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Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study: Methods and Findings to Date

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Abstract

Purpose—To describe baseline and longitudinal findings of the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study.

Methods—The CLEK Study is an eight-year, multi-center, natural history study of 1,209 patients with keratoconus who were examined annually for eight years. Its goals are to prospectively characterize changes in vision, corneal curvature, corneal status, and vision-specific quality of life.

Results—CLEK Study subjects had a mean age at baseline of 39.3 $\pm$ 10.9 years. At study entry, 65% of the patients wore rigid contact lenses, and 14% reported a family history of the disease. Subjects exhibited a seven-year decrease in high- (2.03 letters) and low- (4.06 letters) contrast, best-corrected visual acuity, with 19% demonstrating decreases of 10 or more letters in high-contrast, best-corrected acuity and 31% of subjects demonstrating decreases of 10 or more letters in low-contrast, best-corrected acuity in at least one eye. Subjects exhibited an average eight-year increase in corneal curvature of 1.60 D in the flat corneal meridian, with 24% demonstrating increases of 3.00 D or more. The eight-year incidence of corneal scarring was 20%, with younger age, corneal staining, steeper baseline corneal curvature, contact lens wear, and poorer low-contrast visual acuity predictive of corneal scarring. Data from the National Eye Institute Visual Function Questionnaire suggest that the effect of keratoconus on vision-specific quality of life is disproportionate to its low prevalence and clinical severity.

Conclusion—Although we report measures of disease severity and visual function across the CLEK sample, clinicians can begin to envisage the course of keratoconus in individual patients by determining whether factors predictive of disease progression are present in those patients.

Keywords

keratoconus; visual acuity; corneal scarring; corneal curvature; quality of life

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1. Introduction

1.1. Origins

The American Academy of Optometry Research Committee and the American Optometric Association Council on Research have co-sponsored a semi-annual summer invitational research institute since 1988. At the inaugural institute in Berkeley, California, Joseph T. Barr proposed the following study question: “Does ‘fitting flat’—fitting rigid contact lenses with apical touch—cause apical scarring in patients with keratoconus?” This question was inspired by a paper by Korb et al. (1982), inferring a link between contact lens fitting techniques and apical changes and scarring in keratoconus.[1] Pursuant to the goals of the research institute, this question culminated in a collaborative research proposal that was awarded a National Eye Institute planning grant in 1990 (NIH/NEI R21-EY08652) and funding for a three-year observational study in 1994 (U10-EY10419, U10-EY10069, U10-EY10077). The study subsequently received an administrative extension to complete five additional years of follow-up, and a fourth resource center was funded in 1999 (U10-EY12656). It is noteworthy that this was the first optometry-based, multi-center study funded by the National Eye Institute, National Institutes of Health (Bethesda, Maryland).

1.2. Goals and objectives

Keratoconus is a chronic, non-inflammatory ectasia of the cornea. The condition is characterized by corneal steepening, visual distortion, apical corneal thinning, and central corneal scarring.[2,3] It is a relatively uncommon condition with a reported annual incidence of two per 100,000 and prevalence of 54.5 per 100,000.[4] Rigid contact lenses are frequently the treatment of choice if spectacles do not provide adequate vision.

The Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study is a multi-center, natural history study. Its goals are to prospectively characterize changes in vision, corneal curvature, corneal status (including corneal scarring), and quality of life in patients with keratoconus and to identify the factors associated with these changes over time. In this paper, we summarize baseline characteristics and longitudinal findings to date of over 1,200 subjects with keratoconus.

2. Methods

2.1. Patients

The CLEK Study enrolled 1,209 eligible subjects at 16 participating clinics across the United States between May 31, 1995 and June 29, 1996. All patients provided informed consent according to the protocol approved by each site’s institutional review board. At the time of enrollment, subjects were (1) aged 12 years or older; (2) exhibited an irregular cornea, as determined by distortion of keratometric mires and/or scissoring of the retinoscopic reflex; (3) demonstrated at least one biomicroscopic sign, including Vogt’s striae, Fleicher’s ring of 2 mm or more of arc, or corneal scarring typical of keratoconus; and (4) anticipated being able to participate in the CLEK Study for three or more years. Potential subjects with non-keratoconic ocular disease in both eyes such as cataracts, intraocular lens implants, macular disease, and optic nerve disease other than glaucoma (e.g., optic neuritis, optic atrophy) were not eligible for enrollment.

2.2. Procedures

Clinic personnel were trained and certified in essential procedures, including visual acuity measurements, refraction, keratometry, slit lamp biomicroscopy, videokeratography, corneal photography, fluorescein pattern photography, and contact lens verification. A standardized photography protocol was utilized to document the habitual contact lens fit (Figure 1), apical

corneal scarring (Figure 2), and the First Definite Apical Clearance (FDACL) lens. Exposed but undeveloped film was mailed to the CLEK Photography Reading Center (CPRC) for centralized development and grading by masked examiners.[5] One-hundred thirty-eight patients were randomly selected by the Coordinating Center for inclusion in the test-retest portion of the study, to assess the repeatability of standard test measures for patients with keratoconus, including visual acuity, refraction[6–8], and corneal curvature.[7,9]

Distance visual acuity was measured with high- and low-contrast Bailey-Lovie charts[10] (School of Optometry, University of California, Berkeley, CA) utilizing the Early Treatment Diabetic Retinopathy Study protocol.[11] Visual acuity was initially measured at a test distance of 4 meters and then, if the subject could not read all of the letters on the top line at 4 meters, retested at 1 meter. Visual acuity was measured with a forced-choice protocol, requiring the subject to attempt to read every letter from the top of the chart to the bottom until he or she missed three or more letters on a single line, after attempting to read all five letters on that line. High- and low-contrast, best-corrected visual acuity was measured with a rigid contact lens and spherocylindrical overcorrection. Patients who presented to the examination without habitual rigid contact lenses were evaluated with a rigid lens from the CLEK Study diagnostic lens set with a base curve radius equal to the steep keratometric reading. Distance visual acuity was also measured with manifest refraction (high-contrast only) and with habitual correction (high- and low-contrast).

Corneal curvature was measured with manual keratometry. The range of the keratometer was extended as needed to a maximum curvature of 68.30 diopters (D) with +1.25 D or +2.25 D auxiliary lenses.[12] In addition, a supplementary measure of corneal curvature was developed specifically for the CLEK Study.[13] The First Definite Apical Clearance Lens (FDACL) is the flattest lens in the CLEK Study trial lens set that exhibits an apical clearance fluorescein pattern (assessed in non-grafted eyes only). The CLEK Study diagnostic lenses are characterized by a standard overall diameter and optic zone diameter, with base curve radii ranging from 5.00 to 8.00 mm (Table 1).

Slit lamp biomicroscopy included inspection of the ocular adnexa, conjunctiva, and cornea with documentation of corneal anomalies including Vogt's striae, Fleischer's ring, and the presence and severity of apical corneal scarring (Figure 2) within the 6-mm diameter central cornea. The cornea was categorized by both the clinician and masked examiners as definitely not scarred, probably not scarred, probably scarred, or definitely scarred. An eye was classified as scarred at baseline if either the clinician or the masked examiner at the CPRC categorized the cornea as probably scarred or definitely scarred. An eye with incident scarring was defined as any previously unscarred cornea categorized as probably scarred or definitely scarred at one or more annual follow-up visits by both the clinician and the masked examiner.

Each patient completed a Quality of Life Survey (SF-36) at baseline, a patient history form at baseline and annually thereafter, and the National Eye Institute Visual Function Questionnaire (NEI-VFQ) at the one-year visit and annually thereafter. These instruments collected data on each patient's ocular and medical history, family history of keratoconus, and quality of life. Gender and race were reported using categories utilized by the National Eye Institute at the time of the baseline examination. Study procedures are described in detail elsewhere.[14]

3. Results

3.1. Baseline findings

The CLEK Study patients had a mean age of 39.3 $\pm$ 10.9 years. By self-report, 829 (69%) of the patients were white, 240 (20%) were black, and 99 (8%) were Hispanic. Six hundred eighty-eight (57%) of the subjects were male. Only 14% of patients reported a family history of keratoconus in a parent, sibling, child, aunt or uncle. None reported serious systemic diseases that had been previously reported to be associated with keratoconus, including Down syndrome, Marfan syndrome, focal dermal hypoplasia, Ehlers-Danlos syndrome, infantile tapetoretinal degeneration, oculodentodigital syndrome, osteogenesis imperfecta, or Rieger's anomaly. Six hundred thirty-nine (53%) reported a history of atopy. Approximately half (50%) of the patients reported rubbing one or both eyes vigorously.

Most of the patients (74%) were corrected with contact lenses (either rigid or soft contact lenses) in both eyes; of these, the majority of the patients (64%) were also prescribed spectacles as an adjunct to the primary contact lens correction. Sixty-five percent of the patients wore rigid gas-permeable contact lenses, and the majority of rigid lens wearers (73%) reported that their lenses were comfortable in both eyes. A smaller proportion of patients wore spectacles (16.1%) as their primary vision correction, and an even smaller group (3.6%) reported no vision correction in either eye at baseline.

The majority of the patients exhibited moderate to severe disease, as assessed by a keratometric-based criterion (95% of patients had steep keratometric readings of at least 45.00 D) and relatively good visual acuity (78% had high-contrast, best-corrected visual acuity of at least 20/40 in both eyes). In addition, 86% of the subjects presented with a Fleischer's ring in one (30%) or both (56%) eyes; Vogt's striae in one (35%) or both (30%) eyes; and corneal scarring in one (31%) or both (22%) eyes. One hundred sixteen patients had undergone penetrating keratoplasty prior to study entry, and two patients had undergone epikeratoplasty prior to study entry.

Keratoconus has traditionally been characterized as a bilateral condition with an asymmetric presentation.[3] Baseline study findings demonstrated large between-eye differences in high- (7.30 $\pm$ 6.83 letters correct) and low-contrast (8.53 $\pm$ 7.51 letters correct), best-corrected visual acuity, high- (9.03 $\pm$ 8.40 letters) and low-contrast (9.43 $\pm$ 7.88 letters), entrance visual acuity, spherical equivalent refractive error (3.15 $\pm$ 3.84 D), refractive cylinder power (1.55 $\pm$ 1.42 D), and flat (3.59 $\pm$ 4.46 D) and steep (4.35 $\pm$ 4.41 D) keratometric readings. Twenty percent of the patients demonstrated corneal scarring in only one eye.[15] For the flat keratometric reading, high-contrast, best-corrected acuity, spherical equivalent refractive error, and corneal scarring, the results suggested that the association between disease severity and asymmetry was stronger in patients with more advanced disease.[16]

FDACL was more repeatable than keratometry in severe disease.[9] In addition to providing a measure of corneal curvature, the FDACL lens provides an assessment of the cornea-contact lens base curve fitting relationship for patients wearing rigid lenses. Comparison of the dioptric value of the base curve of the FDACL lens to that of the patients' habitual rigid lenses showed that the majority (88%) of patients wearing rigid lenses were fitted with apical touch. For mild (steep keratometric reading <45.00 D) keratoconic corneas, the average estimate of the base curve-to-cornea fitting relationship was 1.18 D flat (SD $\pm$ 1.84 D); moderate (steep keratometric reading 45.00 D to 52.00 D) corneas were fitted on average 2.38 D flat (SD $\pm$ 2.56 D); and severe (steep keratometric reading >52.00 D) corneas were fitted an average of 4.01 D flat (SD $\pm$ 4.11 D). Overall, rigid gas-permeable lenses were fitted on average 2.86 D (SD $\pm$ 3.31 D) flatter than the first definite apical

clearance lens (FDACL). Despite the possible relationship between contact lens fitting techniques and apical scarring in keratoconus, most CLEK patients wore flat-fitting lenses. [17]

There did not appear to be an association between low patient-reported rigid lens comfort and severe disease, as measured by steep keratometry or FDACL in this sample. The apical fitting relationship (flat versus steep) did not appear to be associated with patient-reported comfort. Minimal peripheral clearance may have contributed to decreased rigid contact lens comfort in keratoconus.[18]

Corneal scarring was associated with a decrease in high- and low-contrast visual acuity with habitual and best correction. Controlling for age, contact lens wear, and disease severity, central scarring was associated with poorer visual acuity and greater patient-reported symptoms of glare.[19,20] Baseline study data suggested that corneal scarring in keratoconus was associated with corneal staining, contact lens wear, a Fleischer's ring, a steeper cornea, and older age.

Of the 761 rigid contact lens-wearing patients at baseline, 41% had a scar at baseline compared with 24% of the non-rigid contact lens wearers (odds ratio [OR], 2.15; 95% confidence interval [CI], 1.35–3.43; $p = 0.001$). Although a greater proportion of the corneas wearing flat-fitting contact lenses were scarred (43% compared with 26% for the steep-fitted eyes; OR = 2.19; 95% CI, 1.37–3.51; $p = 0.001$), the association of rigid contact lens fit and corneal scarring at baseline did not persist after controlling for disease severity (corneal curvature assessed by FDACL; adjusted OR, 1.20; 95% CI, 0.70–2.06; $p = 0.52$). Steeper corneal curvature increased the risk of prevalent corneal scarring by 28% per diopter of increased curvature (adjusted OR, 1.28; 95% CI, 1.23–1.34; $p = 0.0001$).[21]

Visual acuity and corneal curvature had the strongest association with vision-related quality of life.[22] Binocular, entrance visual acuity worse than 20/40 was associated with lower quality of life scores on all scales except General Health and Ocular Pain. A steep keratometric reading (average of both eyes) >52.00 D was associated with lower scores on the Mental Health, Role Difficulty, Driving, Dependency, and Ocular Pain scales. Scores for CLEK patients on all scales were between those of patients with category 3 and 4 age-related macular degeneration (AMD) with two exceptions—General Health in the CLEK patients was better than in AMD patients, while Ocular Pain in CLEK patients was worse than in AMD patients. CLEK patients who wore contact lenses exhibited higher scores compared with non-contact lens wearers on all scales except Distance Activities, Mental Health, and Dependency, indicating overall better function. However, contact lens wearers exhibited lower scores on the Ocular Pain scale, indicating more discomfort.

3.2. Longitudinal findings

Because of a small, anomalous improvement in visual acuity between baseline and year one, seven years of prospective visual acuity data from the CLEK Study cohort from 953 CLEK Study subjects who had no history of penetrating keratoplasty in either eye at baseline were analyzed with respect to changes over time in high- and low- contrast, best-corrected acuity (Table 2). CLEK patients exhibited a gradual decrease in high- (2.03 letters) and low- (4.06 letters) contrast, best-corrected visual acuity during follow-up, with low-contrast acuity deteriorating more rapidly (Figure 3). High- and low-contrast, best-corrected visual acuity decreases of 10 or more letters correct (two lines of acuity) in at least one eye occurred in 19% and 31% of subjects, respectively. Better baseline best-corrected visual acuity, steeper corneas (FDACL), and the presence of corneal scarring were predictive of more significant decreases in visual acuity. Each diopter of increase from baseline FDACL predicted an

increased deterioration of 0.49 and 0.63 high- and low-contrast letters correct, respectively. [23]

There were 1,062 patients with at least one study-eligible eye with at least one slope generated from longitudinal data for FDACL or the flat keratometric reading (Flat K). There were 1,940 eyes from 1,020 patients for FDACL and 1,988 eyes from 1,028 patients for Flat K. CLEK subjects exhibited a gradual increase in corneal curvature during follow-up. The slope of the change in the FDACL (0.18 ± 0.60 D/year) and in the flat keratometric reading ($0.20 \text{ D} \pm 0.80$ D/year) over eight years translated into expected eight-year increases of 1.44 D in the FDACL and 1.60 D in the flat keratometric reading. Corneal curvature increases of 3.00 or more D in either eye had an incidence of 25% for the FDACL and 24% for the flat keratometric reading. Younger age and poorer high-contrast, manifest refraction visual acuity at baseline predicted an increased rate of change in corneal curvature (Table 3).[24]

Of the 878 patients with at least one unscarred cornea at baseline, the five-year incidence of corneal scarring was 14% (120 of 878) overall, 17% (102 of 609) for contact lens-wearing eyes, and 38% (46 of 121) for contact lens-wearing eyes with corneal curvature greater than 52 D. Multivariate analyses of five-year prospective data from the CLEK Study cohort showed that younger age, baseline corneal curvature, contact lens wear, and corneal staining were predictive of incident corneal scarring (Table 4).[25] The eight-year incidence of penetrating keratoplasty was higher (15%) among patients less than 40 years old compared to patients 40 years old or older (8%).[26]

Thirty-two percent of the unscarred eyes at baseline fitted flat developed incident corneal scarring over the course of the study compared to 14% of the eyes fitted steep. Controlling for disease severity (corneal curvature assessed by FDACL), the risk of corneal scarring did not increase with flat versus steep rigid contact lens fit (adjusted OR, 1.83; 95% CI, 0.79–4.23; $p = 0.16$).[21] Steeper corneal curvature increased the risk of corneal scarring by 26% per diopter of increased curvature (adjusted OR, 1.26; 95% CI, 1.17–1.35; $p < 0.0001$).

Rigid contact lens wear at baseline, regardless of how the lenses were fitted, was associated with incident corneal scarring. Of the 370 of 582 non-scarred eyes (64%) wearing rigid contact lenses at baseline, 106 of them (29%) developed corneal scarring by the end of the eighth year of follow up, whereas 42 of the 212 non-rigid contact lens wearers (20%) developed corneal scarring by the end of the eighth year of follow-up (OR, 1.62; 95% CI, 1.08–2.44; $p = 0.02$). This translates to a 62% increase in an eye's risk of scarring if that eye wears a rigid contact lens compared to eyes that did not wear rigid lenses.

The rigid lens fitting method was also associated with incident corneal scarring but only in univariate analyses. Although a greater proportion of the corneas wearing flat-fitting contact lenses were scarred (32% compared with 14% for the steep-fitted eyes; OR, 2.93; 95% CI, 1.34–6.42; $p = 0.007$), after controlling for disease severity (corneal curvature assessed by FDACL) the risk of corneal scarring did not increase with flat versus steep rigid contact lens fit (adjusted OR, 1.83; 95% CI, 0.79–4.23; $p = 0.16$). Steeper corneal curvature increased the risk of prevalent corneal scarring by 26% per diopter of increased curvature (adjusted OR, 1.26; 95% CI, 1.17–1.35; $p < 0.0001$).[21]

As described previously, the NEI-VFQ was administered annually to keratoconus patients for seven years. In multivariate analyses, including the baseline scale score as a covariate, an increase in corneal curvature was significantly associated with a decline in the scores for Dependency, Mental Health, Ocular Pain and Role Difficulties. A decrease in visual acuity was associated with a significant decrease in scores on the Dependency, Driving, Mental Health, and Near Activities scales. It is clear that progression of disease as measured by

changes in visual acuity and corneal curvature resulted in continued decline in vision-related quality of life.[22]

4. Discussion

Baseline data provide clinical insight with which to educate and manage patients with keratoconus. These findings suggest that keratoconus is not associated with increased risk of connective tissue disease, as previously reported in the literature. Even though many researchers believe that individuals may have a genetic predisposition for keratoconus, the relatively small percentage of patients reporting family members diagnosed with the disease is of interest to patients with keratoconus and their families. Baseline findings reaffirm that spectacles may provide a useful ancillary correction for patients with moderate disease severity and, while the majority of patients are comfortable with their contact lenses, a sizable minority are not. Study findings confirm that high-contrast visual acuity underestimates the loss of visual acuity and function in keratoconus. Visual acuity of 20/40 or worse is particularly associated with reduced vision-related quality of life.

Preliminary analyses of the longitudinal findings suggest that the risk of incident scarring in contact lenses wearers is more than two-fold that of non-contact lens wearing patients with keratoconus. These findings suggest a causal contribution of contact lens wear to corneal scarring in keratoconus and imply that clinical intervention in optimizing the contact lens fitting characteristics may potentially affect visual function. However, the linking of advanced disease and flat fit render it nearly impossible to statistically discriminate between the effect of flat contact lens fit and disease severity on visual acuity, contact lens comfort, ocular pain, and incident corneal scarring in this “natural history” sample. A randomized clinical trial would be needed to determine a causal relationship between rigid lenses fit with apical touch and apical corneal scarring, if it exists.

In addition to providing information regarding the cornea-contact lens fitting relationship of the patient’s habitual lenses, adapting the FDA CL procedure to clinical care may provide a useful reference point from which to initiate contact lens fitting, particularly in subjects with moderate to severe disease. Bracketing apical touch and clearance may preclude the prescribing of excessively flat or excessively steep contact lenses.

There have been anecdotal reports that younger age at keratoconus onset is associated with worse disease, faster disease progression, and/or a shorter time to penetrating keratoplasty. Study findings reveal that age appears to be a factor in severity-related outcomes in keratoconus among patients in the CLEK Study. Further analysis should more definitively identify risk factors and protective factors for disease progression.

While keratoconus is a chronic condition that rarely results in blindness, the results of the National Eye Institute Visual Function Questionnaire (NEI-VFQ) suggest that its effect on vision-specific quality of life is worse than expected based on the condition’s relatively low prevalence and clinical severity. Keratoconus is unique among eye diseases, in that it is typically diagnosed during peak education, income-earning, and child-rearing years.

5. Conclusion

CLEK Study patients demonstrated a gradual increase in corneal curvature and decrease in visual acuity. Clinicians and public health officials should be cognizant of the documented impact on quality of life when correlating the disease burden with clinical findings. Although we report average measures of disease severity and visual function, clinicians can begin to envisage the course of keratoconus in individual patients by determining whether factors predictive of progression are present.

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Figure 1.
Fluorescein evaluation is characterized by (A) Definite touch (B) Touch (C) Clearance (D)
Definite clearance

Figure 2.
Apical corneal scarring

Figure 3.

(A) Mean high-contrast best-corrected visual acuity (BCVA), averaged across the right and left eyes, over time. Values are means $\pm$ SEM of both eyes as a function of the follow-up visit. (B) Mean low-contrast BCVA, averaged across the right and left eyes, over time. Values are means $\pm$ SEM of both eyes as a function of the follow-up visit.[23]

Table 1

Parameters of the CLEK Study diagnostic lens set

BCR (mm)	POWER (D)	OAD (mm)	OZD (mm)	SCR (mm)	SCW (mm)	PCR (mm)	PCW (mm)
5.00	-10.00	8.60	6.50	8.50	0.85	11.00	0.20
5.10	-8.00	8.60	6.50	8.50	0.85	11.00	0.20
5.20	-8.00	8.60	6.50	8.50	0.85	11.00	0.20
5.30	-8.00	8.60	6.50	8.50	0.85	11.00	0.20
5.40	-8.00	8.60	6.50	8.50	0.85	11.00	0.20
5.50	-8.00	8.60	6.50	8.50	0.85	11.00	0.20
5.60	-9.00	8.60	6.50	8.50	0.85	11.00	0.20
5.70	-7.00	8.60	6.50	8.50	0.85	11.00	0.20
5.80	-8.00	8.60	6.50	8.50	0.85	11.00	0.20
5.90	-9.00	8.60	6.50	8.50	0.85	11.00	0.20
6.00	-7.00	8.60	6.50	8.50	0.85	11.00	0.20
6.10	-8.00	8.60	6.50	8.50	0.85	11.00	0.20
6.20	-9.00	8.60	6.50	8.50	0.85	11.00	0.20
6.30	-7.00	8.60	6.50	8.50	0.85	11.00	0.20
6.40	-8.00	8.60	6.50	8.50	0.85	11.00	0.20
6.50	-8.00	8.60	6.50	8.50	0.85	11.00	0.20
6.60	-6.00	8.60	6.50	8.50	0.85	11.00	0.20
6.70	-7.00	8.60	6.50	8.50	0.85	11.00	0.20
6.80	-8.00	8.60	6.50	8.50	0.85	11.00	0.20
6.90	-6.00	8.60	6.50	8.50	0.85	11.00	0.20
7.00	-6.00	8.60	6.50	8.50	0.85	11.00	0.20
7.10	-7.00	8.60	6.50	8.50	0.85	11.00	0.20
7.20	-5.00	8.60	6.50	8.50	0.85	11.00	0.20
7.30	-5.00	8.60	6.50	8.50	0.85	11.00	0.20
7.40	-6.00	8.60	6.50	8.50	0.85	11.00	0.20
7.50	-4.00	8.60	6.50	8.50	0.85	11.00	0.20
7.60	-4.00	8.60	6.50	8.50	0.85	11.00	0.20
7.70	-4.00	8.60	6.50	9.00	0.85	11.00	0.20

BCR (mm)	POWER (D)	OAD (mm)	OZD (mm)	SCR (mm)	SCW (mm)	PCR (mm)	PCW (mm)
7.80	-4.00	8.60	6.50	9.00	0.85	11.00	0.20
7.90	-3.00	8.60	6.50	9.00	0.85	11.00	0.20
8.00	-3.00	8.60	6.50	9.00	0.85	11.00	0.20

Table 2

Independent Predictors of the Slope of Change in Best-corrected Visual Acuity (BCVA)

Predictor	Magnitude of Effect ^a	95% Confidence Interval	p-value
High-contrast best-corrected visual acuity			
High-contrast best-corrected visual acuity at year 1	-0.26 +/- 0.02	(-0.30, -0.22)	<0.0001
FDACL at 1 year	-0.07 +/- 0.007	(-0.081, -0.052)	<0.0001
Low-contrast best-corrected visual acuity			
Low-contrast best-corrected visual acuity at year 1	-0.24 +/- 0.02	(-0.28, -0.19)	<0.0001
FDACL at 1 year	-0.09 +/- 0.009	(-0.11, -0.07)	<0.0001

^aDefined 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.

Table 3Independent Predictors of an Increase of FDACL 3.00 D in at Least 1 Eye^a

Predictor	Odds Ratio	95% Confidence Interval	p-value
FDACL			
Younger than aged 35 years	2.45	(1.82, 3.3)	<0.0001
Fewer high contrast manifest refraction visual acuity letters correct ^b	1.19	(1.13, 1.26)	<0.0001
Flat K			
Younger than aged 35 years	3.12	(2.28, 4.27)	<0.0001
Fewer high contrast manifest refraction visual acuity letters correct ^b	1.31	(1.24, 1.38)	<0.0001

^aResults are based upon patient-specific logistic regression analyses.^bPer 5 letters correct

Table 4

Independent Factors Predictive of Incident Corneal Scarring

Predictor	Odds Ratio	95% Confidence Interval	p-value
Age<20 years	6.34	(2.57, 15.00)	<0.0001
FDACL>52 D	4.79	(3.08, 7.45)	<0.0001
Contact lens wear	2.50	(1.40, 4.76)	0.003
Corneal staining	2.38	(1.49, 3.76)	0.0002