Characteristics of Corneal Ectasia After LASIK for Myopia

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Purpose: There are numerous reports of corneal ectasia after laser in situ keratomileusis (LASIK) for myopia without a consistent definition of this condition or a definitive etiology. We conducted a retrospective analysis of published case reports to describe common characteristics of this postoperative event and compared them with findings from a group of successful LASIK patients.

Methods: A MEDLINE search for "LASIK" and "ectasia" yielded 21 relevant articles published before May 2003 (n = 86 eyes, 59 patients). A comparison group (n = 103 eyes, 63 patients) was selected from a clinic-based sample of successful LASIK patients with 12 months of follow-up after treatment. Descriptive statistics are reported as median and interquartile range. Comparisons were performed using the Wilcoxon rank sum, Wilcoxon signed rank, and chi-square tests.

Results: Time to diagnosis of ectasia after LASIK was 13 months (6 to 20 months). Residual myopia in the ectasia group was −3.69 D (−6.00 to −2.13 D) and was significantly greater than the comparison group, −0.38 D (−0.75 to 0.00 D), $P < 0.001$. After surgery, eyes with ectasia had increased corneal toricity 2.87 D (2.00 to 4.9 D) with increased oblique astigmatism 1.3 D (0.23 to 2.89 D) relative to eyes in the comparison group 0.00 D (0.00 to 0.08 D), and a loss of 2 lines (−0.5 to −6 lines) of best spectacle-corrected visual acuity (all $P < 0.001$). Thirty-five percent of reported cases resulted in subsequent corneal transplantation.

Conclusions: Preoperative characteristics of corneal ectasia include worse visual acuity, less corneal thickness, greater residual myopia, and greater corneal toricity than nonectatic eyes. Treatment factors associated with corneal ectasia after LASIK are greater stromal ablation and less residual stromal bed thickness. Postoperative characteristics of corneal ectasia are myopic refractive error with increased astigmatism, worse spectacle-corrected visual acuity, increased corneal toricity with topographic abnormality, and progressive corneal thinning.

Key Words: corneal ectasia, LASIK, refractive surgery, complications, literature review

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Laser in situ keratomileusis (LASIK) is the most common refractive surgical procedure for the treatment of myopia. The safety and success of this elective surgical procedure are widely reported.[1–3] Although the incidence of serious complications is relatively low, the visual consequences in some instances are severe. Corneal ectasia after LASIK is among the more serious complications with visual morbidity that in some cases requires corneal transplantation.

Several studies have attempted to define the preoperative and intraoperative risk factors associated with corneal ectasia after LASIK.[4–6] These studies have failed to converge on a consistent set of risk factors, which may reflect an inconsistent definition of this condition, sampling bias, or merely differences in study design. Alternatively, this may suggest multiple etiologies that do not share the same risk factors but lead to a similar cluster of disease manifestations.

The purpose of this study is to address the lack of a consistent clinical definition of corneal ectasia after LASIK. We describe the common clinical characteristics of corneal ectasia after LASIK by summarizing the findings of cases reported in the peer-reviewed literature and make comparisons with a sample of successful LASIK outcomes. Based on these comparisons, we suggest criteria that support a case definition of corneal ectasia after LASIK.

MATERIALS AND METHODS

This study was designed as a retrospective review of cases of corneal ectasia after LASIK for myopia and myopia with astigmatism reported in the peer-reviewed literature. We compiled individual clinical data from these reported cases and compared them with a convenience sample of successful patients who received LASIK for myopia or myopia with astigmatism. This study was reviewed and approved by the appropriate institutional review boards.

Ectasia Cases

We searched MEDLINE using keywords "LASIK" and "ectasia" in May 2003. This search yielded 60 articles. Careful review of each manuscript provided 21 relevant reports containing the individual case data presented here.[5–22] We included all available data from each individual eye reported. Publications containing summary statistics, or ectasia from other procedures—photorefractive keratectomy, hyperopic LASIK, and radial keratotomy—were not included in this analysis. We analyzed postoperative data reported at the time of diagnosis. This postoperative examination time varied by eye and by study; the median time reported was 13 months.

Comparison Group

We selected a comparison sample from a single clinic population to assess the differences between published cases of corneal ectasia after LASIK and eyes with successful outcomes. This convenience sample consisted of sequential cases of LASIK treated by a single surgeon for myopia with and without astigmatism enrolled between August 1999 and August 2000. All subjects had completed 12 months of postoperative observation. We made no attempt to restrict this sample by range of refractive error or to match the samples on any other characteristics. We compared preoperative and 12-month postoperative data from these eyes to the preoperative and postoperative data of eyes with corneal ectasia at their time of diagnosis.

Clinical Outcomes

Clinical data obtained from the ectasia sample and comparison group before and after surgery included best spectacle-corrected visual acuity, manifest refraction, corneal toricity, and corneal thickness. Snellen visual acuity values were transformed into log minimum angle of resolution (logMAR) values for statistical analyses; we report Snellen equivalents in our results. Surgical parameters obtained included intended ablation depth, intended flap thickness, and stromal bed thickness reported as measured or calculated within each individual study.

Refractive error was transformed into vector components according to the methods proposed by Thibos et al.[23] Mean spherical equivalent power is indicated as *MSE*. We denote with- and against-the-rule astigmatism as the absolute value of the vector component $|J_0|$, and oblique astigmatism is denoted as the $|J_{45}|$ vector component. The magnitudes of these vectors represent approximately half of the magnitude of astigmatism when transformed to conventional prescription format, ie, $|J_{45}| = 2$ D represents 4 D of oblique astigmatism in conventional spectacle prescription form.

Statistical Methods

Statistical analysis was performed with Stata v8.0 (Stata Corp., College Station, TX). Statistical significance was defined as $P < 0.05$. Because much of the analysis in this study depends on the distribution of our data, we present box plots for many of the variables of interest. These plots are constructed with a box that represents the middle 50% of all values, namely, the interquartile range. The median is represented by the horizontal line within the interquartile range. Whiskers extend from the box to delimit the minimum and maximum range of values. Extreme values, greater than 3 times the interquartile range, are plotted as individual points outside the whiskers.

We elected to use nonparametric statistical methods—the Wilcoxon rank sum test for independent sample comparisons and the Wilcoxon sign rank test for paired comparisons—because we could not meet the assumptions required for parametric statistical tests. Specifically, we evaluated the distribution of our outcome variables: best spectacle-corrected visual acuity, manifest refraction, corneal toricity, and corneal thickness. We found that these data were not normally distributed (all $P < 0.001$; Shapiro Wilk test of normality) and found the variance was unequal between the ectasia sample and the comparison group. The descriptive statistics reported are the median and interquartile range (IQR). For comparisons of data with frequent ties between groups, we used χ^2 tests of association with collapsing intervals.

To analyze corneal curvature and toricity, we classified literal descriptions as well as any videokeratography data provided by the authors of these published cases. We grouped the descriptions provided into four categories reflecting the most common features described by the original authors:

1. Spherical or aspheric symmetry, commonly described as "normal" corneal curvature without corneal toricity.
2. Symmetric corneal toricity, often described as "symmetric astigmatism," "regular bowtie," or "normal corneal toricity."
3. Marked central steepening, described as "disproportionately steep centrally" and without evidence of toricity or inferior steepening. All preoperative eyes in this category were >47.5 D
4. Asymmetric corneal toricity with inferior steepening, most frequently described by authors as "asymmetric astigmatism" or "inferior steepening."

TABLE 1. Summary of Demographic and Postoperative Data for Cases of Corneal Ectasia After LASIK for Myopia Reported Before May 1, 2003

	Sample Size (eyes)	Age (years)	Gender (% ♀)	Onset (months)	Residual MSE (diopters)	BSCVA (Snellen)	Pachymetry (μm)
Comparison sample	103	42 (38 to 49)	65	N/A	−0.38 (−0.75 to 0.00)	20/20 (20/15 to 20/20)	514 (488 to 539)
Total Ectasia sample	86†	35 (27 to 45)	55	13 (6 to 20)	−3.69 (−6.00 to −2.13)	20/5 (20/32 to 20/80)	375 (325 to 460)
Amoils[14]	13	32 (27 to 38)	57	17 (2 to 22)	−5.75 (−7.50 to −3.25)	20/80 (20/50 to 20/100)	419 (346 to 470)
Holland[16]	7	35 (35 to 46)	43	N/R	−10.13 (−15.88 to −5.13)	20/200 (20/20 to 20/400)	312 (273 to 450)
Pallikaris[22]	19	42 (27 to 45)	53	15 (9 to 20)	−3.75 (−5.00 to −2.50)	20/33 (20/30 to 20/63)	N/R
Argento[9]	8	34 (21 to 40)	29	15 (12 to 24)	−3.00 (−4.25 to −0.25)	20/40 (20/30 to 20/40)	462 (325 to 476)
Randleman[6]	10	36 (28 to 45)	86	7 (4 to 17)‡	−1.5 (−4.13 to −1.00)	20/25 (20/20 to 20/50)	N/R

Individual data from the 5 largest reports are shown with a comparison sample of eyes undergoing uneventful LASIK. Table values are median and interquartile range; N/R, not reported; N/A, not applicable; MSE, mean spherical equivalent; BSCVA, best spectacle-corrected visual acuity.

†Sample includes only eyes that received LASIK for myopia.

‡Data from Randleman et al (Fig. 8).[6]

Corneal Ectasia Classification

We compared sensitivity, specificity, and accuracy* for each of the postoperative clinical measurements that we found significantly associated with corneal ectasia after LASIK (see Table 3). For each of these clinical characteristics, we calculated the best separation criteria for our two groups using maximal classification accuracy as our criteria. Attribute values exceeding these thresholds were scored 1, values less than threshold or missing data were scored as 0. A corneal ectasia classification score was computed as the sum of each of these 9 attributes.

Sensitivity, specificity, and accuracy vary as a function of the classification threshold criteria. Highly sensitive criteria result in a greater number of false-positive misclassifications. Conversely, highly specific criteria result in a larger proportion of false-negative misclassifications. A useful way to represent the tradeoff between sensitivity and specificity is to plot sensitivity as a function of (1 − Specificity). This plot is known as the receiver operating characteristic (ROC) plot. There are two reasons to use this method to evaluate a classification model. First, this method shows the tradeoff between sensitivity and specificity over the continuum of possible cutpoint criteria. Second, the overall quality of a classifier can be judged by a single metric, the area under the curve, and this area can be compared statistically to other classifiers. After identifying characteristics of corneal ectasia, we used ROC curves to determine the quality of our proposed classification method. We then use ROC plots to compare the performance of our composite corneal ectasia classification model to other classifiers.

*Sensitivity is defined as the number of correct identifications of corneal ectasia from all cases of corneal ectasia in the sample: Sensitivity = True Positive/(True Positive + False Negative). Specificity in this context is defined as the proportion of correct normal identifications of all eyes that are truly normal: Specificity = True Negative/(True Negative + False Positive). Accuracy is the proportion of total correct classifications out of all eyes considered: Accuracy = (True Positive + True Negative)/(Total Sample Size).

RESULTS

Sample Description

The combined sample of individual cases of corneal ectasia after LASIK consisted of 86 eyes from 59 different patients. Approximately 65% (57/86) of the total number of eyes analyzed came from 5 of the 21 published reports.[6,9,14,16,22] Our comparison sample consists of 103 eyes from 63 patients. Demographic variable distributions for the corneal ectasia sample and the comparison group are summarized in Table 1.

Age distributions were significantly different in the ectasia sample and the comparison group (Wilcoxon rank sum statistic, $P < 0.001$; median values were 35 and 42 years, respectively). There is no evidence of a significant association of gender with ectasia in these samples ($\chi^2 = 1.72$; $P = 0.19$).

COMPARISONS OF CLINICAL DATA

Refractive Error

The median and IQR of the preoperative spherical equivalent myopia in the ectasia sample was −10.50 D (−14.00 to −5.75 D) and was −4.75 D (−6.25 to −3.25 D) in the comparison group (Fig. 1A). This difference in preoperative myopia was significant ($P < 0.001$). After LASIK, median residual spherical equivalent refractive error in the ectasia group was −3.69 D (−6.00 to −2.13 D) compared with −0.38 D (−0.75 to

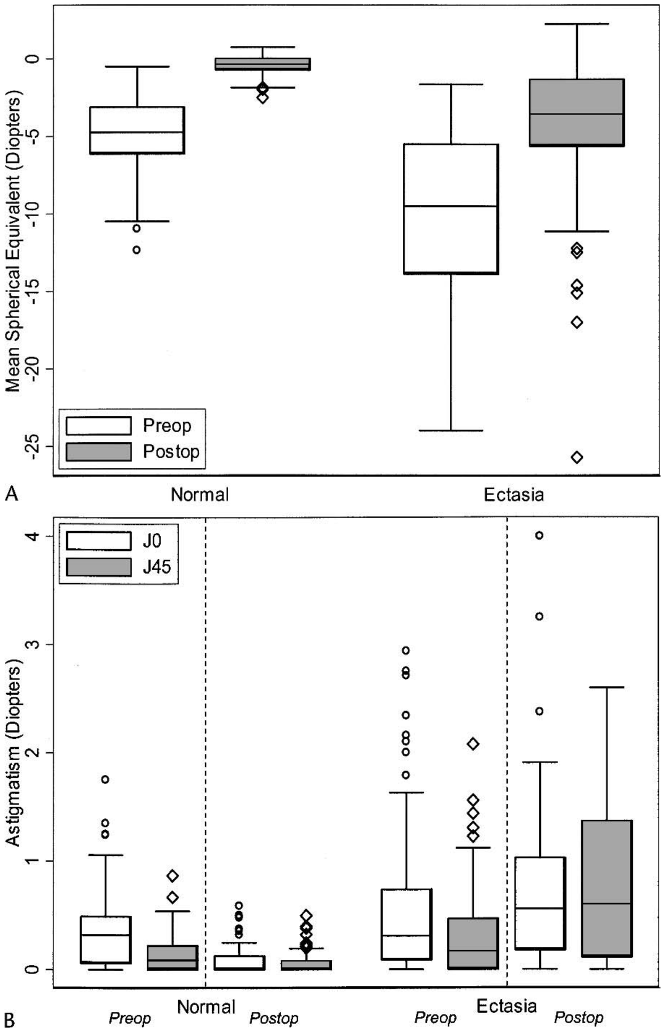

FIGURE 1. A, Distribution of mean spherical equivalent refractive error by sample before and after LASIK: $n_{comparison}$ = 102; $n_{ectasia}$ = 72. B, Distribution of the absolute values of J_0 and J_{45} astigmatic vector magnitudes by sample before and after LASIK; $n_{comparison}$ = 101; $n_{ectasia}$ = 52.

0.00 D) in the comparison sample at 12 months (Fig. 1A), and this difference was also significant ($P < 0.001$).

The distribution of astigmatic refractive error is shown in Figure 1B. Both J_0 and J_{45} astigmatic vectors were greater in the ectasia group than in the comparison group before treatment and increased after treatment. In contrast, both J_0 and J_{45} astigmatic components in the comparison group were reduced effectively by treatment. The magnitudes of the J_0 and J_{45} astigmatic components were significantly different between the two groups after treatment ($P < 0.001$). The magnitude of oblique astigmatism was 1.3 D (0.23 to 2.89 D) for the ectasia group and 0.00 D (0.00 to 0.08 D) in the comparison sample. After LASIK treatment, with- and against-the-rule astigmatism increased in the ectasia sample 1.1 D (0.36 to 2.31 D) and decreased in the comparison group 0.00 D (0.00 to 0.13 D).

Visual Acuity

The distribution of best spectacle-corrected visual acuity before and after LASIK treatment of each group is shown in Figure 2. Preoperatively, the ectasia sample had worse acuity than the comparison sample: 20/25 (20/20 to 20/40). The full range of preoperative visual acuity reported in the ectasia sample was 20/20 to 20/200. The ectasia group was also significantly worse than the comparison group postoperatively 20/50 (20/30 to 20/80). This change represents a median loss of 2 (−0.5 to −6) lines of best spectacle-corrected visual acuity. Best spectacle-corrected visual acuity in the comparison sample varied little before or after treatment. The median preoperative best spectacle-corrected visual acuity for the comparison group was 20/20 (20/10 to 20/30). Best spectacle-corrected visual acuity did not change significantly after treatment in the comparison group: 20/20 (20/15 to 20/20). A χ^2 test of significance showed a statistically significant association between change in postoperative visual acuity and diagnostic category [$\chi^2_{(8)} = 78.85$; $P < 0.001$].

Corneal Curvature

Flat and steep corneal curvatures were similar between the two samples preoperatively (Fig. 3A). After LASIK, the distribution of both flat and steep corneal curvatures widened in the ectasia sample, and curvature of the steepest meridian increased by 0.80 D (−3.15 to 5.38 D). This change was significantly different from change observed in the comparison group ($P < 0.001$). The distribution of corneal curvature narrowed in the comparison group after treatment (Fig. 3A). Correspondingly, the amount of corneal toricity was greater among eyes with ectasia than in the comparison sample (Fig. 3B). The median preoperative corneal toricity in the ectasia sample was 1.50 D (1.00 to 3.00 D) versus 0.75 D (0.40 to 1.09 D) in the

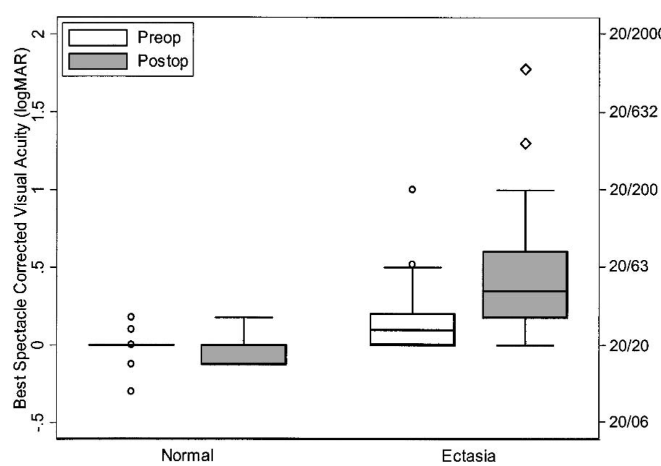

FIGURE 2. Distribution of best spectacle-corrected visual acuity by group before and after surgery: $n_{comparison}$ = 99; $n_{ectasia}$ = 75.

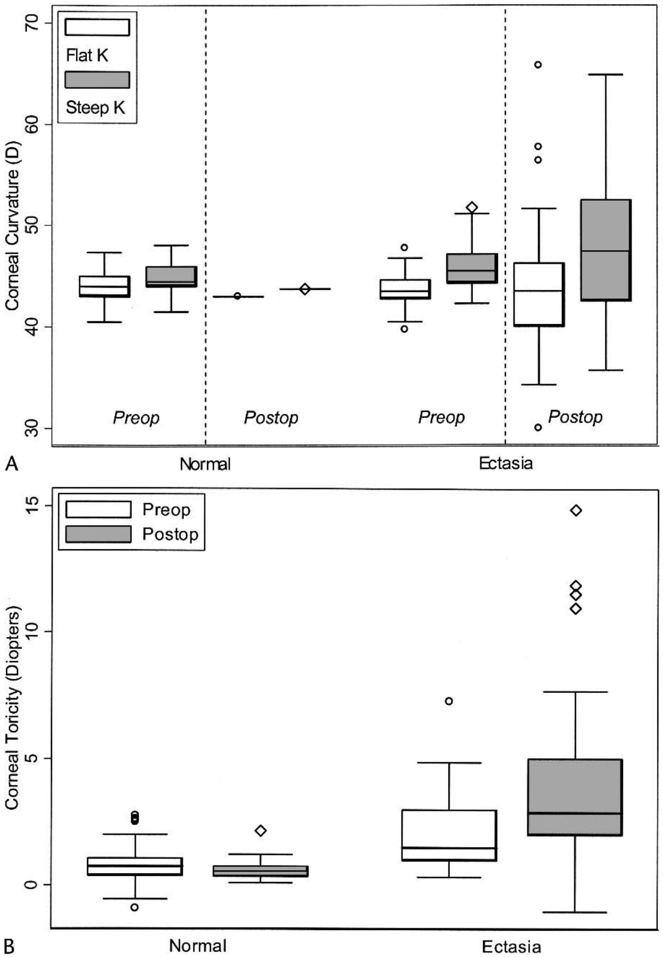

FIGURE 3. A, Comparison of flat and steep corneal curvature distributions for each sample before and after LASIK. B, Distribution of corneal toricity for each sample before and after LASIK for myopia.

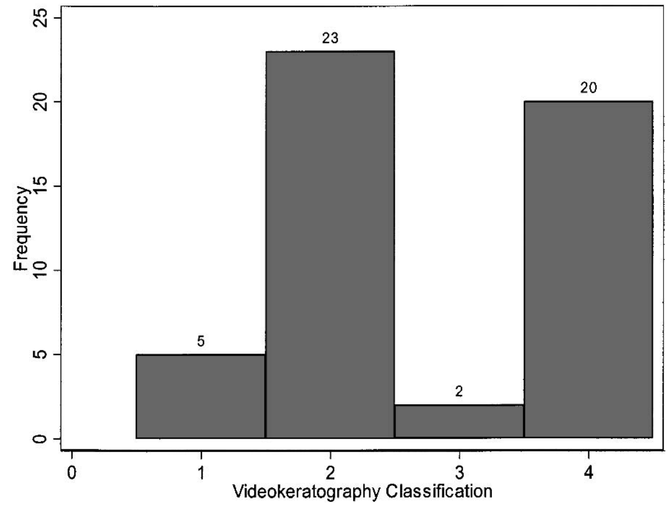

FIGURE 4. Qualitative classification of preoperative videokeratography patterns in eyes diagnosed with corneal ectasia after LASIK. Group 1, spherical or aspheric symmetry; group 2, symmetric corneal toricity; group 3, central steepening; and group 4, asymmetric corneal toricity with inferior steepening; $n_{ectasia}$ = 50.

comparison sample. Postoperatively, corneal toricity in the ectasia sample was 2.87 D (2.00 to 4.90 D) whereas toricity in the comparison sample was reduced to 0.57 D (0.37 to 0.78 D), and this difference was statistically significant ($P < 0.001$).

The distribution of preoperative corneal topographic patterns among the cases of ectasia is shown in Figure 4. After LASIK surgery, all cases of ectasia were described as irregular, with more than 60% (28/42) of reported cases described as having asymmetric corneal toricity with inferior steepening.

Corneal Thickness

We show the distribution of corneal thickness pre- and postoperatively for both samples in Figure 5. Median preoperative corneal thickness in the ectasia group was 512 μm (498 to 530 μm) and was significantly greater in the comparison group 555 μm (523 to 588 μm) ($P < 0.001$).

Because of their higher myopia, eyes in the ectasia sample received significantly deeper ablations, 115 μm (86 to 157 μm), than the comparison group, 47 μm (33 to 62 μm), ($P < 0.001$). These deeper ablations, combined with thinner corneas before treatment, resulted in thinner residual stromal bed thickness among the ectasia sample, 259 μm (210 to 305 μm) versus 334 μm (309 to 359 μm) ($P < 0.001$).

Among eyes that developed corneal ectasia after treatment, the measured change in corneal thickness was +21 μm (−12 to +61 μm) greater than the expected change in corneal thickness (Fig. 6) by the programed ablation depth ($P = 0.03$). Postoperative pachymetry was not available for the comparison group.

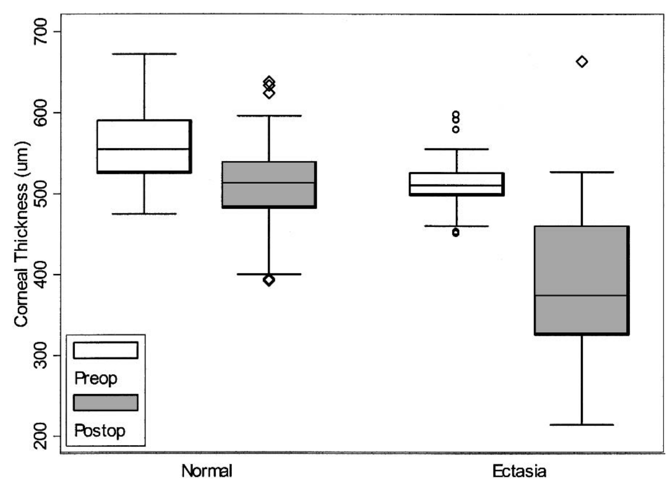

FIGURE 5. Corneal thickness before and after LASIK by sample: $n_{comparison}$ = 103; $n_{ectasia}$ = 74.

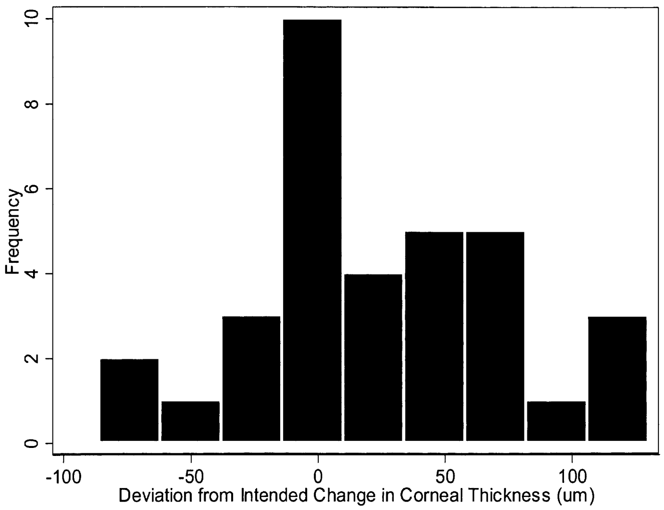

FIGURE 6. Difference of intended change in corneal thickness from measured change in corneal thickness of eyes with ectasia: median = 21, interquartile range = −12 to +61 μm, n = 34.

Time to Diagnosis

The median time to diagnosis of postoperative LASIK ectasia was 13 months (6 to 20 months). The distribution of time to diagnosis for this event was bimodal with nearly 30% (21/76) of cases diagnosed within the first six months after surgery (Fig. 7). This distribution had a second smaller peak at 15 months with a right skewed distribution that extended to 45 months. Stratifying the data with regard to onset before and after 3 months, we found significant differences between earlier onset of corneal ectasia and the clinical variables summarized in Table 2.

Treatment of Ectasia After LASIK

The two most common treatment alternatives for eyes with corneal ectasia after LASIK were rigid gas-permeable contact lenses and penetrating keratoplasty. In this sample of ectasia cases investigators reported what treatment was received after diagnosis in nearly 57% (49/86) of all eyes reported. Of those reporting treatment, 35% (17/49) received penetrating keratoplasty. Rigid gas-permeable contact lenses were used to improve vision in 60% (30/49) of eyes reported. More recently surgeons have attempted to restore optical function using Intacs^{TM} corneal inserts (Addition Technologies, Inc, Des Plaines, IL). This surgical alternative was used in 4% (2/49) of the eyes where treatment was reported.

Evaluation of Classification Criteria

We found 9 postoperative clinical variables that were significantly associated with corneal ectasia after LASIK and list them in Table 3. We determined threshold values that resulted in maximal classification accuracy for each individual variable from the data. We then used maximum likelihood scores from logistic regression to prioritize the order of each variable listed in Table 3.

Defining corneal ectasia by a combination of these individual clinical findings yields a classifier with better overall performance characteristics (Table 4 and Fig. 8). In Table 4, we show that maximum accuracy (94.3%) occurred when 2 or more of the clinical findings exceed threshold. Sensitivity (97%) and specificity (92%) were both high using this classification criterion. For all eyes correctly identified with ectasia by these criteria, 77% (66/86) of eyes had reduced spectacle-corrected visual acuity worse than 20/25. The second and third most frequent findings associated with true positive classification of corneal ectasia among this group were deep ablation, 71% (61/86), and residual myopia, 62% (53/86).

With corneal ectasia defined as a corneal ectasia classification score of two or more positive findings, the area under the ROC curve was 98.6% (95% confidence interval 97.5–99.7%). The total number of misclassifications that occurred by this criterion were 8 false positives and 3 false negatives. With 3 or more positive findings there were 17 misclassifications consisting of 1 false positive and 16 false negatives. With four or more positive findings we achieved 100% specificity; however, the number of false-negative misclassifications rose to 43% (37/86).

DISCUSSION

Evidence from published case reports and comparison with a sample of successful outcomes suggest that both refractive and biometric parameters are useful to distinguish the clinical characteristics of corneal ectasia after LASIK from successful surgical outcomes.

Refractive characteristics of corneal ectasia after LASIK include moderate residual myopia and increased astigmatism

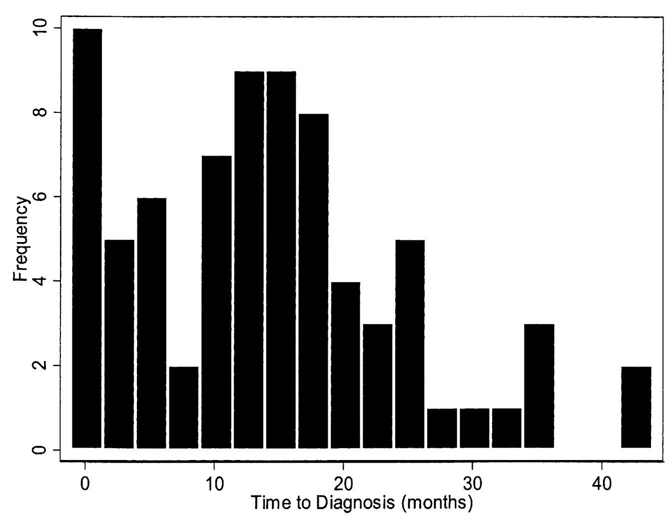

FIGURE 7. Distribution of time to diagnosis among published cases of ectasia: n = 71.

TABLE 2. Factors Associated with Onset of Corneal Ectasia Before and After 3 Months

	Early Onset (3 months or earlier)			Late Onset (after 3 months)			
	N	Median	IQR	N	Median	IQR	P Value
Preop							
BSCVA (Snellen)	14	20/20	20/20 to 20/30	49	20/30	20/20 to 20/32	0.043
Pachymetry (μm)	14	529	516 to 540	56	509	497 to 528	0.028
Postop							
BSCVA* (Snellen)	13	20/80	20/40 to 20/100	53	20/40	20/30 to 20/70	0.014
Loss of BSCVA (lines of acuity)	12	−5	−2 to −7	39	−1	0 to −3	0.020
Corneal toricity (Diopters)	11	4.00	2.11 to 5.80	25	2.23	1.50 to 3.00	0.044

*BSCVA, best spectacle-corrected visual acuity; IQR, interquartile range.

with reduced best spectacle-corrected visual acuity. Corneal shape changes characteristic of ectasia after LASIK include increased corneal toricity, asymmetric inferior steepening, and change in total corneal thickness greater than the intended change from ablation alone.

One of the most distinctive postoperative changes occurring with severe corneal ectasia after LASIK is distortion of anterior corneal shape. However, we found that over half of the reviewed cases of corneal ectasia reporting corneal shape information in this study did not exhibit severe corneal distortion (Fig. 4). Many of these cases were instead categorized with symmetric corneal toricity. Although we could classify these changes and provide some categoric summary of these data, the design of this study limits our ability to quantify this change. Ongoing research of our own and at other institutions may make quantitative comparisons of videokeratography data possible, which would contribute additional information about characteristics of corneal shape associated with corneal ectasia after LASIK. Other investigators have suggested that posterior corneal shape is key to early and correct classification of corneal ectasia.[24,25] Too few reported cases provided posterior corneal shape data to summarize in this study. Although videokeratography was not directly considered as one of our postoperative characteristics of corneal ectasia, corneal shape is captured directly by postoperative toricity and indirectly by residual astigmatism, loss of BSCVA, and postoperative BSCVA. Thus, distortion of corneal shape is well represented in these criteria.

TABLE 3. Postoperative Classification Criteria for Corneal Ectasia After LASIK for Myopia

Clinical Measure	Threshold Value*	Sensitivity (%)	Specificity (%)	Accuracy (%)
BSCVA (Snellen)	Worse than 20/25	92	93	93
Residual astigmatism (diopters)	≥1.25	72	98	90
Corneal toricity (diopters)	≥1.40	87	96	90
MSE refractive error (diopters)	≥−2.00	78	97	89
Pachymetry (μm)	≤400	64	96	86
Estimated ablation depth (μm)	≥76	83	88	86
Loss of BSCVA (logMAR)	≥0.04	79	84	82
Flattening in steepest corneal meridian (diopters)	≤2.00	70	84	75
Difference between intended and achieved reduction in total corneal thickness (μm)	≥25	56	100	89

*Threshold values define the value associated with corneal ectasia for each measure. Sensitivity is the proportion of correctly predicted cases of corneal ectasia. Specificity is the proportion of correctly predicted comparison eyes. Accuracy is the proportion of correct predictions of for both classes combined. BSCVA, best spectacle-corrected visual acuity; MSE, mean spherical equivalent.

TABLE 4. Classifier Performance by Number of Attributes Exceeding Threshold

Criterion*	Sensitivity (%)	Specificity (%)	Accuracy (%)
≥0	100.0	0.0	46.9
≥1	100.0	66.0	82.0
≥2	96.7	92.2	94.3
≥3	82.4	99.0	91.2
≥4	59.3	100.0	80.9
≥5	31.9	100.0	68.0
≥6	17.6	100.0	61.3
≥7	12.1	100.0	58.8
≥8	6.6	100.0	56.2
≥9	0.00	100.0	53.1

*Criterion is defined as the cumulative number of attributes from Table 3 that exceed threshold. Proposed postoperative threshold criteria are visual acuity worse than 20/25, residual astigmatism ≥1.25 D, corneal toricity ≥1.4 D; spherical equivalent refractive error at least −2 D; pachymetry ≤400 μm; ablation depth ≥76 μm; loss of acuity ≥0.5 line; flattening of corneal curvature in the steep corneal meridian less than 2 D; difference between intended and achieved change in total corneal thickness ≥25 μm.

Based on the cases analyzed in this study, corneal ectasia after LASIK is most often associated with a combination of clinical findings. Although we found no single clinical criterion that was characteristic of all cases of corneal ectasia, in most cases a combination of best spectacle-corrected visual acuity of 20/25 or worse, residual astigmatism at least 1.25 D, corneal toricity at least 1.4 D, and residual myopia of −2.00 D or more were all highly specific for this condition. Although we found that area under the ROC curve was maximal with only two of these findings exceeding threshold in our study population, this criterion would be overly sensitive if applied arbitrarily to a population of highly myopic eyes. To achieve better specificity in any group, we recommend 3 or 4 positive findings and thoughtful consideration of the entire clinical picture.

In summary, we found the following clinical criteria were characteristic of corneal ectasia after LASIK for myopia:

- Best spectacle-corrected visual acuity of 20/25 or worse
- Increased astigmatism 1.25 D or more
- Asymmetric corneal toricity of 1.40 D or more by videokeratography
- Residual myopic refractive error at least 2.00 D or more than intended
- Residual total corneal thickness no more than 400 μm
- Estimated ablation depth at least 76 μm
- Reduction in best spectacle-corrected logMAR acuity of 2 or more letters
- Increased corneal power in the steepest meridian relative to preoperative measurements at least 2.00 D by videokeratography
- Difference between intended and achieved reduction in total corneal thickness at least 25 μm.

Randleman et al defined corneal ectasia as inferior topographic steepening of 5 D or more compared with immediate postoperative appearance, loss of 2 or more lines of Snellen acuity, and a change in manifest refraction of 2 D or more of either sphere or cylinder.[6] We agree that these criteria are specific (99%), but they lack sensitivity (71%) and accuracy (86%) compared with our proposed definition (Fig. 8 and Table 4). Area under the ROC curve for the Randleman et al definition was 85% (95% confidence interval 85–90%). This was significantly less than the area under the ROC curve for our proposed definition of ectasia ($\chi^2 = 22.98$; $P < 0.001$).

Using their definition of corneal ectasia after LASIK, Randleman et al defined risk factors from an ectasia sample of 10 eyes from 7 patients and 2 comparison groups consisting of 100 eyes each—one group with moderate myopia and another with high myopia. They report preoperative risk factors as myopia greater than −8.00 D, forme fruste keratoconus, and residual stromal bed thickness less than 250 μm.

Applying risk factors they identified to this sample, we find that 74% (35/47) of eyes with myopia over −8.00 D were correctly classified by this risk factor alone. The sensitivity of this risk factor was 59%; however, the specificity was 87%. If we apply the criteria of residual stromal bed thickness less than 250 μm to these data, we find that we correctly identify 74% (128/173) of all eyes. By itself, stromal bed thickness was not very sensitive, explaining only 45% (34/75) of ectasia cases in

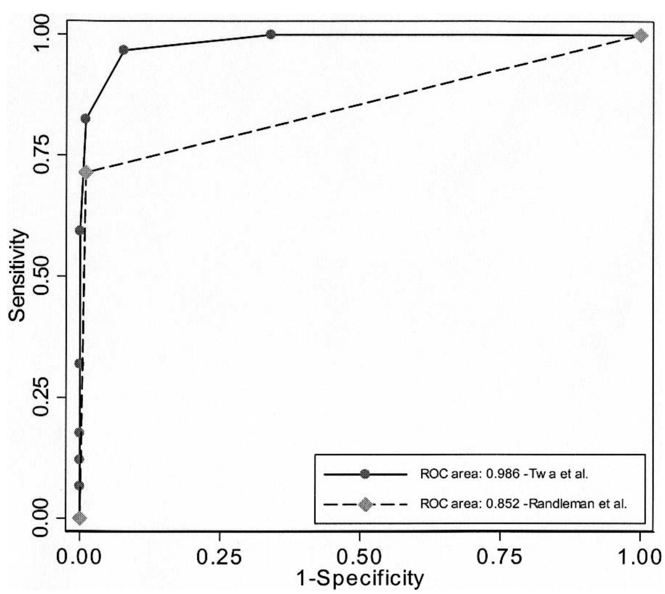

FIGURE 8. ROC comparison of sensitivity and (1-specificity) for two proposed definitions of corneal ectasia after LASIK for myopia. Better classification performance is represented by greater area under the ROC curve. These two curves were significantly different: $\chi^2 = 22.98$, $P < 0.001$.

this study. However, of all eyes identified with residual stromal bed thickness less than 250 μm, 90% (34/38) of them were correctly classified as ectasia. So, although these criteria are not highly sensitive, they are fairly specific for corneal ectasia after LASIK. Unfortunately, it was not possible to evaluate the videokeratography data of our study using the same criteria of Randleman et al.

An ideal clinical test would be both extremely sensitive and highly specific. However, selection of appropriate criteria for optimal sensitivity and specificity must be weighed in context of the costs associated with corresponding false-positive and false-negative misclassifications. To develop screening criteria that will identify all cases of disease, one would prefer a test criterion that is biased toward sensitivity. This would also result in a higher proportion of false-positive misclassifications. If the cost of erroneously classifying healthy patients as diseased is of primary concern, one would prefer a highly specific criterion that only identifies true cases of disease but will have limited ability to detect all cases.

Debate on how best to identify corneal ectasia must also consider the frequency of disease. Although sensitivity and specificity of a classification model do not depend on disease frequency in a population, the predictive value of classification results for any given individual do depend on disease frequency. When disease is less frequent, cases identified are more likely to be false-positive misclassifications. So, we would expect any classification criteria for corneal ectasia to yield a higher proportion of false-positive classifications because of the presumably low frequency of corneal ectasia among the general LASIK population than it would if corneal ectasia were relatively common.

Considering these known constraints, and based on available samples, we developed a corneal ectasia classification score that is a composite of several common clinical observations. Combined, these criteria are highly sensitive and specific. However, alone they are insufficient to make a diagnosis of corneal ectasia. Instead we prefer an alternative interpretation in which greater similarity to the characteristics we describe is merely associated with increased probability of this condition. This classification criterion must still be couched in the entire clinical context for each individual patient.

Sampling bias is an important limitation of our study as well as previous publications on this topic. For example, 35% of these cases eventually received corneal transplantation. It is unknown if this proportion of corneal transplants fairly represents the population of all eyes that develop corneal ectasia after LASIK.

Likewise, the comparison group is a convenience sample that may be biased as well. Because our intent was to identify pre- and postoperative characteristics of ectasia patients, we chose a practice-based comparison group with no limitations on the range of refractive error, corneal thickness, preoperative corneal topography, or other patient characteristics. This comparison group appears to fairly represent the range of refractive error seen in the control groups of other published reports,[6] and we believe it to be fairly representative of common clinical practice. Although age was significantly younger in our sample of eyes with ectasia, additional study is needed to confirm that this finding is real and not a reflection of bias in our sample selection. We found significant correlations (Spearman rank, $P < 0.05$) between age and postoperative MSE, postoperative best spectacle-corrected visual acuity, and change in best spectacle-corrected visual acuity. Although it may not be biologically plausible, it is possible that age alone could explain these group differences.

Unlike the study by Randleman et al, we have not matched our eyes with ectasia on refractive error for our comparison group. One advantage of this approach is that we can determine the association between magnitude of refractive error and corneal ectasia after LASIK. A limitation of not providing a comparison group of highly myopic eyes is that we may underestimate the impact of other factors.

Sanders and Vukich recently published a case series of LASIK in highly myopic eyes.[26] In our comparison group, 16% of patients lost 1 line of best spectacle-corrected visual acuity, giving a specificity of 84%. In Sanders and Vukich's cohort of highly myopic eyes, 15% (28/182) lost 1 line, giving a specificity of 85%. In our comparison group, 3% were undercorrected by at least 2.00 D, giving a specificity of 97%. In Sanders and Vukich's cohort, 3% (6/191) were undercorrected by at least 2.00 D, also giving a specificity of 97%. In summary, their data for LASIK in highly myopic eyes gives very similar specificity to our cohort and should not lead to excessive false positives. Although LASIK for high myopia is more likely to result in some residual myopia and worse spectacle-corrected visual acuity postoperatively than outcomes for lower myopia, critical reviews of published studies in this population show that very few normal outcomes exceed our proposed classification criteria thresholds.[26–29] Additional studies comparing the performance of this proposed corneal ectasia classification criteria with highly myopic eyes as well as other patient populations are needed.

In spite of these limitations, our analyses can be used to make important inferences about corneal ectasia after LASIK. First, we observed a bimodal distribution of the time to diagnosis of this event. Although many cases were diagnosed within the first 3 months following LASIK treatment, a second peak was clustered with a median time to diagnosis of 15 months. The early peak of this distribution may indicate that ectatic disease such as keratoconus or pellucid marginal degeneration was present but unrecognized. Alternatively, those diagnosed early may represent disproportionately greater magnitudes of treatment or less preoperative corneal thickness. Those diagnosed later may reflect an artifact of normal follow-up schedules, or they may suggest other causes, such as a slowly progressive degenerative physiologic response to treatment (ie, extraordinary keratocyte degeneration or neurotrophic degeneration). These ideas warrant further research.

We did find an association between treatment parameters such as ablation depth and incidence of ectasia in our sample, as other studies have shown, suggesting that the magnitude of treatment relative to preoperative corneal thickness is an important factor in the development of corneal ectasia after LASIK.[5,9,15,22,30] By comparing the intended change in corneal thickness from planned ablation parameters with observed change in corneal thickness from clinical measurements, we found that median corneal thickness was reduced more than was intended in eyes with ectasia. There are several possible interpretations of this finding, including poor reliability of clinical measurements, a systematic bias of the ablation algorithm for this class of patients that is related to treatment magnitude, or more effective tissue ablation in these eyes. We speculate that this effect could also be caused by a greater than usual loss of keratocytes with subsequent stromal degeneration.

Preoperative differences in clinical outcomes included worse spectacle-corrected visual acuity, less corneal thickness, greater myopia, and greater corneal toricity in the ectatic group. Treatment factors associated with corneal ectasia after LASIK included greater stromal ablation and thinner residual stromal bed thickness. Our findings suggest that eyes that develop corneal ectasia after LASIK may be associated with identifiable refractive, visual function and biometric characteristics preoperatively as well as treatment parameters that differ from those of eyes that do not develop ectasia postoperatively.

Considering the numbers of patients who elect to have this surgical procedure each year, additional study is needed to establish the causes and risk factors associated with corneal ectasia after LASIK as well as the morbidity associated with this condition. Although many case reports have been published, there have been no rigorous clinical studies that provide firm evidence for clinical guidelines to avoid corneal ectasia after LASIK.

Progress toward predicting and preventing corneal ectasia after LASIK requires a consistent definition of this condition that includes viable diagnostic criteria. A significant challenge to meeting this objective is the spectrum of clinical observations that are currently classified as corneal ectasia after LASIK. We find differences between eyes that develop ectasia and those that do not that are similar to findings from previous reports; however, it is not possible to know if our convergence on a similar definition of this condition merely reflects an intrinsic bias of the literature.

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REFERENCES

1. Sugar A, Rapuano CJ, Culbertson WW, et al. Laser in situ keratomileusis for myopia and astigmatism: Safety and efficacy: A report by the american academy of ophthalmology. *Ophthalmology*. 2002;109:175–187.
2. Gimbel HV, van Westenbrugge JA, Penno EE, et al. Simultaneous bilateral laser in situ keratomileusis: Safety and efficacy. *Ophthalmology*. 1999;106:1461–1467; discussion 1467–1468.
3. Waring GO 3rd, Carr JD, Stulting RD, et al. Prospective, randomized comparison of simultaneous and sequential bilateral lasik for the correction of myopia. *Trans Am Ophthalmol Soc*. 1997;95:271–284.
4. Vinciguerra P, Camesasca FI. Prevention of corneal ectasia in laser in situ keratomileusis. *J Refract Surg*. 2001;17:S187–S189.
5. Rao SN, Epstein RJ. Early onset ectasia following laser in situ keratomileusus: Case report and literature review. *J Refract Surg*. 2002;18:177–184.
6. Randleman JB, Russell B, Ward MA, et al. Risk factors and prognosis for corneal ectasia after LASIK. *Ophthalmology*. 2003;110:267–275.
7. Ou RJ, Shaw EL, Glasgow BJ. Keratectasia after laser in situ keratomileusis (LASIK): Evaluation of the calculated residual stromal bed thickness. *Am J Ophthalmol*. 2002;134:771–773.
8. Haw WW, Manche EE. Iatrogenic keratectasia after a deep primary keratotomy during laser in situ keratomileusis. *Am J Ophthalmol*. 2001;132: 920–921.
9. Argento C, Cosentino MJ, Tytiun A, et al. Corneal ectasia after laser in situ keratomileusis. *J Cataract Refract Surg*. 2001;27:1440–1448.
10. Eggink FA, Beekhuis WH. Contact lens fitting in a patient with keratectasia after laser in situ keratomileusis. *J Cataract Refract Surg*. 2001;27: 1119–1123.
11. Magallanes R, Shah S, Zadok D, et al. Stability after laser in situ keratomileusis in moderately and extremely myopic eyes. *J Cataract Refract Surg*. 2001;27:1007–1012.
12. Ozdamar A, Aras C, Ustundag C, et al. Corneal iron ring associated with iatrogenic keratectasia after myopic laser in situ keratomileusis. *J Cataract Refract Surg*. 2000;26:1684–1686.
13. Lipshitz I, Dotan G. Central corneal pachymetry and lasik. *Ophthalmology*. 2000;107:1967–1968.
14. Amoils SP, Deist MB, Gous P, et al. Iatrogenic keratectasia after laser in situ keratomileusis for less than −4.0 to −7.0 diopters of myopia. *J Cataract Refract Surg*. 2000;26:967–977.
15. Schmitt-Bernard CF, Lesage C, Arnaud B. Keratectasia induced by laser in situ keratomileusis in keratoconus. *J Refract Surg*. 2000;16:368–370.
16. Holland SP, Srivannaboon S, Reinstein DZ. Avoiding serious corneal complications of laser assisted in situ keratomileusis and photorefractive keratectomy. *Ophthalmology*. 2000;107:640–652.
17. Joo CK, Kim TG. Corneal ectasia detected after laser in situ keratomileusis for correction of less than −12 diopters of myopia. *J Cataract Refract Surg*. 2000;26:292–295.
18. McLeod SD, Kisla TA, Caro NC, et al. Iatrogenic keratoconus: Corneal ectasia following laser in situ keratomileusis for myopia. *Arch Ophthalmol*. 2000;118:282–284.
19. Joo CK, Kim TG. Corneal perforation during laser in situ keratomileusis. *J Cataract Refract Surg*. 1999;25:1165–1167.
20. Geggel HS, Talley AR. Delayed onset keratectasia following laser in situ keratomileusis. *J Cataract Refract Surg*. 1999;25:582–586.
21. Seiler T, Quurke AW. Iatrogenic keratectasia after lasik in a case of forme fruste keratoconus. *J Cataract Refract Surg*. 1998;24:1007–1009.
22. Pallikaris IG, Kymionis GD, Astyrakakis NI. Corneal ectasia induced by laser in situ keratomileusis. *J Cataract Refract Surg*. 2001;27:1796–1802.
23. Thibos LN, Wheeler W, Horner D. Power vectors: An application of Fourier analysis to the description and statistical analysis of refractive error. *Optom Vis Sci*. 1997;74:367–375.
24. Rao SN, Raviv T, Majmudar PA, et al. Role of Orbscan II in screening keratoconus suspects before refractive corneal surgery. *Ophthalmology*. 2002;109:1642–1646.

25. Seitz B, Torres F, Langenbucher A, et al. Posterior corneal curvature changes after myopic laser in situ keratomileusis. *Ophthalmology*. 2001; 108:666–672, discussion 73.
26. Sanders DR, Vukich JA. Comparison of implantable contact lens and laser assisted in situ keratomileusis for moderate to high myopia. *Cornea*. 2003;22:324–331.
27. Knorz MC, Wiesinger B, Liermann A, et al. Laser in situ keratomileusis for moderate and high myopia and myopic astigmatism. *Ophthalmology*. 1998;105:932–940.
28. Dada T, Sudan R, Sinha R, et al. Results of laser in situ keratomileusis for myopia of −10 to −19 diopters with a Technolas 217 laser. *J Refract Surg*. 2003;19:44–47.
29. Stojanovic A, Nitter TA. 200 Hz flying-spot technology of the lasersight LSX excimer laser in the treatment of myopic astigmatism: Six and 12 month outcomes of laser in situ keratomileusis and photorefractive keratectomy. *J Cataract Refract Surg*. 2001;27:1263–1277.
30. Spadea L, Palmieri G, Mosca L, et al. Latrogenic keratectasia following laser in situ keratomileusis. *J Refract Surg*. 2002;18:475–480.

