# Longitudinal Changes in Visual Acuity in Keratoconus

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PURPOSE. The present investigation aimed to identify factors that predict reduced visual acuity in keratoconus from a prospective, longitudinal study.

METHODS. This report from the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study used 7 years of follow-up data from 953 CLEK subjects who did not have penetrating keratoplasty in either eye at baseline and who provided enough data to compute the slope of the change over time in high- or low-contrast best-corrected visual acuity (BCVA). Outcome measures included these slopes and whether the number of letters correctly read decreased by 10 letters or more in at least one eye in 7 years.

RESULTS. Mean age of the subjects at the first follow-up visit was $40.2 \pm 11.0$ years (mean $\pm$ SD). Overall, 44.4% were female, and 71.9% were white. The slope of the change in high- and low-contrast BCVA ($-0.29 \pm 1.5$ and $-0.58 \pm 1.7$ letters correct/year, respectively) translated into expected 7-year decreases of 2.03 high- and 4.06 low-contrast letters correct. High- and low-contrast visual acuity decreases of 10 or more letters correct occurred in 19.0% and 30.8% of subjects, respectively. Independent predictors of reduced high- and low-contrast BCVA included better baseline acuity, steeper first definite apical clearance lens (FDACL), and fundus abnormalities. Each diopter of steeper baseline FDACL predicted an increased deterioration of 0.49 high- and 0.63 low-contrast letters correct.

CONCLUSIONS. CLEK Study subjects with keratoconus exhibited a slow but clear decrease in BCVA during follow-up, with low-contrast acuity deteriorating more rapidly than high-contrast. Better baseline BCVA, steeper FDACL, and fundus abnormalities were predictive of greater acuity loss with time. (*Invest Ophthalmol Vis Sci.* 2006;47:489–500) DOI:10.1167/iovs.05-0381

Keratoconus is an asymmetric, bilateral, progressive corneal ectasia and thinning that is noninflammatory in nature.[1-3] These corneal changes may result in irregular astigmatism and corneal scarring, both of which reduce the best-corrected visual acuity (BCVA) of the patient.[3] In mild cases, spectacle correction may provide adequate vision.[3] As the disease progresses, rigid contact lenses are the preferred treatment modality when the vision corrected with spectacles or soft contact lenses is no longer acceptable to the patient.[4,5] Approximately 10% to 20% of patients with keratoconus undergo penetrating keratoplasty when rigid contact lenses no longer provide adequate vision or when the patient becomes intolerant to the rigid lenses.[4,6] Most clinicians would agree that the BCVA of patients with keratoconus decreases over the course of the disease, but no prospective study has yet verified this finding.

Various degrees of visual change have been sporadically reported in the literature. Most studies indicate a loss of vision or contrast sensitivity as the disease progresses[1]; however, one retrospective study showed that the average BCVA in a group of nonsurgical patients with keratoconus improved from 20/30 to 20/25 over the 4-year study period.[4] Reports in the literature suggest that BCVA of 20/50 or worse is a predictor of the need for surgical treatment of keratoconus with penetrating keratoplasty.[4] A longitudinal evaluation of BCVA and the factors relating to visual acuity changes in patients with keratoconus is important. Clinicians will be able to use this information to counsel patients and formulate treatment plans.

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## METHODS

The Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study is a 16-center, longitudinal observational study of patients with keratoconus. A total of 1209 eligible patients were enrolled between May 31, 1995 and June 29, 1996. The protocol used for the study is described in detail elsewhere.[7] The procedures outlined below are those relevant to the present report. The CLEK Study protocol was approved by each clinic's institutional review board, in compliance with the tenets of the Declaration of Helsinki, and the clinics obtained informed consent from each patient.

### Study Sample

The database used in this analysis was selected from the original CLEK Study sample of 2416 eyes from 1209 subjects, with the number of eyes being reduced by 142 because of subjects who did not complete the year 1 examination, the examination that served as baseline for this report for reasons discussed in the next section. In addition, 282 eyes were excluded because of our a priori decision to eliminate all subjects

who had penetrating keratoplasty in either eye at the year 1 visit. We also excluded 16 eyes that were characterized as probably or definitely visually unstable due to a fundus abnormality of the macula, paramacula, or periphery and 48 eyes because their visual acuity measurement was made at a 1-m viewing distance at baseline. Finally, we excluded 73 eyes because the available data did not permit the calculation of the slope of the change in either high- or low-contrast BCVA, where the slope was defined as appropriate for evaluation only if there were usable acuity measures at year 1 and at least two subsequent regular CLEK visits that preceded an incident penetrating keratoplasty in the relevant eye. This set of exclusion criteria removed 561 eyes from analysis and produced an analysis dataset that contained 1855 eyes from 953 subjects, 51 with one eye that could be evaluated and 902 with two eyes that could be evaluated.

## Duration of Follow-up

The CLEK Study included annual visits at baseline and for 8 years of subsequent follow-up. Because of an apparent learning curve on the part of the patients that yielded a presumably anomalous measured improvement in visual acuity between baseline and year 1 (a difference of $0.85 \pm 5.66$ and $1.53 \pm 1.53$ letters correct [mean $\pm$ SD] for high- and low-contrast acuity, respectively), an assessment of change in visual acuity could have been biased if it included the baseline visit in the analysis. This improvement was assumed to be anomalous because there is no evidence that vision in keratoconus generally improves with time and disease progression. As a result, the present report presents data that reflect changes over time between the year 1 visit and the year 8 visit, with the year 1 visit designated as "baseline" in all analyses presented.

## Visual Acuity Assessment

Bailey-Lovie[8] distance visual acuities were measured using the available high- and low-contrast (Michelson contrast 10%) Bailey-Lovie charts. The chart was located at 4 m, and the white background of the chart had a standard luminance ($70–110$ cd/m$^2$), calibrated weekly. If the patient could not correctly identify all five of the letters on the top line of the Bailey-Lovie chart at 4 m, the patient was moved forward to a 1-m test distance.

Visual acuity was measured in three ways: (1) entrance visual acuity: high- and low-contrast with habitual correction, for each eye separately and with both eyes together; (2) BCVA: high- and low-contrast with best correction (for rigid contact lens wearers, their rigid contact lenses with optimal overrefraction; for other patients, a CLEK Study trial contact lens with base curve radius equal to the steep keratometric reading plus optimal overrefraction), for each eye separately; and (3) manifest refraction visual acuity: high-contrast Bailey-Lovie visual acuity with manifest refraction, for each eye separately. Patients read the chart beginning at the top during each measure until they missed at least three letters on a line on which they attempted to read every letter. Visual acuity scores were recorded as the total number of letters correct.

## First Definite Apical Clearance Lens (FDACL)

A protocol for determining the first definite apical clearance lens (FDACL) to provide a measure of corneal curvature was developed specifically for the CLEK Study.[7] A rigid contact lens from the CLEK Study trial lens set with a base curve radius equal to the steep keratometric reading was applied. If the initial trial lens was judged to be flat centrally, a steeper trial lens was applied to the eye for fluorescein pattern evaluation. This procedure was repeated until an apical clearance pattern was achieved. Therefore, the objective of the contact lens fitting procedure was to find the flattest lens in the trial lens set that exhibited a definite apical clearance fluorescein pattern such that the sagittal depth of the base-curve chord diameter was greater than the sagittal depth of the cornea for the same chord diameter. If the initial trial lens was judged to be steep centrally, a flatter trial lens was applied to the cornea for fluorescein pattern evaluation. This proce-

dure was repeated until apical touch was observed. The FDACL protocol was not performed on grafted eyes. The CLEK Study trial lens set's base curve radii were measured monthly to ensure that the lenses were in the proper order and that none of the lenses was warped. The fluorescein pattern of the FDACL and the lens with base curve radius 0.2 mm flatter were photographed. Exposed but undeveloped film was mailed to the CLEK Photography Reading Center for centralized development, labeling, and grading.

## Outcome Measures

We report results on two outcomes that measure change in high-contrast BCVA and two outcomes that measure change in low-contrast BCVA. The first high-contrast BCVA outcome is an eye-specific measure of change that is quantified using the slope of the within-eye regression line that describes changes over 7 years. The calculated slope is a measure of the change per year in the number of high-contrast letters correctly read. It can be multiplied by 7 to compute the projected change in the number of letters correctly read over a 7-year period. The slope was coded as missing for a given eye if, in addition to the year 1 assessment, there were $<2$ valid data points that preceded any incident penetrating keratoplasty in the relevant eye. Second, high-contrast BCVA is presented as a dichotomous outcome variable measuring subject-specific change in high-contrast BCVA, defined by whether the year 1 to 8 deterioration in the outcome was $\geq 10$ letters (0.2 log MAR or 2 lines) in one or more eyes that could be evaluated for a given patient. A 10-letter reduction in visual acuity corresponds to a 2-line decrease in visual acuity. We considered this to be clinically significant and to result in a subjective decrease in vision, as well. Chia and coworkers defined visual impairment as visual acuity $< 20/40$,[9] which, for patients presenting with "normal" (i.e., 20/20) visual acuity at baseline, would be consistent with a two-line reduction in visual acuity. For the purposes of this variable, a decrement of $\geq 10$ letters was defined as having occurred during the 7-year period if the slope of the regression line for that eye was $< -1.43$ letters/year, a figure which, when multiplied by 7, yields a decrease of 10 letters. The corresponding outcome measures that quantify change in low-contrast BCVA are precisely analogous to those just described for high-contrast BCVA.

## Statistical Methods

Initial analyses focused on evaluating univariate associations between potential predictors and each of the outcome measures; these univariate associations were used to identify candidate predictors for subsequent multivariate modeling. For the regression slopes (the eye-specific outcome measures), univariate associations involving patient-specific covariates like age and gender were analyzed using the mean slope across eyes when data for a patient were available for both eyes. In this setting, Pearson correlation coefficients were used to assess the relations between the mean slope and the continuous predictors, and *t*-tests or analyses of variance were used to compare the mean slopes across the categories of dichotomous and polychotomous predictors. For eye-specific covariates like FDACL and year 1 acuity measures, Pearson correlation coefficients were computed to assess the relations between slopes and predictors on an eye-specific basis. Predictors whose univariate associations with within-eye regression slopes yielded a $P$-value $< 0.1$ were included in stepwise mixed-model analyses where the eye was the unit of analysis and where the correlation between eyes was taken into account. Statistical contrasts were computed to perform pairwise comparisons of polychotomous predictors (e.g., the number of eyes that were scarred). The least square means option of the MIXED procedure in SAS[10] was then used to quantify and produce confidence bounds on the adjusted difference between the effect on the regression slope of having, say, one scarred eye compared with having zero scarred eyes.

When the outcome was a dichotomous, subject-specific measure of whether visual acuity in at least one eye in a given subject deteriorated by $\geq 10$ letters correct, all analyses were performed on a subject-

TABLE 1. Characteristics of the CLEK Study Sample

| Variable | Mean ± SD or Percentage (*n*) |
|---|---|
| ***Subject-Specific Covariates*** | |
| Age (y) | 40.2 ± 11 (953) |
| Gender | |
| Female | 44.4% (423/953) |
| Male | 55.6% (530/953) |
| Race | |
| American Indian/Alaska native | 0.6% (6/953) |
| Asian or Pacific Islander | 1.8% (17/953) |
| Black, non-Hispanic | 17.4% (166/953) |
| Hispanic | 7.1% (68/953) |
| White, non-Hispanic | 71.9% (685/953) |
| Other | 1.2% (11/953) |
| Family history of keratoconus | 13.4% (128/953) |
| Atopy (hay fever, allergies, asthma, atopic dermatitis) | 58.8% (560/953) |
| ***Eye-Specific Covariates at Year 1*** | |
| Contact lens wearing time (hours) | 12.6 ± 4.8 (1556) |
| Contact lens comfort (1–5, 5 = worst) | 2.48 ± 1.2 (1549) |
| FDACL (D) | 50.4 ± 5.2 (1852) |
| Flat keratometric reading (D) | 47.5 ± 5.0 (1850) |
| Steep keratometric reading (D) | 50.5 ± 5.6 (1847) |
| ***Acuity Measures (Letters Correct) at Year 1*** | |
| High-contrast BCVA | 49.3 ± 8.1 (1854) |
| Low-contrast BCVA | 35.7 ± 9.6 (1834) |
| High-contrast entrance | 46.4 ± 9.7 (1820) |
| Low-contrast entrance | 33.7 ± 10.2 (1754) |
| ***Covariates Quantified by Number of Eyes Affected*** | |
| Probable/definite scar | |
| 0 | 53.3% (508/953) |
| 1 | 27.7% (264/953) |
| 2 | 19.1% (181/953) |
| Contact lenses | |
| 0 | 14.7% (140/953) |
| 1 | 4.0% (38/953) |
| 2 | 81.3% (775/953) |
| RGP-type lenses | |
| 0 | 15.6% (145/932) |
| 1 | 5.3% (49/932) |
| 2 | 79.2% (738/932) |
| Vogt's striae | |
| 0 | 34.5% (329/953) |
| 1 | 33.1% (315/953) |
| 2 | 32.4% (309/953) |
| Fleischer's ring | |
| 0 | 10.0% (95/953) |
| 1 | 21.7% (207/953) |
| 2 | 68.3% (651/953) |
| Eye rubbing | |
| 0 | 47.7% (439/921) |
| 1 | 1.6% (15/921) |
| 2 | 50.7% (467/921) |
| Corneal staining | |
| 0 | 64.3% (613/953) |
| 1 | 21.2% (202/953) |
| 2 | 14.5% (138/953) |
| Ocular trauma | |
| 0 | 91.3% (865/947) |
| 1 | 7.1% (67/947) |
| 2 | 1.6% (15/947) |
| Lens opacity | |
| 0 | 95.5% (910/953) |
| 1 | 1.3% (12/953) |
| 2 | 3.3% (31/953) |
| Abnormal macula | |
| 0 | 98.3% (937/953) |
| 1 | 1.2% (11/953) |
| 2 | 0.5% (5/953) |

TABLE 1. (*continued*). Characteristics of the CLEK Study Sample

| Variable | Mean ± SD or Percentage (*n*) |
|---|---|
| Fundus (other findings) | |
| 0 | 85.0% (810/953) |
| 1 | 9.3% (89/953) |
| 2 | 5.7% (54/953) |
| Abnormal paramacular periphery | |
| 0 | 92.4% (881/953) |
| 1 | 4.8% (46/953) |
| 2 | 2.7% (26/953) |
| ***Outcome Measures*** | |
| Slope | |
| High-contrast BCVA change | −0.29 ± 1.5 (1853) |
| Low-contrast BCVA change | −0.58 ± 1.7 (1834) |
| 10-letter decrease in BCVA (either eye) | |
| High-contrast | 19.0% (181/951) |
| Low-contrast | 30.8% (293/951) |

Means for continuous variables computed using all eyes for which data were available. The year 1 assessment defined initial baseline measurements. A 10-letter decrease in high- or low-contrast visual acuity is equivalent to 0.2 log MAR (0.02 log MAR/letter).

specific basis that used the mean of all eye-specific predictors in the analyses. With these outcomes, the initial analyses included Pearson correlation coefficients for continuous predictors, *t*-tests for dichotomous predictors, and analyses of variance for polychotomous predictors. All variables that produced a *P*-value < 0.1 were then included in stepwise logistic regression analyses that produced a best set of independent predictors. Odds ratios and associated 95% confidence bounds were computed to quantify the magnitude of the significant effects. When the predictor was a measure of letters correctly read at year 1, the variable was entered into the model after dividing by 5 so that odds ratios would refer specifically to the effect on the outcome measure of a difference of a full line instead of a single letter correct.

## RESULTS

From our dataset of 1855 eyes from 953 subjects, the regression slope describing the change from year 1 to 8 in high-contrast BCVA could be calculated in 1853 eyes from 951 subjects. The slope for low-contrast BCVA was available in 1834 eyes from 951 subjects. Table 1 contains year 1 descriptive statistics for all subject- and eye-specific outcome measures and covariates. For completeness, it also contains data on visual acuity measures and measures of contact lens wear and comfort, variables that are not subsequently evaluated as covariates. Table 1 indicates that the mean age of the study sample subjects was 40.2 ± 11 years. Overall, 423 (44.4%) of 953 subjects were female, and 685 (71.9%) of 953 were white. When averaged across all eyes, the slope of the change in high-contrast BCVA over the 7-year follow-up period was −0.29 ± 1.5 letters correct per year. The corresponding slope for low-contrast BCVA was −0.58 ± 1.7 letters correct per year. In interpreting these slopes, it is important to emphasize that because the tabulated values are in letters correct per year and because the follow-up period was 7 years, one must multiply the slope by 7 to compute mean expected changes over the entire follow-up period. Thus, the mean expected decrease in high-contrast BCVA over 7 years was 0.29 × 7 or 2.03 letters correct, while the corresponding expected decrease in low-contrast acuity was 0.58 × 7 or 4.06 letters correct. Table 1 also indicates that 19.0% of subjects had a projected 7-year decrease in high-contrast BCVA of ≥10 letters correct in at least one eye, where the projections were calculated using the eye-specific regression slope to compute projected changes

from year 1 to 8. The corresponding rate at which low-contrast BCVA decreased by ≥10 letters correct was 30.8%.

Figures 1 and 2 depict the mean high- and low-contrast visual acuity as a function of year of examination. There was an overall decrease in the mean high-contrast acuity from 49.28 to 47.61 letters correct over 7 years of follow-up, with a corresponding decrease from 35.62 to 32.32 letters correct in mean low-contrast acuity.

Table 2 describes the unadjusted association between potential predictors and the slope of the line describing change over time in high- and low-contrast BCVA. The negative correlation coefficients between the slope of the change in high-contrast acuity and year 1 values of FDACL ($r = -0.084$, $P = 0.0003$), the flat keratometric reading ($r = -0.052$, $P = 0.026$), the steep keratometric reading ($r = -0.070$, $P = 0.003$), high-contrast BCVA ($r = -0.184$, $P < 0.0001$), and low-contrast BCVA ($r = -0.073$, $P = 0.002$) all indicate that the greater the year 1 value of these predictors, the greater the deterioration in high-contrast BCVA by year 8. The third section of Table 2 indicates that high-contrast BCVA was significantly associated with the number of eyes that had a probable or definite scar ($P = 0.005$), the number of eyes with Vogt's striae ($P = 0.028$), and the number of eyes with fundus abnormalities other than an abnormal macula or an abnormal paramacular periphery ($P = 0.015$). It should be noted in the latter context that because Table 2 demonstrates an ordered relation between the high-contrast BCVA slope and the number of eyes with Vogt's striae, Vogt's striae was treated as an ordered variable with a value ranging from 0 to 2. However, because Table 2 shows no such ordering with respect to scarring and other fundus findings, the latter variables were treated as strictly categorical variables taking on the values 0, 1, or 2. Because the data about low-contrast BCVA in Table 2 are fully analogous to the high-contrast BCVA data, the details are not discussed here, but the detailed consideration of the associations reported are contained in Table 2.

Table 3 presents the results of stepwise mixed-model analyses of covariance focused on determining independent predictors of the slope of the change in high- and low-contrast BCVA (Tables 3A and 3B, respectively). With two exceptions, candidate variables for these models included all variables in Table 2 that had a significant ($P < 0.05$) or borderline significant ($P < 0.1$) association with the outcome measure. The first exception was that because of the high correlation between FDACL, the flat keratometric reading, and the steep keratomet-

ric reading, FDACL was selected as the only candidate variable among these three because it had the highest correlation with both outcome measures. The second exception was that the year 1 high-contrast BCVA measure was not included as a potential predictor of low-contrast BCVA slope and did not include the year 1 low-contrast BCVA measure as a potential predictor of high-contrast BCVA slope.

Table 3A indicates that year 1 high-contrast BCVA ($P < 0.0001$), FDACL ($P < 0.0001$), the number of eyes with scars at year 1 ($P = 0.006$), and the number of eyes with other fundus findings at year 1 ($P = 0.023$) were the only significant independent predictors of the slope of the change in high-contrast BCVA. Visual acuity data were entered into the model after dividing the number of letters correct by 5, meaning that the regression coefficient should be interpreted as making predictions about changes in regression slope as a function of the number of lines that were correctly read during year 1. Thus, the tabulated regression slope of $-0.26 \pm 0.02$ (95% confidence bounds: $-0.30$ to $-0.22$) for high-contrast BCVA means that, after adjusting for covariates, the visual acuity of an eye that could discern one line more than another eye at year 1 could be expected to deteriorate at a rate of ~0.26 letters/year more or by a total of $0.26 \times 7 = 1.82$ letters more over a 7-year period. If the year 1 difference in lines read is 3 at year 1, then the corresponding adjusted difference in the expected deterioration is 0.78 letters/year or 5.46 letters over a 7-year period. A similar interpretation can be applied to the tabulated FDACL regression coefficient of $-0.7 \pm 0.007$, with the exception that FDACL was quantified in the model in terms of a single diopter. Thus, each diopter of FDACL predicted an increased deterioration of $0.7 \times 7 = 0.49$ high-contrast letters correct.

Effect sizes for categorical variables in Table 3 were quantified using a different approach. For example, Table 3A indicates that the comparison of subjects with one versus neither eye scarred at year 1 yields an expected covariate-adjusted difference in change in the slope of the within-subject regression line of $0.12 \pm 0.08$ letters/year, or 0.84 letters over a 7-year period. The positive coefficient of 0.12 means that the visual acuity of an eye of a subject with one eye scarred as opposed to no eyes scarred is expected to deteriorate by a greater magnitude than that of a subject with no scars at year 1. The negative effect size of $-0.32 \pm 0.10$ in the comparison of the eyes of subjects with one versus two scars at year 1 means that the visual acuity of an eye of a subject with two eyes scarred can be expected to deteriorate by a smaller mag-
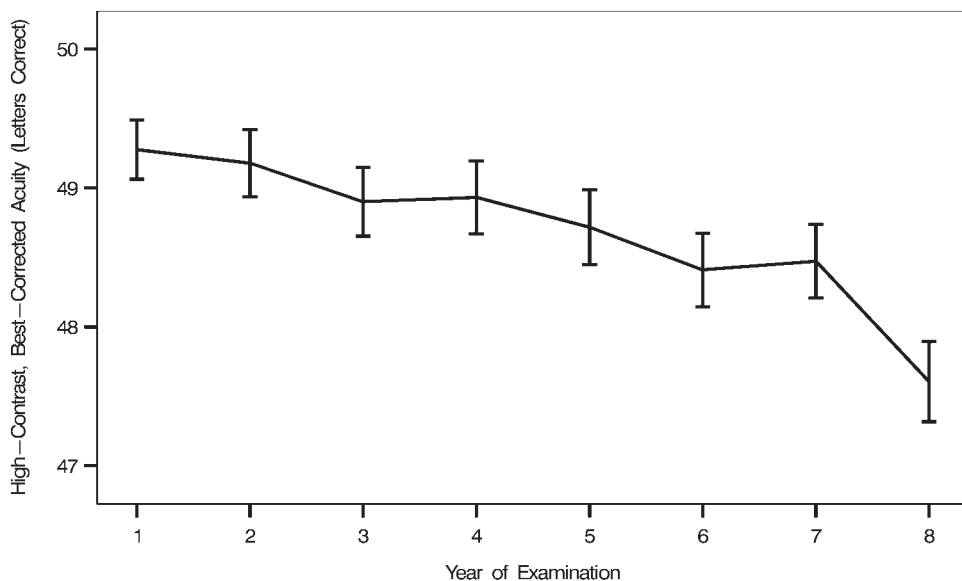


**FIGURE 1.** Mean high-contrast BCVA, averaged across the right and left eyes, over time. Values are means ± SEM of both eyes as a function of the follow-up visit.
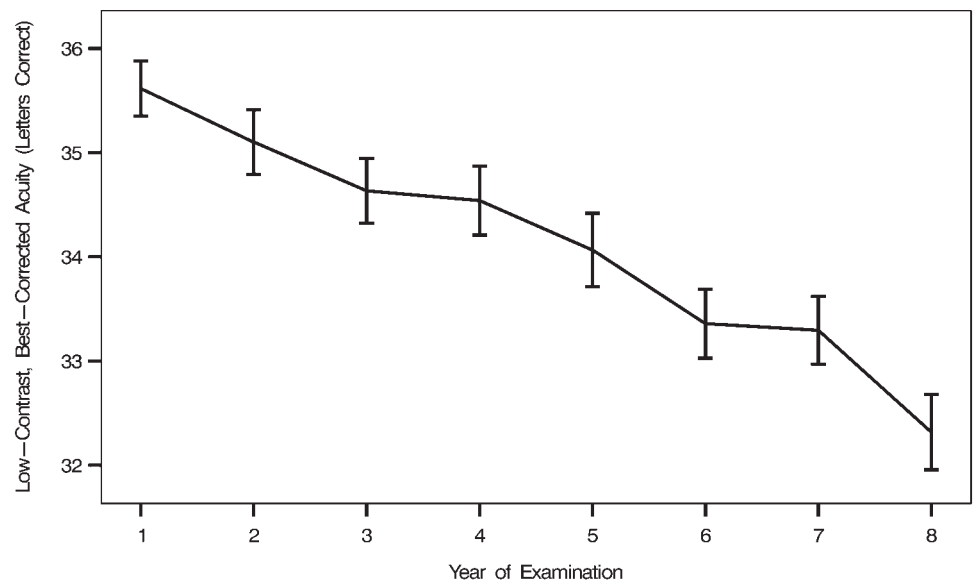
FIGURE 2. Mean low-contrast BCVA, averaged across the right and left eyes, over time. Values are means ± SEM of both eyes as a function of the follow-up visit.

nitude (0.32 letters/year or 2.24 letters over 7 years) than that of a subject with one scar. In interpreting these data, it should be emphasized that the visual acuity of fewer than 3% of eyes enabled subjects to read <30 (20/40 Snellen equivalent) or >65 (20/8 Snellen equivalent) letters at year 1. Thus, the application of these results to eyes outside this specified range is highly uncertain due to small sample sizes in the outlying ranges.

Table 3B shows that the only predictors of low-contrast BCVA were the year 1 low-contrast BCVA ($P < 0.0001$) and FDACL ($P < 0.0001$), with less impressive prediction by the number of eyes with corneal scarring ($P = 0.044$) and an abnormal macula at year 1 ($P = 0.075$). The interpretation of the tabulated measures of the size of the effect follows the same logic discussed above.

Table 4 presents unadjusted bivariate data measuring the association between potential predictors and two dichotomous, patient-specific outcome measures. The outcome measures are whether, in accordance with the definition in the Methods section, the patient experienced a deterioration in high-contrast and low-contrast BCVA of ≥10 letters in either eye. Because the outcome measures are patient specific, patient-specific predictors were generated using the mean of all eye-specific measures as the value of the predictor whenever data were available from two eyes. The first column in Table 4 indicates that factors associated with an increased likelihood of deterioration by ≥10 letters in high-contrast BCVA were race other than non-Hispanic white ($P = 0.015$), steeper FDACL ($P < 0.0001$), steeper flat keratometric reading ($P = 0.023$), steeper steep keratometric reading ($P = 0.006$), corneal scarring ($P = 0.058$), Vogt's striae ($P = 0.003$), Fleischer's ring ($P = 0.034$), eye rubbing ($P = 0.024$), corneal staining ($P = 0.039$), and an abnormal macula ($P = 0.018$). Variables that had a univariate association with a deterioration of ≥10 letters in low-contrast BCVA included race other than non-Hispanic white ($P = 0.002$), steeper FDACL ($P = 0.0003$), steeper steep keratometric reading ($P = 0.016$), better year 1 low-contrast BCVA ($P = 0.077$), and Vogt's striae ($P = 0.022$).

Table 5 presents the results of a stepwise logistic regression that generates a model consisting of independent predictors of a decrease of ≥10 letters in at least one eye, with all variables with an independent $P$-value < 0.1 included in the model. Table 5A indicates that the significant independent predictors of deterioration in high-contrast acuity were a steeper FDACL (odds ratio/D = 1.07, $P = 0.0002$) and, to a lesser extent, the

number of eyes affected by Vogt's striae ($P = 0.033$, odds ratio = 1.75 [comparing 1 vs. 2 eyes]; 1.61 [2 vs. 0 eyes]), the number of eyes affected by Fleischer's ring ($P = 0.056$, odds ratio = 0.54 for both 1 vs. 0 and 2 vs. 0 eyes), and race other than non-Hispanic white (odds ratio = 1.39, $P = 0.073$). Note that these data indicate that the presence of Vogt's striae at baseline increases the odds of a decrease of 10 letters in high-contrast acuity, whereas the presence of Fleischer's ring at baseline has the opposite effect on high-contrast acuity. The only independent predictors of a decrease in low-contrast BCVA of ≥10 letters in at least one eye were better year 1 low-contrast BCVA (odds ratio per visual acuity line = 1.20, $P = 0.0002$), steeper FDACL (odds ratio/D = 1.04, $P = 0.0003$), and race other than non-Hispanic white (odds ratio = 1.51, $P = 0.008$).

## DISCUSSION

The frequency with which poor visual acuity is reported as the primary reason for penetrating keratoplasty varies. Lim and Vogt[11] identified inadequate visual acuity as the primary reason for surgery in 8.5% of keratoconus patients undergoing penetrating keratoplasty. Contact lens intolerance or instability of the contact lens fit was reported in the remaining 91.5% of patients who received surgery. Because an inadequate contact lens fit or poor contact lens comfort also means that the patient cannot see clearly, Lim and Vogt[11] essentially cited visual acuity as an indirect or direct reason for all cases of penetrating keratoplasty for keratoconus. Dana and co-workers[12] retrospectively examined the reason for surgery in 99 consecutive patients with keratoconus who had undergone penetrating keratoplasty and found that the primary reasons were visual acuity, 43% of cases; contact lens intolerance, 32% of cases; frequent lens displacement, 13% of cases; and peripheral corneal thinning, 12% of cases. Visual performance is therefore an essential factor when determining whether surgical intervention should be considered and as an outcome measure of the success of surgery.[5] Also, both clinicians and patients have a keen interest in the rate and degree of visual acuity change associated with keratoconus along with the effect of other clinical findings that influence such change. In addition to quantifying the progressive reduction in visual acuity, we identify risk factors associated with diminishing visual acuity in a large cross-sectional sample of patients who presented with

TABLE 2. Univariate Associations with the Slope of Change in High- and Low-Contrast BCVA

| Variable | High-Contrast BCVA | | Low-Contrast BCVA | |
|---|---|---|---|---|
| | Slope or Correlation | *P* | Slope or Correlation | *P* |
| ***Subject-Specific Covariates**** | | | | |
| Age | *r* = 0.033 | 0.31 | *r* = 0.037 | 0.255 |
| Gender | | 0.12 | | 0.79 |
| Female | −0.37 ± 1.3 | | −0.58 ± 1.3 | |
| Male | −0.25 ± 1.0 | | −0.60 ± 1.6 | |
| Race | | 0.11 | | 0.058 |
| White, non-Hispanic | −0.26 ± 1.0 | | −0.53 ± 1.5 | |
| Other | −0.40 ± 1.5 | | −0.74 ± 1.4 | |
| Family history | | 0.36 | | 0.21 |
| No | −0.31 ± 1.2 | | −0.61 ± 1.5 | |
| Yes | −0.21 ± 0.9 | | −0.43 ± 1.4 | |
| Atopy | | 0.09 | | 0.68 |
| No | 0.38 ± 1.2 | | −0.61 ± 1.3 | |
| Yes | −0.25 ± 1.1 | | −0.57 ± 1.6 | |
| ***Eye-Specific Covariates at Year 1†*** | | | | |
| FDACL | *r* = −0.084 | 0.0003 | *r* = −0.118 | <0.0001 |
| Flat keratometric reading | *r* = −0.052 | 0.026 | *r* = −0.064 | 0.006 |
| Steep keratometric reading | *r* = −0.070 | 0.003 | *r* = −0.089 | 0.0001 |
| High-contrast BCVA | *r* = −0.184 | <0.0001 | *r* = −0.075 | 0.001 |
| Low-contrast BCVA | *r* = −0.073 | 0.002 | *r* = −0.153 | <0.0001 |
| ***Number of Eyes Affected**** | | | | |
| Probable/definite scar | | 0.005 | | 0.028 |
| 0 (*n* = 508) | −0.25 ± 1.0 | | −0.50 ± 1.4 | |
| 1 (*n* = 263) | −0.49 ± 1.5 | | −0.80 ± 1.9 | |
| 2 (*n* = 181) | −0.16 ± 1.0 | | −0.52 ± 1.1 | |
| Contact lenses | | 0.23 | | 0.93 |
| 0 (*n* = 140) | −0.23 ± 1.3 | | −0.58 ± 1.4 | |
| 1 (*n* = 38) | −0.59 ± 2.7 | | −0.50 ± 1.3 | |
| 2 (*n* = 774) | −0.30 ± 1.0 | | −0.60 ± 1.5 | |
| RGP-type lenses | | 0.20 | | 0.83 |
| 0 (*n* = 145) | −0.21 ± 1.3 | | −0.56 ± 1.4 | |
| 1 (*n* = 49) | −0.55 ± 2.4 | | −0.45 ± 1.4 | |
| 2 (*n* = 737) | −0.29 ± 1.0 | | −0.58 ± 1.5 | |
| Vogt's striae‡ | | 0.028 | | 0.004 |
| 0 (*n* = 329) | −0.21 ± 0.9 | | −0.43 ± 1.4 | |
| 1 (*n* = 315) | −0.28 ± 1.5 | | −0.58 ± 1.3 | |
| 2 (*n* = 308) | −0.42 ± 1.1 | | −0.77 ± 1.8 | |
| Fleischer's ring | | 0.52 | | 0.22 |
| 0 (*n* = 95) | −0.21 ± 1.5 | | −0.55 ± 1.7 | |
| 1 (*n* = 206) | −0.25 ± 0.9 | | −0.44 ± 1.5 | |
| 2 (*n* = 648) | −0.33 ± 1.2 | | −0.64 ± 1.5 | |
| Eye rubbing | | 0.88 | | 0.84 |
| 0 (*n* = 439) | −0.30 ± 1.0 | | −0.59 ± 1.3 | |
| 1 (*n* = 15) | −0.44 ± 1.1 | | −0.35 ± 1.7 | |
| 2 (*n* = 466) | −0.29 ± 1.3 | | −0.59 ± 1.6 | |
| Corneal staining | | 0.18 | | 0.32 |
| 0 (*n* = 612) | −0.29 ± 1.2 | | −0.56 ± 1.6 | |
| 1 (*n* = 202) | −0.22 ± 1.0 | | −0.57 ± 1.1 | |
| 2 (*n* = 138) | −0.46 ± 1.2 | | −0.77 ± 1.4 | |
| Ocular trauma | | 0.25 | | 0.13 |
| 0 (*n* = 864) | −0.32 ± 1.1 | | −0.61 ± 1.5 | |
| 1 (*n* = 67) | −0.08 ± 1.2 | | −0.26 ± 1.1 | |
| 2 (*n* = 15) | −0.45 ± 1.3 | | −0.93 ± 2.2 | |
| Lens opacity | | 0.22 | | 0.72 |
| 0 (*n* = 909) | −0.29 ± 1.2 | | −0.60 ± 1.5 | |
| 1 (*n* = 12) | −0.87 ± 1.1 | | −0.70 ± 1.4 | |
| 2 (*n* = 31) | −0.29 ± 1.1 | | −0.38 ± 1.5 | |
| Abnormal macula | | 0.16 | | 0.10 |
| 0 (*n* = 936) | −0.30 ± 1.2 | | −0.58 ± 1.5 | |
| 1 (*n* = 11) | −0.15 ± 0.5 | | −0.55 ± 0.9 | |
| 2 (*n* = 5) | −1.3 ± 1.1 | | −2.0 ± 2.2 | |
| Fundus other findings | | 0.015 | | 0.42 |
| 0 (*n* = 809) | −0.28 ± 1.1 | | −0.61 ± 1.6 | |
| 1 (*n* = 89) | −0.22 ± 0.7 | | −0.39 ± 1.1 | |
| 2 (*n* = 54) | −0.74 ± 2.1 | | −0.66 ± 1.1 | |

(*continues*)

**TABLE 2.** (*continued*). Univariate Associations with the Slope of Change in High- and Low-Contrast BCVA

| | High-Contrast BCVA | | Low-Contrast BCVA | |
|---|---|---|---|---|
| **Variable** | **Slope or Correlation** | **P** | **Slope or Correlation** | **P** |
| ***Number of Eyes Affected\* (continued)*** | | | | |
| Abnormal paramacular periphery | | 0.31 | | 0.25 |
| 0 (*n* = 880) | −0.30 ± 1.2 | | −0.60 ± 1.5 | |
| 1 (*n* = 46) | −0.12 ± 0.7 | | −0.29 ± 1.2 | |
| 2 (*n* = 26) | −0.56 ± 0.7 | | −0.88 ± 1.3 | |

    \* Results based on mean BCVA across eyes when data on both eyes were available. Values are means ± SD.

    † Correlation coefficients computed across all eyes; positive coefficient indicates that larger year 1 value of the predictor is associated with less deterioration in the outcome measure.

    ‡ *P*-value computed treating number of eyes affected as an ordered variable.

moderate to advanced keratoconus and who have been followed for 7 years.

## Eye-Specific Predictors of Increased Deterioration

The results show a modest, progressive, eye-specific average reduction in BCVA over a period of 7 years. The average 7-year reduction in low-contrast visual acuity (4.06 letters correct) was twice that measured for high-contrast visual acuity (2.03 letters correct). A reduction in contrast sensitivity function before a measurable decrease in visual acuity in eyes with keratoconus has been reported previously.[13] Thus, these data,

based on low-contrast visual acuity rather than contrast sensitivity, agree with previous results.

Perhaps the most important conclusions from these data are the eye-specific characteristics associated with rapid deterioration of visual acuity. The presence of typical clinical measures indicative of more severe disease severity (e.g., steeper corneal curvatures, corneal scars, and the presence of Vogt's striae)[7,14] were associated with more rapid deterioration of vision. Because reduced visual acuity is present before penetrating keratoplasty, our results corroborate the results of a previous retrospective study reported by Sray et al.[15] They found that

**TABLE 3.** Independent Predictors of the Slope of Change in BCVA

| | | | *P* | |
|---|---|---|---|---|
| **Predictor** | **Magnitude of Effect\*** | **95% Confidence Bounds** | **Contrast†** | **Main Effect** |
| ***A. High-Contrast BCVA (R² = 0.085)*** | | | | |
| High-contrast BCVA at year 1‡ | −0.26 ± 0.02 | −0.30, −0.22 | | <0.0001 |
| FDACL at year 1 | −0.07 ± 0.007 | −0.081, −0.052 | | <0.0001 |
| Eyes with scars at year 1§ | | | | 0.006 |
|    0 vs. 1 | 0.12 ± 0.08 | −0.04, 0.27 | 0.15 | |
|    0 vs. 2 | −0.20 ± 0.10 | −0.39, −0.02 | 0.03 | |
|    1 vs. 2 | −0.32 ± 0.10 | −0.52, −0.12 | 0.001 | |
| Eyes with other fundus findings at year 1§ | | | | 0.023 |
|    0 vs. 1 | −0.02 ± 0.11 | −0.25, 0.20 | 0.84 | |
|    0 vs. 2 | 0.39 ± 0.14 | 0.11, 0.67 | 0.007 | |
|    1 vs. 2 | 0.41 ± 0.18 | 0.07, 0.76 | 0.020 | |
| ***B. Low-Contrast BCVA (R² = 0.072)*** | | | | |
| Low-contrast BCVA at year 1‡ | −0.24 ± 0.02 | −0.28, −0.19 | | <0.0001 |
| FDACL at year 1 | −0.09 ± 0.009 | −0.11, −0.07 | | <0.0001 |
| Eyes with scars at year 1§ | | | | 0.04 |
|    0 vs. 1 | 0.18 ± 0.11 | −0.02, 0.39 | 0.08 | |
|    0 vs. 2 | −0.13 ± 0.13 | −0.38, 0.11 | 0.29 | |
|    1 vs. 2 | −0.32 ± 0.13 | −0.58, −0.06 | 0.016 | |
| Fundus abnormal macula at year 1‖ | | | | 0.08 |
|    0 vs. 1 or 2 | 0.63 ± 0.35 | −0.06, 1.32 | | |

    Results based on mixed-model stepwise analyses of covariance that account for correlation between eyes and use backward elimination to select the final set of predictors.

    \* Defined as the adjusted regression coefficient for continuous variables (baseline BCVA and FDACL) and as the adjusted (least square mean) estimate of the difference for each contrast for categorical variables (scarring and other fundus findings). Values are means ± SD.

    † Only relevant for predictors that have three categories and that are treated as categorical variables.

    ‡ BCVA quantified in units of 5 letters correct.

    § A positive effect value indicates that the greater the number of eyes affected, the greater the adjusted deterioration in high-contrast acuity over time.

    ‖ The 1- and 2-eye categories were combined because of the small number of cases.

TABLE 4. Subject Characteristics by Projected Decrease in Both High- and Low-Contrast BCVA of ≥10 Letters in at Least One Eye over 7 Years

| Variable | High-Contrast BCVA Decrease ≥ 10 Letters Correct (19.0%) | | Low-Contrast BCVA Decrease ≥ 10 Letters Correct (30.8%) | |
| --- | --- | --- | --- | --- |
| | Mean ± SD or Percentage | *P* | Mean ± SD or Percentage | *P* |
| *Patient-Specific Covariates* | | | | |
| Age (y) | | 0.41 | | 0.200 |
| Decrease < 10 letters correct | 40.4 ± 10 | | 40.5 ± 10 | |
| Decrease ≥ 10 letters correct | 39.6 ± 13 | | 39.6 ± 12 | |
| Gender | | 0.54 | | 0.89 |
| Female | 19.9% | | 30.6% | |
| Male | 18.3% | | 31.0% | |
| Race | | 0.015 | | 0.002 |
| White, non-Hispanic | 17.1% | | 27.9% | |
| Other | 24.0% | | 38.2% | |
| Family history | | 0.74 | | 0.62 |
| No | 19.2% | | 31.1% | |
| Yes | 18.0% | | 28.9% | |
| Atopy | | 0.46 | | 0.46 |
| No | 20.2% | | 32.1% | |
| Yes | 18.3% | | 29.9% | |
| *Eye-Specific Covariates at Year 1** | | | | |
| FDACL (D) | | 0.0001 | | 0.0003 |
| Decrease < 10 letters correct | 50.2 ± 4.4 | | 50.1 ± 4.2 | |
| Decrease ≥ 10 letters correct | 51.8 ± 4.6 | | 51.2 ± 5.0 | |
| Flat keratometric reading (D) | | 0.02 | | 0.30 |
| Decrease < 10 letters correct | 47.3 ± 4.3 | | 47.4 ± 4.2 | |
| Decrease ≥ 10 letters correct | 48.1 ± 4.4 | | 47.7 ± 4.5 | |
| Steep keratometric reading (D) | | 0.006 | | 0.016 |
| Decrease < 10 letters correct | 50.2 ± 4.6 | | 50.2 ± 4.5 | |
| Decrease ≥ 10 letters correct | 51.5 ± 4.9 | | 51.0 ± 5.0 | |
| High-contrast BCVA (letters correct) | | 0.71 | | 0.85 |
| Decrease < 10 letters correct | 49.3 ± 6.6 | | 49.3 ± 6.6 | |
| Decrease ≥ 10 letters correct | 49.1 ± 6.8 | | 49.2 ± 6.7 | |
| Low-contrast BCVA (letters correct) | | 0.20 | | 0.08 |
| Decrease < 10 letters correct | 35.8 ± 8.0 | | 35.3 ± 8.0 | |
| Decrease ≥ 10 letters correct | 34.9 ± 8.5 | | 36.3 ± 8.5 | |
| *Number of Eyes Affected* | | | | |
| Probable/definite scar | | 0.058 | | 0.62 |
| 0 | 16.5% | | 29.5% | |
| 1 | 23.7% | | 31.7% | |
| 2 | 19.3% | | 33.2% | |
| Contact lenses | | 0.60 | | 0.28 |
| 0 | 22.1% | | 36.4% | |
| 1 | 18.9% | | 32.4% | |
| 2 | 18.5% | | 29.7% | |
| RGP-type lenses | | 0.51 | | 0.23 |
| 0 | 21.4% | | 35.2% | |
| 1 | 22.9% | | 37.5% | |
| 2 | 18.2% | | 29.4% | |
| Vogt's striae | | 0.003 | | 0.022 |
| 0 | 13.1% | | 25.2% | |
| 1 | 22.3% | | 34.7% | |
| 2 | 22.1% | | 32.8% | |
| Fleischer's ring | | 0.034 | | 0.85 |
| 0 | 28.4% | | 28.4% | |
| 1 | 15.9% | | 30.4% | |
| 2 | 18.6% | | 31.3% | |
| Eye rubbing | | 0.024 | | 0.67 |
| 0 | 18.7% | | 32.4% | |
| 1 | 46.7% | | 33.3% | |
| 2 | 18.7% | | 29.7% | |
| Corneal staining | | 0.039 | | 0.24 |
| 0 | 18.0% | | 30.0% | |
| 1 | 16.8% | | 29.2% | |
| 2 | 26.8% | | 37.0% | |

(*continues*)

TABLE 4. (*continued*). Subject Characteristics by Projected Decrease in Both High- and Low-Contrast BCVA of ≥10 Letters in at Least One Eye over 7 Years

| Variable | High-Contrast BCVA Decrease ≥ 10 Letters Correct (19.0%) | | Low-Contrast BCVA Decrease ≥ 10 Letters Correct (30.8%) | |
|---|---|---|---|---|
| | Mean ± SD or Percentage | *P* | Mean ± SD or Percentage | *P* |
| ***Number of Eyes Affected*** (*continued*) | | | | |
| Ocular trauma | | 0.65 | | 0.23 |
|   0 | 19.1% | | 31.4% | |
|   1 | 16.4% | | 22.4% | |
|   2 | 26.7% | | 40.0% | |
| Lens opacity | | 0.13 | | 0.83 |
|   0 | 18.8% | | 30.6% | |
|   1 | 41.7% | | 33.3% | |
|   2 | 16.1% | | 35.5% | |
| Abnormal macula | | 0.018 | | 0.24 |
|   0 | 19.0% | | 30.8% | |
|   1 | 0.0% | | 18.2% | |
|   2 | 60.0% | | 60.0% | |
| Fundus other findings | | 0.54 | | 0.39 |
|   0 | 19.4% | | 31.3% | |
|   1 | 19.1% | | 24.7% | |
|   2 | 13.2% | | 34.0% | |
| Abnormal paramacular periphery | | 0.31 | | 0.72 |
|   0 | 19.6% | | 30.9% | |
|   1 | 10.9% | | 26.1% | |
|   2 | 15.4% | | 34.6% | |

Projections for each subject are based on the within-subject regression line. Because the outcome measures were subject specific, the computation of mean values across subjects for eye-specific predictors were generated after averaging within-subject values for both eyes. Entries for continuous variables are means ± SD for subjects whose visual acuity did and did not decrease by ≥10 letters; entries for categorical variables are percentages whose visual acuity decreased ≥10 letters.

\* Based on mean of two eyes when available.

corneal scarring and steeper keratometry values were significant risk factors for penetrating keratoplasty in a retrospective sample of 109 keratoconus patients in a corneal referral practice. Interestingly in our study, subjects having two unscarred eyes or two scarred eyes showed a slower rate of monocular visual acuity decrease than those having just one scarred eye. Our results suggest that patients experience a period of more rapid change in the indicators of disease severity, including deterioration of visual acuity, after the development of a scar in one eye.

Although not specific to keratoconus, visual acuity initially deteriorated more rapidly in eyes with fundus abnormalities. Paradoxically, visual function in eyes with better visual acuity at baseline deteriorated more rapidly over the course of the study. This result is at first counterintuitive when combined with the other influential measures that indicate that visual acuity deteriorates more rapidly in eyes having more severe disease. One might at first conclude that eyes with more severe disease would have worse visual acuity, including that measured under conditions of best visual correction. However, the application of a rigid contact lens and overrefraction (present for the measure of BCVA) provide for good neutralization of optical abnormalities even in the majority of eyes having severe disease. One plausible explanation is that eyes having better visual acuity at baseline have "more to lose" as the disease progresses. Small shifts in disease severity are more influential on the visual quality of an eye with better visual acuity compared to an eye with poorer visual acuity. This has not been reported previously. Also, the results could be influenced by the sample selected for analysis. Our rationale for excluding subjects was primarily to eliminate eyes that may have shown a change in visual acuity—better or worse—from baseline for

reasons unrelated to the progression of keratoconus. It is recognized therefore that a disproportionate number of subjects having the most severe disease could have been deleted from the sample, thereby reducing the power to detect the influence of disease severity.

The two negative effects of the decision to exclude subjects who had penetrating keratoplasty in either eye were to produce results that cannot be confidently generalized to a corneal transplant group and to reduce both the overall sample size and the number of subjects with severe disease, thereby reducing statistical power. Because the CLEK Study had substantial power due to its large sample size, these negative effects are probably not prohibitive. Despite these effects, subjects who had undergone penetrating keratoplasty were excluded for the following reasons. All data from eyes that had undergone penetrating keratoplasty were excluded, because such data would reflect disease status in a way that is wholly different from the information provided by eyes that had not undergone penetrating keratoplasty and because such data might not even be a reflection of the underlying disease. Thus, including eyes with penetrating keratoplasty would substantially complicate data interpretation. If one eye had undergone penetrating keratoplasty, the fellow eye was excluded because the experience of penetrating keratoplasty might alter data from the other eye and alter the decision-making process that could lead to penetrating keratoplasty in the nonoperated eye. These factors could lead to biased results.

## Patient-Specific Results

Our data also define the independent, disease-specific predictors of a loss of ≥10 letters in at least one eye as a substantial

TABLE 5. Independent Predictors of a Decrease in BCVA of ≥10 Letters in at Least One Eye

| Predictor | Odds Ratio | Confidence Bounds | P Contrast | P Main Effect |
|---|---|---|---|---|
| **A. High-Contrast Acuity** | | | | |
| FDACL at year 1 | 1.07 | 1.03, 1.11 | | 0.0002 |
| Eyes with Vogt's striae at year 1* | | | | 0.03 |
| 1 vs. 0 | 1.75 | 1.15, 2.68 | 0.01 | |
| 2 vs. 0 | 1.51 | 0.97, 2.35 | 0.07 | |
| 2 vs. 1 | 0.86 | 0.58, 1.29 | 0.48 | |
| Eyes with Fleischer's ring at year 1* | | | | 0.04 |
| 1 vs. 0 | 0.53 | 0.30, 0.97 | 0.04 | |
| 2 vs. 0 | 0.54 | 0.32, 0.87 | 0.013 | |
| 2 vs. 1 | 0.98 | 0.63, 1.53 | 0.93 | |
| Race other than non-Hispanic white | 1.42 | 1.00, 2.03 | | 0.052 |
| **B. Low-Contrast Acuity** | | | | |
| BCVA at year 1† | 1.20 | 1.09, 1.33 | | 0.0002 |
| FDACL at year 1 | 1.04 | 1.02, 1.06 | | 0.0003 |
| Race other than non-Hispanic white | 1.51 | 1.11, 2.05 | | 0.008 |

Results based on subject-specific stepwise logistic regression analyses.

* Odds ratio > 1 indicates that an increased number of affected eyes is associated with greater risk; for odds ratio < 1, an increased number of affected eyes is associated with reduced risk.

† BCVA quantified in units of 5 letters correct.

decrease in vision. One in five to nearly one in three patients (19% or 30% if measured by high- or low-contrast BCVA, respectively) experienced a substantial reduction in visual performance in at least one eye over the course of the study period. Predictors for a patient to experience a two-line (10-letter) reduction in visual acuity in at least one eye include better initial low-contrast BCVA, steeper corneal curvature, the presence of Vogt's striae in one or both eyes, and race other than non-Hispanic white. Our data also establish ratios to be used by clinicians as they counsel patients regarding the likelihood of substantial vision loss over the next 5 to 7 years. Each diopter of change in corneal curvature is associated with an odds ratio (for a 10-letter change) of 1.07 for high- and 1.04 for low-contrast visual acuity. For example, a patient presenting with a FDACL-measured corneal curvature of 51.50 D (1.00 D steeper than the mean) would have a 7% increased risk for a 10-letter loss of high-contrast BCVA and a 4% increased risk of a 10-letter loss of low-contrast BCVA.

An additional important patient-specific association with ≥10-letter decrease in BCVA is race other than non-Hispanic white. These individuals have a 39% to 51% increased risk of deterioration of ≥ 10 letters in at least one eye in 7 years (in high- and low-contrast acuity, respectively). This suggests that ethnic origin may influence the progression and severity of keratoconus.

Patient factors at baseline associated with a subsequent reduction in high- or low-contrast BCVA over the 7-year follow-up period included better best-corrected visual acuity, steeper corneal curvature as measured by FDACL, the presence of Vogt's striae, and race other than non-Hispanic white. Likewise, patients with keratoconus who had better visual acuity, steeper corneal curvatures (>50.40 D as measured by FDACL), Vogt's striae, and are not non-Hispanic white were more likely to experience a substantial reduction in visual acuity (≥10 letters in at least one eye over a period of 7 years).

Clinicians should now begin to be able to predict visual acuity loss in keratoconus by determining whether these factors associated with a future loss of visual acuity are present. A critical assessment of the clinical measures described in this article for each patient with keratoconus will help to clarify projections for visual performance and provide an estimate of

what the patient is at an increased risk of experiencing over the next 5 to 7 years. These results from the CLEK Study provide much-needed quantitative measures of visual acuity changes with time in keratoconus and estimates that may be applied to predict what is frequently the most important clinical measure for patients with keratoconus—visual acuity.

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## APPENDIX: THE CLEK STUDY GROUP (AS OF APRIL 2004)

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(Co-investigator), Arti S. Shah (Co-investigator), Lisa A. Barnhart (Co-investigator, 1995-2001), and Karen K. Yeung (Co-investigator, 1999–2001).

*University of Missouri—St. Louis College of Optometry, St. Louis, MO:* Larry J. Davis (Principal Investigator), Edward S. Bennett (Co-investigator), Beth A. Henderson (Co-investigator), Bruce W. Morgan (Co-investigator), Patricia Sanders (Study Coordinator), Ivetta S. Siedlecki (Co-investigator), Zansheree L. Blue (Study Coordinator, 2000–2001), Monica J. Harris (Co-investigator, 2000–2001), Amber A. Reeves (Study Coordinator, 1998–2000), Nancy M. Duquette (Study Coordinator, 1995–1998), and Janene R. Sims (Co-investigator, 2000–2002).

*State University of New York State College of Optometry, New York, NY:* David P. Libassi (Principal Investigator) and Ralph E. Gundel (Co-investigator).

*Northeastern Eye Institute, Scranton, PA:* Joseph P. Shovlin (Principal Investigator), John W. Boyle (Co-investigator), J. Bradley Flickinger (Co-investigator), M. Elizabeth Flickinger (Co-investigator), Stephen C. Gushue (Photographer), Patricia McMasters (Study Coordinator), Cheryl Haefele (Study Coordinator, 1994–2000), and Stephen E. Pascucci (Medical Monitor).

*Nova Southeastern University College of Optometry, Ft. Lauderdale, FL:* Heidi Wagner (Principal Investigator), Andrea M. Janoff (Co-investigator), Chris Woodruff (Photographer), Arnie Patrick (Study Coordinator), Julie A. Tyler (Study Coordinator), and Karla E. Rumsey (Co-investigator, 1995).

*The Ohio State University College of Optometry, Columbus, OH:* Barbara A. Fink (Principal Investigator), Lindsay Florkey (Study Coordinator), Gregory J. Nixon (Co-investigator), Jason J. Nichols (Co-investigator; Coordinator, 1996–2001), Susan L. Sabers (Study Coordinator, 1994–1996), and Lisa Badowski (Co-investigator, 1995–1996).

*Pennsylvania College of Optometry, Philadelphia, PA:* Joel A. Silbert (Principal Investigator), Kenneth M. Daniels (Co-investigator), Mary Jameson (Backup Study Coordinator), Theresa E. Sanogo (Study Coordinator), and David T. Gubman (Co-investigator, 1998–2000).

*Southern California College of Optometry, Fullerton, CA:* Julie Yu (Principal Investigator), Raymond H. Chu (Co-investigator), Timothy B. Edrington (Co-investigator; Principal Investigator, 1994–2002), Eunice Myung (Co-Investigator), Julie A. Schornack, (Co-investigator), and Terry Y. Tsang (Co-investigator, 1998–2000).

*John Moran Eye Center, Department of Ophthalmology, University of Utah, Salt Lake City, UT:* Harald E. Olafsson (Principal Investigator), Doug M. Blanchard (Photographer), Deborah Y. Harrison (Study Coordinator), Mark McKay (Co-investigator), Paula F. Morris (Photographer), Kimberley Wegner (Study Coordinator/Technician), Libbi A. Tracy (Co-investigator, 1995-1998), Kate M. Landro (Study Coordinator, 1995-1998), Lizbeth A. Malmquist (Technician, 1998), Marie Cason (Technician, 1995-1999), and Craig M. Fehr (Technician, 1997-1999).

### Former Clinical Centers

*Health Science Center, Department of Ophthalmology, University of Texas at San Antonio, San Antonio, TX (1996):* Julie A. Yu (Principal Investigator), Beth Ann Benetz (Photographer), E. Joseph Zayac (Principal Investigator, 1994–1996), Paul D. Comeau (Photographer, 1994–1996), Ray V. Reil (Photographer, 1994–1996), and Sandra J. Hunt (Technician, 1994–1996).

### Resource Centers

*Chairman's Office, The Ohio State University College of Optometry, Columbus, OH:* Karla Zadnik (Chairman), Lanna Blue

(Secretary), Jodi M. Malone (Study Coordinator), Jeffrey J. Walline (Optometrist), Dione Allen (Secretary, 1997–2000), and Nora McFadden (Secretary, 2000–2002).

*CLEK Photography Reading Center, The Ohio State University College of Optometry, Columbus, OH:* Joseph T. Barr (Director), Gilbert E. Pierce (Reader), Marjorie J. Rah (Reader, based at the New England College of Optometry), Mohinder Merchea (Reader, based at Bausch & Lomb), Beth Oglevee (Study Coordinator), Gloria Scott-Tibbs (Study Coordinator), Robert Steffen (Reader, 1994–1995), and Roanne Flom (Reader, 1998–2001).

*Coordinating Center, Department of Ophthalmology and Visual Sciences and the Division of Biostatistics, Washington University Medical School, St. Louis, MO:* Mae O. Gordon (Director), Joel Achtenberg (Senior Research Analyst), Patricia A. Nugent (Data Assistant), Teresa A. Roediger (Project Manager), Kenneth B. Schechtman (Statistician), Brad S. Wilson (Statistical Data Analyst), Steven Kymes (Statistical Data Analyst), Karen Steger-May (Statistical Data Analyst), and Michael Richman (Project Manager, 1994–1996).

*CLEK Topography Reading Center, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, IL:* Timothy T. McMahon (Director), Robert J. Anderson (Biostatistician), Michi Goto (Research Assistant), Cynthia Roberts (Consultant), George A. Rosas (Study Coordinator), Loretta B. Szczotka (Consultant), Mark Wright (Programmer/Analyst), Stephanie K. Schoepfer-Grosskurth (Reader), Stephanie Walter Cooper (Reader, 1998), Thomas W. Raasch (Consultant, 2000–2002), and Dasia Corado (Reader, 2001).

*Project Office, National Eye Institute, Rockville, MD:* Donald F. Everett.

## Committees

*Executive Committee:* Karla Zadnik (Chair), Joseph T. Barr, Mae O. Gordon, Timothy B. Edrington, Donald F. Everett, and Timothy T. McMahon.

*CLEK Topography Analysis Group:* Loretta B. Szczotka (Co-chair), Timothy T. McMahon (Co-chair), Robert J. Anderson, Nina E. Friedman, Larry J. Davis, and Thomas W. Raasch.

*Data Monitoring and Oversight Committee:* Gary R. Cutter (Chair), Robin L. Chalmers, and Bruce A. Barron.