular pain (odds ratio, 1.92) and mental health (odds ratio, 3.49) scales and on both scales was the most potent predictor of a 10-point decline for that scale. As previously noted, these two scales had very low scores at baseline and showed a mean increase in the scores over 7 years of follow-up. This provided further evidence of the responsiveness of the NEI-VFQ to a clinically significant change in a subgroup of patients.

Our exclusion of people with penetrating keratoplasty at baseline, as well as censoring all observations at PK, limits the generalizability of our findings to people who have not had PK or to people who may be contemplating the procedure. PK is a preferred method to manage keratoconus in people who become contact lens intolerant.[17] The CLEK investigators have shown that lower scores on the NEI-VFQ Ocular Pain and Distance Vision scores are modestly predictive of PK after adjustment for other clinical factors.[18] Our group has also shown in preliminary analyses that PK patients report substantially improved V-QoL, particularly after transplantation of the fellow eye (Kymes SM, et al. IOVS 2004;45:ARVO E-Abstract 1376). However, our intention in this investigation was to demonstrate the influence on changes in commonly measured clinical factors (visual acuity, corneal curvature, corneal characteristics, etc.) on V-QoL for the "average" person with keratoconus. More complete consideration of PK on V-QoL will have to be the subject of future investigations.

We characterized change in V-QoL as a slope of responses given at a minimum of three CLEK examination visits. The purpose of this method was to minimize the influence of extreme reports on the change in V-QoL. In taking this approach, we may have understated or overstated changes in quality of life. If that is the case, the result may be a biased estimation of the reported associations. However, because the trend seen in most scales is negative (indicating a decline in V-QoL), our smoothing technique more likely resulted in an underestimation of the change in V-QoL rather than an overestimation. This being the case the associations reported here likely represents a conservative estimate of the relation between changes in clinical factors and self-reported quality of life.

Clinical examination of people with keratoconus typically reveals normal entrance and best-corrected visual acuity as well as modest ocular comorbidity. As a consequence, the common clinical wisdom is to assume keratoconus to be a disease of modest consequence to those who bear its burden. Combining the results here with our previous report, we have shown that its impact on patients, from their perspective, highly significant, and gets worse with time. We

hope with these findings we have lain to rest the concept that keratoconus is a disease of modest consequence, and that policymakers will be inspired to ensure that clinicians and researchers have the resources necessary to address the needs of those who suffer the consequences of keratoconus.

Acknowledgments

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Table 1

Demographic Measures for 925 Collaborative Longitudinal Evaluation of Keratoconus Study (CLEK) Participants Included in This Study[a]

Characteristics	N or Mean	% or SD
Age (y)	40.4	10.8
Age >35 years	630	68.2%
Gender (male)	510	55.1%
Race		
African American	158	17.1%
Asian/Pacific Islander	17	1.8%
Hispanic	69	7.5%
Native American	6	0.6%
White	665	71.9%
Other	10	1.1%
Education level		
High school not completed	33	3.6%
High school graduate	140	15.1%
Some college	254	27.5%
College	213	23.0%
Some graduate school	285	30.8%
Contact lens wear (at baseline)		
None	139	15.0%
One eye only	34	2.7%
Both eyes	752	81.3%

Abbreviation: SD, standard deviation

[a]Where the measure is continuous, the final column provides the mean. Where it is categorical, the frequency is provided.

Table 2

Baseline Clinical Measures and Slopes Measuring Change Over Seven Years of Follow-up for 925 CLEK Participants[a]

Variable	N	Baseline Mean(SD or N [%])	N	Slope Mean (SD or N [%])
Visual acuity (letters correct, high contrast)				
Entrance binocular	924	52.2 (6.65)	919	−0.15 (1.18)
Baseline visual acuity worse than 20/40	33	3.6%		
Loss of ≥ 10 letters during follow-up			170	18.5%
Corneal curvature (diopters, steep keratometry)				
Average of left and right eyes	917	50.5 (4.63)	918	0.16 (0.48)
Baseline steep keratotomy ≥ 52 D	280	30.3%		
Increase of >3.00 D during follow-up			115	12.4%
Corneal scarring present (at baseline)	283	30.6%		
Incident scar during follow-up			149	16.1%
Penetrating keratoplasty during follow-up	52	5.6%		
NEI-VFQ scale scores				
General vision	924	74.7 (14.6)	924	−0.06 (3.00)
Ocular pain	925	75.6 (17.2)	925	0.23 (3.79)
Near activities	925	79.1 (18.2)	925	−0.24 (2.84)
Distance activities	925	78.4 (17.3)	925	−0.03 (2.71)
Social function	925	91.7 (14.4)	925	−0.17 (2.59)
Mental health	925	74.9 (21.2)	925	0.48 (3.50)
Role difficulties	924	81.9 (21.9)	924	−0.23 (3.76)
Dependency	923	94.4 (13.1)	923	−0.55 (2.95)
Driving	886	80.4 (17.0)	883	−0.12 (2.91)
Color vision	924	96.9 (11.1)	923	−0.19 (2.28)
Peripheral vision	924	81.9 (21.9)	923	−0.44 (3.30)

Abbreviation: SD, standard deviation

[a]Where the "N" does not equal 925, this indicates missing data for that measure for some participants. Slopes represent expected change for one year.

Table 3

Average Annual Change in NEI-VFQ[a] Scales Stratified by Clinical Indicators[b]

Scale	Baseline Visual Acuity Worse than 20/40[c]		Baseline Corneal Curvature ≥52 D[d]		Decline in Visual Acuity ≥10 Letters[c]		Increase in Corneal Curvature ≥3.00 D[d]		Incident Scar During 7-year Follow-up	
	Yes (n = 33)	No (n = 892)	Yes (n = 280)	No (n = 645)	Yes (n = 170)	No (n = 749)	Yes (n = 115)	No (n = 809)	Yes (n = 149)	No (n = 775)
General vision	0.42	−0.08	−0.27	0.02	−0.938	0.125[e]	−0.980	0.066[e]	−0.694	0.058[e]
Ocular pain	1.40	0.18	0.40	0.15	−0.022	0.283	−0.389	0.320	−0.614	0.390[e]
Near activities	−0.46	−0.23	−0.21	−0.24	−0.888	−0.098[e]	−0.884	−0.148[e]	−0.640	−0.162
Distance activities	0.36	−0.04	−0.10	0.01	−0.885	0.160[e]	−0.840	0.087[e]	−0.655	0.092[e]
Social function	0.49	−0.19	−0.35	−0.08	−0.703	−0.067[e]	−0.432	−0.132	−0.412	−0.123
Mental health	0.21	0.49	0.68	0.39	−0.365	0.663[e]	−0.219	0.583[e]	−0.130	0.601[e]
Role difficulties	−0.24	−0.23	−0.58	−0.08	−0.976	−0.022[e]	−1.349	−0.074[e]	−1.064	−0.073[e]
Dependency	−1.09	−0.52	−1.03	−0.33[e]	−1.305	−0.365[e]	−1.952	−0.349[e]	−1.417	−0.381[e]
Driving	0.43	−0.13	−0.39	−0.01	−0.879	0.038[e]	−0.868	−0.014[e]	−0.610	−0.027[e]
Color vision	0.11	−0.20	−0.39	−0.10	−0.535	−0.121[e]	−0.070	−0.208	−0.644	−0.104[e]
Peripheral vision	0.77	−0.48	−0.72	−0.31	−1.129	−0.310[e]	−1.268	−0.320[e]	−0.702	−0.387

[a] Annual slope of change in NEI-VFQ scale score

[b] A positive slope indicates improvement in reported quality of life, a negative slope indicates a decline.

[c] Entrance High Contrast Binocular Vision

[d] Average of left and right eye

[e] Significant at $p < 0.05$

Table 4

Odds Ratios for a 10-point Decline in NEI-VFQ Scale Score Over Seven Years After Adjustment for Race, Education Baseline NEI-VFQ Scale Score, Incident Scarring Baseline VA and Curvature, and Changes in VA and Curvature[a]

Scale	N	Number with 10-Point Decline (%)	Baseline Visual Acuity Worse than <20/40[b] (n = 33)	Baseline Steep Keratotomy ≥52 D[c] (n = 280)	Any Incident Scar (n = 149)	Decrease in Visual Acuity ≥10 Letters[b] (n = 170)	Increase in Steep Keratotomy >3.00 D[c] (n = 115)
General vision	924	204 (22)	0.72(0.19–2.66)	1.51(1.02–2.22)	1.81(1.17–2.81)	1.67(1.10–2.54)	1.29 (0.76–2.18)
Ocular pain	925	201 (22)	0.25 (0.06–1.11)	1.03 (0.70–1.51)	1.57 (1.04–2.39)	1.20 (0.80–1.81)	2.30 (1.42–3.72)
Near activities	925	226 (24)	1.36(0.52–3.58)	1.14(0.80–1.64)	1.07(0.70–1.65)	1.86(1.27–2.74)	1.62(1.00–2.60)
Distance activities	925	189 (20)	0.47(0.12–1.81)	1.18(0.81–1.73)	1.24(0.80–1.93)	2.19(1.48–3.24)	2.02(1.25–3.25)
Social function	925	155 (17)	0.41(0.08–2.20)	1.41(0.92–2.18)	1.18(0.72–1.94)	1.78(1.15–2.77)	1.68(0.92–3.05)
Mental health	925	154 (17)	0.86(0.27–2.72)	1.01(0.67–1.52)	1.47(0.93–2.32)	2.07(1.36–3.15)	3.49(2.15–5.66)
Role difficulties	924	227 (24)	0.26(0.06–1.21)	1.04(0.70–1.53)	1.42(0.94–2.18)	1.69(1.14–2.50)	1.88(1.11–3.16)
Dependency	923	157 (17)	0.81(0.27–2.41)	1.40(0.94–2.09)	1.76(1.12–2.77)	1.80(1.17–2.79)	2.80(1.73–4.52)
Driving	883	161 (18)	0.55(0.12–2.54)	1.12(0.75–1.67)	1.08(0.67–1.74)	1.51(0.98–2.33)	1.99(1.18–3.33)
Color vision	923	117 (13)	0.79(0.22–2.82)	1.92(1.24–2.95)	1.08(0.63–1.87)	1.70(1.05–2.74)	1.43(0.80–2.58)
Peripheral vision	923	227 (24)	0.99(0.32–3.07)	0.99(0.67–1.47)	0.92(0.58–1.45)	1.64(1.11–2.44)	1.99(1.17–3.39)

[a] Adjusted for race, education baseline NEI-VFQ scale score, incident scarring baseline VA and curvature, and changes in VA and curvature

[b] Entrance High Contrast Binocular Vision

[c] Average of left and right eye