Baseline Findings in the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study

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PURPOSE. To describe the baseline findings in patients enrolled in the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study.

METHODS. This is a longitudinal observational study of 1209 patients with keratoconus enrolled at 16 clinical centers. Its main outcome measures are corneal scarring, visual acuity, keratometry, and quality of life.

RESULTS. The CLEK Study patients had a mean age of 39.29 ± 10.90 years with moderate to severe disease, assessed by a keratometric-based criterion (95.4% of patients had steep keratometric readings of at least 45 D) and relatively good visual acuity (77.9% had best corrected visual acuity of at least 20/40 in both eyes). Sixty-five percent of the patients wore rigid gas-permeable contact lenses, and most of those (75%) reported that their lenses were comfortable. Only 13.5% of patients reported a family history of keratoconus. None reported serious systemic diseases that had been previously reported to be associated with keratoconus. Many (53%) reported a history of atopy. Fifty-three percent had corneal scarring in one or both eyes.

CONCLUSIONS. Baseline findings suggest that keratoconus is not associated with increased risk of connective tissue disease and that most patients in the CLEK Study sample represent mild to moderate keratoconus. Additional follow-up of at least 3 years will provide new information about the progression of keratoconus, identify factors associated with progression, and assess its impact on quality of life. (Invest Ophtalmol Vis Sci. 1998;39:2537-2546)

The Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study is a multicenter observational study supported by the National Eye Institute, Bethesda, Maryland. The purpose of the CLEK Study is to characterize prospectively the changes in vision, corneal curvature, corneal status (i.e., corneal scarring), and quality of life in patients with keratoconus and to determine the factors associated with these changes across time. In this article, we summarize the study design and baseline characteristics of patients enrolled in the study.

Keratoconus is a progressive, asymmetric, noninflammatory disease of the cornea characterized by steepening and distortion, apical thinning, and central scarring of the cornea. These corneal changes cause a mild to marked decrease in vision secondary to high irregular astigmatism and frequently to central corneal scarring. There are several characteristic biomicroscopic corneal signs that become more prevalent as the disease progresses. These include an inferiorly displaced, thinned protrusion of the cornea, corneal thinning over the apex of the cone, Vogt's strie in the posterior stroma, scars in Bowman's layer, and Fleischer's ring, an either full or partial ring of iron in the corneal epithelium at the base of the cone. Although its cause is unknown, keratoconus has been putatively associated with atopic disease, eye rubbing, inheritance, and contact lens wear.

Management varies with disease severity. Nonsurgical alternatives are used primarily in treating patients with keratoconus. Although the visual disturbances in keratoconus may be managed with spectacles or hydrogel lenses early in the disease process, rigid gas-permeable contact lenses are the treatment of choice for the irregular astigmatism associated with the disease. Occasionally, hydrogel lenses are used in later stages in conjunction with rigid lenses in a piggyback lens design.

Patients are generally referred for penetrating keratoplasty when they can no longer tolerate contact lenses or when contact lenses provide inadequate vision. Poor vision with contact lenses is often accompanied by apical corneal scarring, but vision can be compromised even with optimal contact lens correction and no corneal scarring. With concerted effort,
most patients initially referred for corneal transplants can be successfully refitted without surgery, yielding improved visual acuity and increased contact lens wearing time.\textsuperscript{14-16}

Previous, large-scale studies of keratoconus have been focused on describing the disease's incidence and prevalence,\textsuperscript{17} on attempting to establish the disease's cause,\textsuperscript{5,12} or on trends in the clinical management of keratoconus.\textsuperscript{2,5,13,18,19} Few have characterized the course of the disease and its associated factors in large samples of affected patients.\textsuperscript{20} With the exception of our previous CLEK survey,\textsuperscript{2} all previous studies have relied on retrospective evaluation of patients' medical records. None of the previous studies has characterized the interrelations among corneal curvature, biomicroscopic findings, and vision in keratoconus. Although visual function (other than visual acuity) has been described in small samples of patients with keratoconus,\textsuperscript{21} none of the large-scale studies has characterized vision and visual function beyond retrospective Snellen visual acuity measurements recorded by an examining clinician. No surveys of quality of life in keratoconus have been performed. No data exist comparing patients' visual symptoms with their clinically measured visual performance. None of the attempts to stage and classify keratoconus has been performed in a standardized manner.

The CLEK Study is a multicenter, prospective, observational study designed to describe the course of keratoconus and to describe the associations among its visual and physiological manifestations. Over the course of 13 months, 1209 patients were enrolled at 16 clinics. Patients will be examined annually for at least 3 years. Baseline and annual visit examinations include visual acuity (high- and low-contrast), patient-reported quality of life, manifest refraction, keratometry, photodocumentation of the cornea, photodocumentation of the patient's habitual rigid contact lenses, and photodocumentation of the flattest rigid contact lens from the CLEK Study trial lens set to show apical clearance (the First Definite Apical Clearance Lens [FDACL]). The CLEK Study's goal is to identify risk factors that determine disease severity and progression in keratoconus.

A specific purpose of the CLEK Study is to provide a description of the distribution and rate of change in best corrected high- and low-contrast visual acuity and corneal curvature and to determine the proportion of patients with incident corneal scarring and the proportion of patients requiring penetrating keratoplasty. Another specific purpose of this study is to identify factors associated with changes over time in visual acuity, corneal curvature, and corneal scarring.

\textbf{MATERIALS AND METHODS}

\textbf{CLEK Study Design}

The CLEK Study is a 16-center observational study of patients with keratoconus, as described. The sample size goal was to recruit at least 1000 patients, allowing for a 5\% loss to follow-up in 3 years. In total, 1209 eligible patients were enrolled between May 31, 1995, and June 29, 1996.

\textbf{Training and Certification of Study Personnel}

All examination procedures were performed by clinicians and technicians who had completed training, who had successfully demonstrated the ability to perform each measurement according to the protocol, and who had successfully completed written and verbal evaluations by the CLEK Study chairman's office. CLEK clinic personnel were trained and certified on nine key tasks: study coordination, visual acuity measurement, refraction, keratometry, slit lamp biomicroscopy, corneal topography, corneal photography, fluorescein photography, and contact lens verification.

\textbf{Visit Schedule}

Each CLEK clinic was expected to recruit 80 patients. Each patient, whether an established patient at a clinic or an outside referral patient, was screened for the entry criteria (Table 1). After confirmation of eligibility, each patient was scheduled for his or her baseline visit. Each patient will be seen annually for a minimum of 3 years of follow-up (at least four visits). Investigators at each clinic obtained informed consent from their patients. The CLEK Study protocol was approved by each clinic's institutional review board, in accordance with the tenets of the Declaration of Helsinki.

\textbf{Patient-Completed Items}

Each patient completed a patient background form and a Quality of Life Survey (SF-36) at baseline\textsuperscript{22}, a patient history form during the baseline visit and annually thereafter; and the National Eye Institute Visual Functioning Questionnaire,\textsuperscript{23} beginning at the first annual visit and annually thereafter. These survey instruments collected data on the patient's ocular and medical history, family history, history of contact lens wear, and health-related and vision-related quality of life.

\textbf{Interview}

Questions about the patient's ocular general health and contact lens history were answered in an interview format. These

\begin{table}[h]
\centering
\begin{tabular}{|l|l|}
\hline
\textbf{Inclusion Criteria} & \textbf{Exclusion Criteria} \\
\hline
Age & At least 12 years old \\
Irregular corneal surface & In either eye, identified by distortion of the keratometric mires, scissoring of the retinoscopic reflex, or irregularity in the red reflex observed with the direct ophthalmoscope. \\
Slit lamp biomicroscopic findings & Vogt's striae or a Fleischer's ring of at least 2 mm arc or corneal scarring characteristic of keratoconus in either eye. \\
Follow-up status & Able to complete at least 3 years of follow-up \\
Surgical status & No bilateral corneal transplants \\
Other ocular disease & No nonkeratoconic ocular disease in both eyes, that is, no cataract, intraocular lens implants, macular disease, or optic nerve disease other than glaucoma (e.g., optic neuritis, optic atrophy).
\hline
\end{tabular}
\caption{Study Eligibility Criteria}
\end{table}
included assessment of a family history of keratoconus, presence of systemic disease, eye rubbing, contact lens wearing time, and contact lens comfort.

**Examination**

A detailed examination was performed on each eligible patient. Distance visual acuity was measured using the high- and low- (Michelson contrast 10%) contrast Bailey-Lovie chart (School of Optometry, University of California, Berkeley). The chart is located at 4 m, and the white background of the chart has a standard luminance, 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: entrance visual acuity, high- and low-contrast with habitual correction in each eye and then in both eyes; best corrected visual acuity, high- and low-contrast with best correction (in rigid contact lens wearers, their rigid contact lenses with optimal overrefraction; in those patients who do not wear rigid contact lenses, a CLEK Study trial contact lens with base curve radius in the steep keratometric reading plus optimal overrefraction) in each eye; and manifest refraction visual acuity, high contrast Bailey-Lovie visual acuity with manifest refraction in each eye. 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 number of letters read correctly.

Manifest refraction was performed according to standard subjective techniques with additional methods—for example, larger steps between subjective lens choices, higher power Jackson crossed cylinder, and subjective cylinder axis adjustment, tailored to patients with poorer vision. The same technique was used to perform overrefractions over the patient’s habitual contact lenses or trial lenses from the CLEK Study trial lens set.

Fluorescein patterns of habitual contact lenses were assessed. Fluorescein was instilled, and the contact lens fit was observed by slit lamp biomicroscopy with cobalt and Wratten 12 (or Tiffen yellow) filters in place. A grading system using photographic standards specifying the central fluorescein pattern as definite touch, touch, clearance, or definite clearance for each observation was used. Peripheral clearance was graded as minimum-unacceptable, minimum-acceptable, average, maximum-acceptable, or excessive-bubbles.

Keratometry was performed by taking two readings in the flattest and steepest meridians, which may or may not be 90° apart. The keratometer was calibrated to steel balls of known flattest and steepest meridians, which may or may not be 90° apart. The keratometer was calibrated to steel balls of known curvature weekly. Keratometry range was extended with the flattest lens in the trial lens set that exhibited a definite apical clearance pattern. Keratometry was performed by taking two readings in the flattest and steepest meridians, which may or may not be 90° apart. The keratometer was calibrated to steel balls of known curvature weekly. Keratometry range was extended with the flattest lens in the trial lens set that exhibited a definite apical clearance pattern. Keratometry was performed by taking two readings in the flattest and steepest meridians, which may or may not be 90° apart. The keratometer was calibrated to steel balls of known curvature weekly. Keratometry range was extended with the flattest lens in the trial lens set that exhibited a definite apical clearance pattern.

A protocol for determining the FDACL to provide a measure of corneal curvature was developed specifically for the CLEK Study. 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 so that the sagittal depth of the base curve chord diameter was greater than the sagittal depth of the cornea, when using 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 procedure 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 are in the proper order and that none of the lenses were 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. Rigid contact lens parameters were measured. Parameters measured included base curve radius, contact lens power, overall diameter, optic zone diameter, and center thickness.

Video keratography was performed at each clinic using the instrument available to the respective clinic. Eight clinics have TMS-1 devices (Tomey Technology, Cambridge, MA) units, four of the clinics have EyeSys units (EyeSys Premier, Irvine, CA) units, two of the clinics have Visioptic EH270 (Alcon Surgical, Fort Worth, TX) units, and one clinic has a Humphrey Mastervue (Humphrey Instruments, San Leandro, CA) unit. At the time of the grant submission and start of the study, a recognized method for analyzing corneal topography data was not apparent; therefore, a large expenditure to equip each site with the same instrument was impractical. Study investigators opted to collect corneal topography data with the existing instrument at each site with the intent of analyzing these data later. It was recognized early that developing a method for pooling data from a variety of instruments would be a challenge. Strategies are in development for analyzing the data.

Four central parallelepipeds photographs of the central cornea were taken, and the CLEK standardized corneal photography protocol was used to document the presence or absence of corneal scarring. After pupillary dilation, two oblique photographs were taken of the entire cornea. Exposed but undeveloped film was mailed to the CLEK Photography Reading Center at The Ohio State University College of Optometry, Columbus, for centralized development, labeling, and grading. Dilated fundus examination was performed, and intraocular pressure was measured at each visit.
TABLE 2. Power for Detecting Risk Factors

<table>
<thead>
<tr>
<th>Percentage with Risk Factor</th>
<th>P1 = 0.10</th>
<th>P1 = 0.15</th>
<th>P1 = 0.20</th>
<th>P1 = 0.25</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P2 = 0.18</td>
<td>P2 = 0.26</td>
<td>P2 = 0.33</td>
<td>P2 = 0.40</td>
</tr>
<tr>
<td>15</td>
<td>0.748</td>
<td>0.875</td>
<td>0.918</td>
<td>0.953</td>
</tr>
<tr>
<td>20</td>
<td>0.838</td>
<td>0.935</td>
<td>0.963</td>
<td>0.983</td>
</tr>
<tr>
<td>25</td>
<td>0.890</td>
<td>0.964</td>
<td>0.982</td>
<td>0.993</td>
</tr>
</tbody>
</table>

Total sample size, 1000. Odds ratio of ≥2.00. P1, the probability of the event in the group without the risk factor; P2, the probability of the event in the group with the risk factor.24

Statistical Methods: Sample Size Rationale

The minimum overall target sample of 1000 was selected to provide adequately narrow 95% confidence intervals for estimates of means (e.g., keratometry, visual acuity, quality of life) and proportions (e.g., corneal scarring) of the primary outcome variables. A sample size of 1000 patients provides reasonable power for detecting risk factors for events of relatively low incidence, such as central corneal scarring (Table 2). A sample of 1000 patients provides sufficient power to detect risk factors that explain 10% of the variation in continuous variables such as keratometry, visual acuity, and quality of life.27

RESULTS

One thousand two hundred nine patients were enrolled in the CLEK Study (Fig. 1). By self-report, 829 (68.5%) of the patients were white, 240 (19.9%) were black, 99 (8.2%) were Hispanic, and 41 (3.4%) were a mix of other ethnic categories. Men comprised 55.9% of the sample. The age distribution of the patients is shown in Figure 2 (mean age, 39.29 ± 10.90 years [SD]). One hundred eighteen of the patients (9.8%) entered the CLEK Study having undergone a penetrating keratoplasty in one eye before the baseline visit (54 in the right eye and 64 in the left eye). The educational level of the CLEK Study patients is shown in Table 3. Eighty percent of the patients had at least some college education.

The mode of visual correction in the patients is shown in Tables 4 and 5. Most of the patients' vision was corrected with contact lenses in both eyes (892 [74%] of 1209); of these, 571 (64%) of 892 also used glasses in some capacity (Table 6). A small proportion of patients (3-6%) used no visual correction in either eye at baseline. Seven hundred ninety (65%) patients wore rigid contact lenses in both eyes, and 94 (8%) wore rigid contact lenses in one eye (Table 5).

The patients responded to various questions designed to assess the burden of having keratoconus. Only 15 (1.4%) of 1096 patients at baseline reported having changed jobs because of keratoconus, and only 23 (2.1%) of 1073 received keratoconus-related disability, but 124 (11.5%) of 1080 patients...
reported missing work because of keratoconus. One hundred (10.1%) of 988 contact lens-wearing patients reported that they were unable to wear their contact lenses for leisure activities, and 174 (17.6%) of 986 contact lens-wearing patients reported that they could not wear their contact lenses to read at night. Six hundred forty-one (35.1%) of 988 contact lens-wearing patients reported a refitting of their contact lenses in the year before their baseline visit.

Patients were asked whether they rubbed their eyes vigorously, and they were allowed to answer the question for each eye. Of the 1207 patients who responded to the eye rubbing question, 582 patients (48.2%) reported rubbing both eyes vigorously, whereas only 27 patients (2.2%) reported rubbing only one eye vigorously. Five hundred fifty-nine patients (46.3%) reported that they rubbed neither eye. Thirty-nine patients (3.2%) were unsure whether they rubbed their eyes.

No patient reported a history of 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 patients (52.9%) had hay fever or allergies, 180 (14.9%) had asthma, and 101 (8.4%) had atopic dermatitis. Cardiovascular disease was present in 74 patients (6.1%), diabetes mellitus in 23 (1.9%), and cystic fibrosis in 2 (0.16%).

Table 4. Type of Visual Correction Worn by Study Patients at Baseline

<table>
<thead>
<tr>
<th>Type of Correction</th>
<th>Number of Patients</th>
<th>Percentage of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Same in both eyes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unaided</td>
<td>43</td>
<td>3.6</td>
</tr>
<tr>
<td>Glasses</td>
<td>194</td>
<td>16.1</td>
</tr>
<tr>
<td>Contact lenses</td>
<td>321</td>
<td>26.6</td>
</tr>
<tr>
<td>Glasses and contact lenses</td>
<td>571</td>
<td>47.2</td>
</tr>
<tr>
<td>Different in each eye</td>
<td></td>
<td></td>
</tr>
<tr>
<td>One eye: Unaided</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fellow eye: Contact lenses</td>
<td>37</td>
<td>3.1</td>
</tr>
<tr>
<td>One eye: Glasses and contact lenses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fellow eye:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unaided</td>
<td>2</td>
<td>0.2</td>
</tr>
<tr>
<td>Contact lenses</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>Glasses</td>
<td>40</td>
<td>3.6</td>
</tr>
<tr>
<td>Total</td>
<td>1209</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 5. Patients Wearing Specific Types of Contact Lenses at Baseline

<table>
<thead>
<tr>
<th>Type of Correction</th>
<th>One Eye</th>
<th>Two Eyes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rigid contact lenses*</td>
<td>94 (8)</td>
<td>790 (65)</td>
</tr>
<tr>
<td>Soft contact lenses</td>
<td>21 (2)</td>
<td>30 (2)</td>
</tr>
<tr>
<td>Piggyback contact lenses</td>
<td>18 (1)</td>
<td>17 (1)</td>
</tr>
<tr>
<td>Hybrid (Softperm)</td>
<td>17 (1)</td>
<td>24 (2)</td>
</tr>
</tbody>
</table>

Eyes may be represented more than once if patient wears more than one type of contact lens in an eye.
Values are number of patients with corrective lenses, with percentage in parentheses.
* Rigid gas-permeable contact lenses or conventional hard polymethylmethacrylate contact lenses.

Of the 896 patients in whom contact lens comfort was assessed at baseline, 652 (72.8%) reported that their contact lenses were comfortable in both eyes. Ninety-six patients (10.7%) reported that contact lenses were irritating in both eyes, and 147 patients (16.4%) reported that one lens was comfortable and the other irritating. One hundred sixty-three patients (13.5%) reported a family history of keratoconus in a parent, sibling, child, aunt, or uncle.

High-contrast entrance visual acuity and best corrected visual acuity for the better eye are summarized in Table 6. Ninety percent of the patients had entrance acuity of 20/40 or better, and 95.5% had best corrected acuity of 20/40 or better. Monocular entrance visual acuity results by better eye and worse eye are shown in Table 7. Forty-five percent of patients had similar entrance visual acuity in both eyes. Sixty-three percent had entrance visual acuity of 20/40 or better in both eyes.

The best corrected high-contrast monocular visual acuity data by better and worse eye are shown in Table 8. Approximately one-half of the patients had equal visual acuity in both eyes. Compared with the entrance visual acuity, a higher proportion of patients achieved at least 20/20 best corrected visual acuity in both eyes. A small proportion of patients had best corrected visual acuity worse than 20/60 in either eye. The subjective refraction yielded sphere results of $-5.04 \pm 1.84$ D and cylinder results of $-2.49 \pm 1.84$ D (randomly selected, one eye per person; $n = 1205$).

Disease severity by central keratometry is depicted in Table 9. As expected, the flat keratometric reading was steeper with more severe disease, and the magnitude of corneal toric...
ity was greater with more severe disease. A profile of disease severity in the CLEK Study sample was also developed (see Table 11) that is distinctly skewed in the direction of moderate to severe disease, when measured by the steep keratometric reading.

When corneal curvature was assessed by the base curve radius of the flattest contact lens that vaulted the cornea (FDACL), the mean base curve radius of the FDACL was 50.94 ± 5.70 D for the 1182 patients for whom this assessment was made. The correlation of FDACL with the steep keratometric reading was 0.89 (Pearson correlation; \( P = 0.001 \)).

The slit lamp biomicroscopic signs of keratoconus (Vogt’s striae, Fleischer’s ring, and corneal scarring) are listed in Table 10. Although the majority of patients had a Fleischer’s ring in both eyes, the presence of Vogt’s striae was noted in both eyes of only one-third of the patients. One half of the patients entered the study with no corneal scarring in either eye.

**DISCUSSION**

The 1209 patients with keratoconus enrolled in the CLEK Study represent the most systematically studied and carefully characterized sample of patients with keratoconus ever prospectively examined. Previous samples have been studied retrospectively,\(^{2,5,13,17-20,28-30}\) but, because of the rarity of the disease,\(^{17}\) all studies, including ours, were clinic-based (Table 11). In contrast to previous studies, the CLEK Study patient-based entry criteria were rigorously adhered to by the CLEK clinic personnel. The requirement that each patient have a slit lamp biomicroscopic sign of keratoconus (Vogt’s striae, Fleischer’s ring of at least 2 mm of arc, or corneal scarring characteristic of keratoconus in at least one eye) resulted in a sample with some fellow eyes that could be classified as exhibiting early or preclinical keratoconus. Conversely, some patients had moderate or advanced keratoconus in one eye and had a penetrating keratoplasty in the fellow eye. The result of these carefully applied entry criteria is a large sample of patients whose disease encompasses the entire spectrum of the disease that we clinically label as keratoconus.

The CLEK Study patients represent a highly educated sample. We postulate this may be because of selection bias. Volunteers for studies are typically more educated,\(^{31,32}\) and many of our clinics are in academic settings. Our ethnic distribution approximates that of the United States population. The age distribution of the CLEK Study patients is distinctly skewed toward younger ages, similar to those in other studies (Fig. 2). This may be because of several factors, including study exclusion criteria, but the age pattern is counter-intuitive because keratoconus is a chronic disease. Thus, a larger proportion of older people with the disease would have been expected in the sample. One prospective study found no increased mortality associated with keratoconus.\(^{17}\) Perhaps older patients with keratoconus are not as dependent on contact lens wear, have undergone bilateral penetrating keratoplasty, or do not receive routine eye care at our 16 clinics.

Most of the patients enrolled in the CLEK Study wore rigid gas-permeable contact lenses. These data parallel those of our preliminary CLEK survey, which showed that vision in 75% of the

**TABLE 7. Entrance High-Contrast Monocular Visual Acuity for 1208 Study Patients at Baseline**

<table>
<thead>
<tr>
<th>Snellen Visual Acuity, Better Eye</th>
<th>20/20 or better</th>
<th>20/21 to 20/40</th>
<th>20/41 to 20/69</th>
<th>20/70 to 20/199</th>
<th>20/200 or worse</th>
</tr>
</thead>
<tbody>
<tr>
<td>20/20 or better</td>
<td>65 (5.4)*</td>
<td>278 (23.0)</td>
<td>35 (2.9)</td>
<td>19 (1.6)</td>
<td>12 (1.0)</td>
</tr>
<tr>
<td>20/21 to 20/40</td>
<td>418 (34.6)*</td>
<td>178 (14.7)</td>
<td>64 (5.3)</td>
<td>33 (2.7)</td>
<td>15 (1.2)</td>
</tr>
<tr>
<td>20/41 to 20/69</td>
<td></td>
<td>40 (3.3)*</td>
<td></td>
<td>29 (2.4)</td>
<td></td>
</tr>
<tr>
<td>20/70 to 20/199</td>
<td></td>
<td></td>
<td>12 (1.0)*</td>
<td>6 (0.5)</td>
<td></td>
</tr>
<tr>
<td>20/200 or worse</td>
<td></td>
<td></td>
<td></td>
<td>4 (0.3)</td>
<td></td>
</tr>
</tbody>
</table>

Each table entry represents the number of patients classified by the visual acuity level in each eye, with the percentage of patients in parentheses.

* Equal acuity in both eyes. Empty cells are logically impossible.

**TABLE 8. Best Corrected High-Contrast Monocular Visual Acuity for 1204 Study Patients at Baseline**

<table>
<thead>
<tr>
<th>Snellen Visual Acuity, Worse Eye</th>
<th>20/20 or better</th>
<th>20/21 to 20/40</th>
<th>20/41 to 20/69</th>
<th>20/70 to 20/199</th>
<th>20/200 or worse</th>
</tr>
</thead>
<tbody>
<tr>
<td>20/20 or better</td>
<td>169 (14.0)*</td>
<td>331 (27.5)</td>
<td>27 (2.2)</td>
<td>8 (0.7)</td>
<td>3 (0.3)</td>
</tr>
<tr>
<td>20/21 to 20/40</td>
<td>438 (36.4)</td>
<td>128 (10.6)</td>
<td>39 (3.2)</td>
<td>7 (0.6)</td>
<td></td>
</tr>
<tr>
<td>20/41 to 20/69</td>
<td>28 (2.3)*</td>
<td>14 (1.2)</td>
<td>10 (0.8)*</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>20/70 to 20/199</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 (0.1)*</td>
</tr>
<tr>
<td>20/200 or worse</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Each table entry represents the number of patients classified by the visual acuity level in each eye, with the percentage of patients in parentheses.

* Equal acuity in both eyes. Empty cells are logically impossible.
patients was corrected with rigid contact lenses and agrees with data collected by other investigators. Some previous reports do not document the proportion of patients corrected with contact lenses. Some reports of small samples suggest approximately equal numbers of patients treated with either contact lenses or surgery. Previous studies have shown that patients classified as surgical candidates could be fitted with rigid gas-permeable contact lenses when an additional contact lens refit was attempted before surgery. Large variability in reports of contact lens correction among patients with keratoconus may reflect unique features of patient samples associated with given investigators or institutions.

In evaluating contact lens comfort, the majority of CLEK Study patients reported their lenses to be comfortable. However, 10% to 18% of them could not wear their lenses adequately during leisure activities or when reading at the end of the day. Perhaps the patients reported on the comfort at the time of the question (i.e., during the study visit) and may not have assessed comfort based on the duration of lens wear throughout a given day or during several days. Our patient-reported findings on spectacle correction show, however, the value of spectacles as an adjunct to contact lens wear. Patients may benefit from spectacles fitted to wear over their rigid contact lenses to eliminate uncorrected astigmatism, or they may benefit from bifocals or reading glasses for presbyopia. Many patients reported possession of spectacles as back-up to their contact lenses, presumably for use when they were unable to tolerate their contact lenses—for example, on awakening or at night.

### Table 9. Flat Keratometric Reading and Corneal Toricity for Three Categories of Steep Keratometric Reading

<table>
<thead>
<tr>
<th>Steep Keratometric Reading</th>
<th>Number of Patients*</th>
<th>Flat Keratometric Reading (D)†</th>
<th>Corneal Toricity†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (&lt;45 D)</td>
<td>55 (4.6)</td>
<td>42.48 ± 1.09</td>
<td>1.41 ± 1.06</td>
</tr>
<tr>
<td>Moderate (45–52 D)</td>
<td>586 (48.7)</td>
<td>45.73 ± 2.44</td>
<td>3.28 ± 2.23</td>
</tr>
<tr>
<td>Severe (&gt;52 D)</td>
<td>562 (46.7)</td>
<td>53.87 ± 5.70</td>
<td>4.01 ± 3.45</td>
</tr>
<tr>
<td>Overall</td>
<td>1203 (100.0)</td>
<td>49.49 ± 6.01</td>
<td>3.53 ± 2.87</td>
</tr>
</tbody>
</table>

All values are for the worse, or more advanced eye, as categorized by the steep keratometric reading. Based on 1203 patients for whom flat and steep keratometric readings are available at baseline.

* Values in parentheses are percentages.
† Values are means ± SD.

The association between eye rubbing and keratoconus dates back many years. A problem with documenting this association and its magnitude is the definition of an appropriate comparison group. For example, no comparison between rigid contact lens–wearing patients with and without keratoconus has ever been conducted.

Most clinicians associate atopic disease with keratoconus. They expect affected patients to exhibit the signs and symptoms of hay fever, allergy, asthma, and atopic dermatitis more frequently than the general population. A reasonable estimate for the prevalence of atopy in the general population is 10% to 20%. Obviously, this estimate is geography- and sample-dependent. Previous reports of the prevalence of atopy in patients with keratoconus have ranged from 24% to 42% to a high of 53%. Our highest estimate is 53% for hay fever and allergies and is in keeping with estimates in these reports. The clinical significance of this association is unknown. Perhaps patients with keratoconus who also have atopic disease are especially prone to eye rubbing, simply because their eyes itch, and eye rubbing is associated with but not causative of keratoconus.

Previous case reports or small case series of patients with rare systemic diseases and keratoconus were not confirmed by the CLEK Study sample. It may be that anywhere from none to a small proportion of patients with keratoconus also have connective tissue disorders, but such disorders are certainly not present in the majority of patients.

Reported rates of a positive family history of keratoconus are in the range of 6% to 8% with one study reporting 15% compared with our report of 13.5%. One study of the corneal topography of 28 family members of 5 patients with keratoconus showed an increased prevalence of abnormal but nonkeratoconic corneal topography, suggesting an inheritance pattern with variable penetrance in some cases of the disease. Visual acuity in the CLEK Study patients is relatively good. Comparison of our data on entrance with that of best corrected visual acuity shows that the CLEK Study patients have the potential of seeing better than they do with their habitual visual correction. These results may lead eye care practitioners to evaluate their patients’ current mode of correction more critically and to attempt to improve visual acuity.

The CLEK Study patients are classified overwhelmingly into the steep keratometric reading-based categories of moderate and severe. Twenty-one percent of Thalainen’s much smaller sample of patients with keratoconus had steep keratometric readings 52.00 D or steeper compared with 47% of others.
### Table 11. Summary of Previous Epidemiologic Studies of Patients with Keratoconus

<table>
<thead>
<tr>
<th>Study</th>
<th>Source of Patients</th>
<th>Number of Eyes/Patients</th>
<th>Disease Severity</th>
<th>Method of Severity Characterization</th>
<th>Age Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kennedy et al., 1986</td>
<td>Mayo Clinic</td>
<td>102/64</td>
<td>Diagnostic criteria only</td>
<td>Not applicable</td>
<td>Age at diagnosis only</td>
</tr>
<tr>
<td>Macsai et al., 1990</td>
<td>Cornea specialty practice</td>
<td>398/199</td>
<td>Mild (55%); moderate (41%); severe (4%)</td>
<td>Spectacle-corrected visual acuity</td>
<td>Mean ~ early 30s; no one older than 56 years</td>
</tr>
<tr>
<td>Eggink et al., 1988</td>
<td>Academic and nonacademic clinical centers</td>
<td>??/874</td>
<td>Not given</td>
<td>Not applicable</td>
<td>Age at diagnosis only</td>
</tr>
<tr>
<td>Lass et al., 1990</td>
<td>Three cornea specialty practices</td>
<td>834/417</td>
<td>No categorical designations</td>
<td>Categories by best corrected visual acuity and average keratometric reading</td>
<td>Mean, 35 ± 11 years; 90% ≤ 50 years of age</td>
</tr>
<tr>
<td>Swann and Waldron, 1986</td>
<td>Private optometry practice</td>
<td>87/57</td>
<td>No discussion</td>
<td>Not applicable</td>
<td>Mean, 28.5 years; distribution unknown</td>
</tr>
<tr>
<td>Ihalainen, 1986</td>
<td>University hospital</td>
<td>??/212</td>
<td>Degrees I through IV</td>
<td>Steep keratometric reading categories</td>
<td>Mean, 27.7 ± 10.6 years; 92% &lt; 50 years of age</td>
</tr>
<tr>
<td>Crews et al., 1994</td>
<td>Cornea and contact lens specialty practice</td>
<td>118/66</td>
<td>Categorization by type of management only</td>
<td>Mean keratometric reading</td>
<td>Mean, 28 years; range, 10–83 years; distribution unknown</td>
</tr>
<tr>
<td>Tuft et al., 1994</td>
<td>Specialty contact lens clinic</td>
<td>5242/2723</td>
<td>Presented only in context of surgical intervention</td>
<td>Presented only in context of surgical intervention</td>
<td>Age at diagnosis only</td>
</tr>
<tr>
<td>Zadnik et al., 1996</td>
<td>38 clinical centers</td>
<td>2379/1579</td>
<td>No categorical designations</td>
<td>Categories by best-corrected visual acuity and average keratometric reading</td>
<td>Mean, 37 years; range, 10–89 years; 88% &lt; 50 years of age</td>
</tr>
</tbody>
</table>

?, number of eyes not specified.

This represents the baseline results from the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study. The patients are young with moderate to severe disease by a keratometric-based criterion, with good visual acuity. They are predominantly rigid gas-permeable contact lens wearers whose lenses are mostly comfortable. Few of them report a positive family history of keratoconus. None of them report the serious systemic diseases that have been associated with keratoconus, and many of them report a history of atopy. Many of them exhibit the slit lamp biomicroscopic signs of keratoconus, but most of them have at least one cornea in which corneal scarring has not developed. This cohort of 1209 patients spans the spectrum of keratoconus and will be observed for a period of at least 3 years to develop a picture of the progression of keratoconus and risk factors associated with progression of the disease.
Acknowledgments

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References