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# KISA% index: A quantitative videokeratography algorithm embodying minimal topographic criteria for diagnosing keratoconus

Yaron S. Rabinowitz, MD, Karim Rasheed, MD, MSc, MRCOphth

## ABSTRACT

**Purpose:** To formulate and test an algorithm using minimal topographic criteria for accurately diagnosing clinical keratoconus.

**Setting:** Subspecialty cornea practice and Keratoconus Genetic Research Project.

**Methods:** Both eyes of 86 keratoconic patients who had never worn contact lenses and 195 normal participants were studied with the TMS-1 videokeratoscope to evaluate the KISA% index, an algorithm that topographically quantifies the phenotypic features of keratoconus. The diagnostic efficacy of the KISA% index was compared with that of the modified Rabinowitz/McDonnell (K- and I-S values) and the Maeda/Klyce (KCI% and KPI) indices. The same indices were calculated for an additional 8 eyes with keratoconus-suspect topography and 12 eyes with early keratoconus.

**Results:** The mean KISA% was significantly greater in the keratoconus group (103.82%) than in the normal control group (20.44%) with minimal overlap. At a cutoff point for KISA% of 100, 280 of 281 participants (99.6%) were correctly classified. In contrast, the correct classification rate for the other indices were KCI%, 274 of 281 (97.5%); KPI, 249 of 281 (88.6%); K, 272 of 281 (96.8%); I-S, 269 of 281 (95.7%). Six of the 8 eyes with keratoconus-suspect topography had a KISA% between 60% and 100%, and 11 of the 12 eyes with early keratoconus had a KISA% greater than 100%.

**Conclusions:** The KISA% index set at 100 was highly sensitive and specific for diagnosing keratoconus; a range of 60% to 100% may be useful for designating suspects. This index is more useful than any of the other currently available tools for classifying patients with keratoconus for computerized segregation analysis and for distinguishing eyes with keratoconus from normal eyes in topographic screening of refractive surgical candidates. *J Cataract Refract Surg* 1999; 25:1327-1335 © 1999 ASCRS and ESCRS

Videokeratography is an excellent tool for confirming the diagnosis of keratoconus even when signs of the disease are not obviously apparent at the slitlamp.<sup>1-4</sup>

As clinicians increasingly use this technology, they are becoming more familiar with the videokeratography patterns that depict overt keratoconus.<sup>5,6</sup> Computer programs with quantitative indices have also been devised to aid clinicians in their subjective interpretation of keratoconus-like videokeratographs.<sup>7-10</sup> There is little agreement, however, as to what constitutes the minimal topographic criteria for making the diagnosis of kerato-

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Reprint requests to Yaron S. Rabinowitz, MD, Cornea-Genetic Eye Institute, Cedars-Sinai Medical Center, Mark Goodson Building, Suite 1102, 444 South San Vicente Boulevard, Los Angeles, California 90048, USA.

conus based solely on videokeratography; hence, the introduction of the term *keratoconus suspect* to describe videokeratographs the clinician suspects might progress to keratoconus based solely on a subjective impression.<sup>11,12</sup>

To clearly define the modes of heredity of keratoconus using techniques such as computer-assisted complex segregation analysis and for screening candidates for refractive surgery, it would be useful to quantify the minimal topographic criteria for diagnosing keratoconus that have direct correlation to clinical disease status and designate topographic criteria for keratoconus suspects who have minimal overlap with the normal population.<sup>13,14</sup> We describe a new algorithm—the KISA% index—embodying features of previously described algorithms that quantify the phenotypic features of keratoconus in an attempt to achieve this goal.

## Patients and Methods

Eighty-six patients were selected from a database of more than 400 patients with keratoconus recruited for longitudinal videokeratography and genetic studies of keratoconus at the Cedars-Sinai Medical Center (CSMC), Los Angeles, California. Inclusion criteria included slitlamp or retroillumination signs of keratoconus in at least 1 eye, absence of corneal scarring, no history of contact lens wear of any type, no signs or history of other corneal disease, and no previous ocular surgery.

One hundred ninety-five normal control participants were also studied. Their demographic data and selection criteria have been reported.<sup>15</sup>

### *Clinical Examination Methods*

Before being entered into the study, all participants were asked to review a patient information sheet approved by the institutional review board for protection of human subjects. They were then asked to complete a questionnaire regarding their family, medical, and surgical histories. The clinical examinations performed on each patient included slitlamp biomicroscopy and direct ophthalmoscopy as well as retinoscopy to determine retroillumination signs of keratoconus (e.g., oil droplet, scissors reflex).

Videokeratography was performed on both eyes of each study participant with the TMS-1 (software version

1.61, Computed Anatomy, Inc.). This software embodies an algorithm that uses axial radius-of-curvature calculations to display topographic maps. The following measures were taken to ensure quality control and reproducibility of video images: At least 4 pictures of each eye were taken; at least the inner 22 of the 25 rings had to be fully digitized; lids had to be kept wide open and off the cornea without assistance or eyelid compression; all pictures had to be within 0.25 diopter (D) of one another as measured by simulated keratometry (Sim K) readings;<sup>16</sup> to ensure proper fixation and alignment, the cross-hair had to be in the center of the pupil for each examination. The best videokeratograph of the 4 was selected based on the quality of the keratoscope mires, determined by visual inspection.

### *Videokeratography-Derived Quantitative Indices*

*Modified Rabinowitz/McDonnell.* In these indices, K is the central K-reading, an index that quantifies the central steepening occurring in keratoconus. The method for calculating this index has been described.<sup>10</sup> The cutoff value was modified by Tomey Inc. before inclusion in version 1.61 of the TMS-1 software.<sup>9</sup> When used alone, a K-value of more than 47.2 D is suggestive of keratoconus.

The indices also use the I-S value, which quantifies the inferior-superior dioptric asymmetry occurring in keratoconus. The method for calculating this index has been described.<sup>10</sup> The cutoff value was also modified by Tomey Inc. before including it in version 1.61 of the TMS-1 software.<sup>9</sup> When used alone, an I-S value greater than 1.4 D is suggestive of keratoconus.

*Maeda/Klyce.* In these indices, KPI is the keratoconus prediction index, which is derived from 8 other quantitative videokeratography-derived indices. The method for calculating this index has been described; Maeda and coauthors<sup>7</sup> suggest that a value greater than 0.23 is indicative of keratoconus.

Also in these indices, the KCI% is derived using a binary decision-making tree that was input from the KPI and 4 other indices described by Klyce and Maeda. The degree of the keratoconus-like pattern is determined and expressed as a percentage, which is the KCI%. The method for calculating this index has been described by Maeda and coauthors,<sup>7</sup> who suggest that a value greater than zero is indicative of keratoconus.

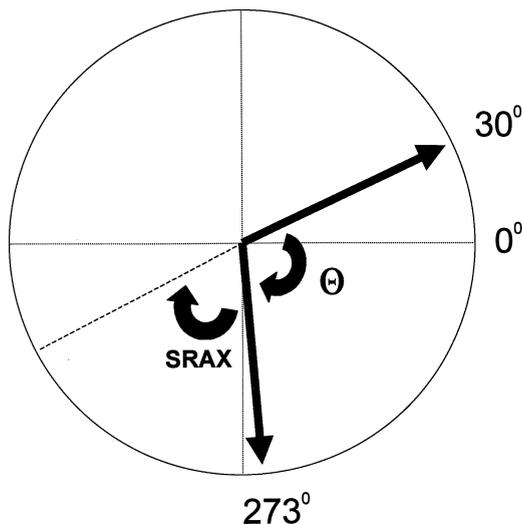
*Derivation of the KISA% index.* The KISA% index quantifies the topographic features seen in patients with clinical keratoconus. It is derived from the product of 4 indices: the K-value, an expression of central corneal steepening; the I-S value, an expression of inferior-superior dioptric asymmetry; the AST index, which quantifies the degree of regular corneal astigmatism (Sim K1 - Sim K2); the skewed radial axis (SRAX) index, an expression of irregular astigmatism occurring in keratoconus. These individual indices and the methods by which they are calculated have been described.<sup>10</sup> The method for calculating the SRAX index was slightly modified as shown in Figure 1.

The algorithm for calculating the KISA% index was initially derived as follows:

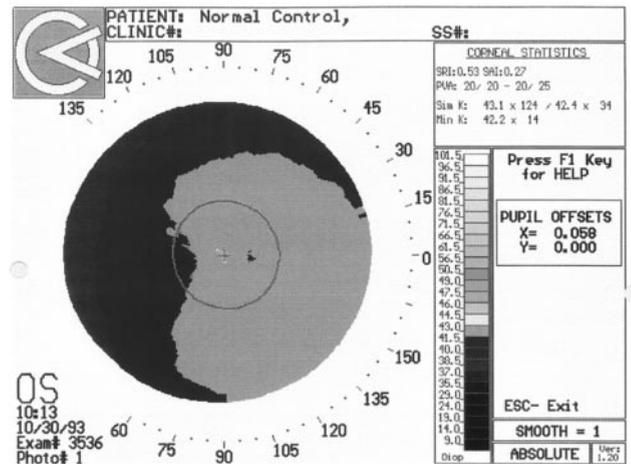
$$KISA\% = (K) \times (I-S) \times (AST) \times (SRAX) \times 100$$

As each individual index quantifies a topographic feature of keratoconus, when they are multiplied by one another, an abnormality in 1 amplifies the resultant product. In addition to the above, the following rules apply:

1. To amplify any abnormality, the value 1 was substituted in the equation whenever a calculated index had a value of less than 1.
2. Only absolute values were used. For example, if the



**Figure 1.** (Rabinowitz) Calculation of the SRAX for the topography map in Figure 4. The steepest radius above the horizontal meridian is at 30 degrees. The steepest radius below the horizontal is at 273 degrees. The SRAX is 180 minus the smaller of the 2 angles (angle  $\theta$ ) between these 2 radii. For this calculation, radii in the 10 degrees above and below the horizontal diameter are ignored.



**Figure 2.** (Rabinowitz) Normal cornea; The steepest radius above the horizontal meridian is at 66 degrees; the steepest inferior radius is at 236 degrees. The SRAX is, therefore, 10 degrees. The other indices are as follows: K = 45.51 D; I-S = 0.80 D; AST = 0.70 D. The KISA% is, therefore, as follows:  $(1 \times 1 \times 1 \times 10) \times 100/300 = 3.3\%$ .

I-S value was -2.0 D, it was corrected to 2.0 D; there can, therefore, be no negative values in the KISA%.

3. The K-value used was that which was in excess of 47.2 D (i.e., K-47.2). For values less than 47.2 D, a value of 1.0 was substituted in the calculation.

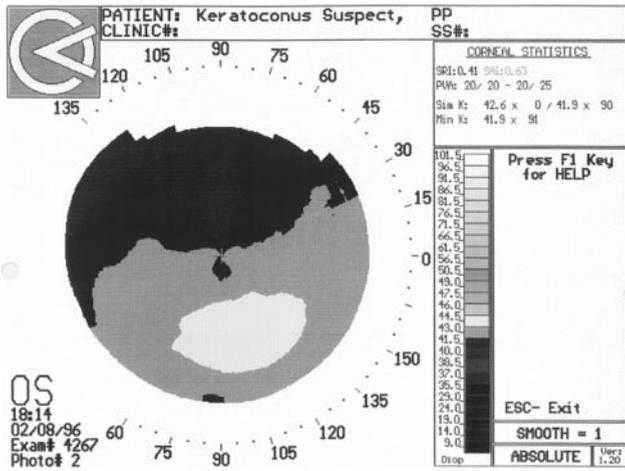
This index was calculated for all 86 keratoconus patients in our database. The eye with the lowest KISA% value but that still had minimal clinical signs of keratoconus (i.e., scissoring of the red reflex and a topographic pattern consistent with keratoconus) had a KISA of 3090. As the goal was to have an index on which a patient with the minimal clinical features of keratoconus was as close to 100% as possible, this index was divided by 300, giving this patient a KISA% value of 103%. The KISA% index is thus calculated as follows:

$$KISA\% = \frac{(K) \times (I-S) \times (AST) \times (SRAX) \times 100}{300}$$

To further illustrate how this index was calculated for individual videokeratographs, the KISA% index was calculated for a normal control eye (Figure 2), a patient with keratoconus-suspect topography (Figure 3), a patient with early keratoconus (Figure 4), and a patient with advanced keratoconus (Figure 5).

*Data Extraction and Analysis*

A computer program was written that extracted the dioptric powers calculated for each of the 256 points on

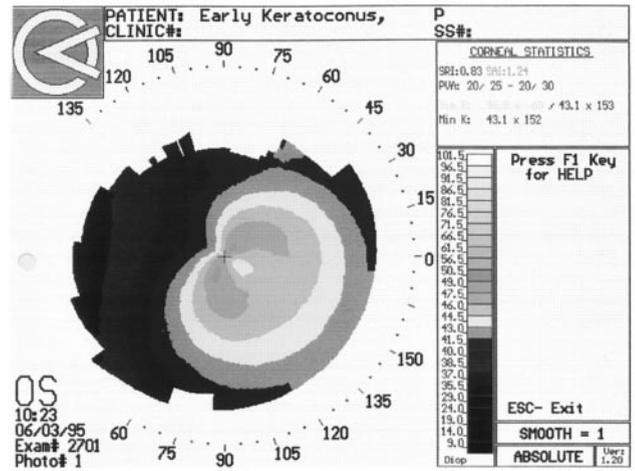


**Figure 3.** (Rabinowitz) Keratoconus suspect; the steepest radius above the horizontal meridian is at 10 degrees; the steepest inferior radius is at 100 degrees. The SRAX, therefore, is 90 degrees. The other indices are as follows: K = 42.10 D; I-S = 2.75 D; AST = 0.70 D. The KISA% is, therefore, as follows:  $(1 \times 2.75 \times 1 \times 90) \times 100/300 = 82.5\%$ .

the 25 rings projected on the cornea. Using these values, the K, I-S, AST, SRAX, and the KISA% index were calculated for each videokeratograph selected. The keratoconus detection software available with the TMS-1 software version 1.61 was used to calculate the KCI% and the KPI (Computed Anatomy Inc.).<sup>9</sup> Because it was considered that the diagnosis of keratoconus in 1 eye of a patient identifies him or her as having the keratoconus phenotype, an analysis was used that would maximize the detection of keratoconus by using the index value that was the greater of the 2 eyes (i.e., the Max K, Max I-S, Max KISA%, Max KCI, and Max KPI). All data were entered into a computer spreadsheet, and the optimum cutoff point for the Max KISA% was determined to separate the keratoconus group from the normal control group.

*Testing the KISA% Index for Detecting Early Keratoconus and Keratoconus Suspects*

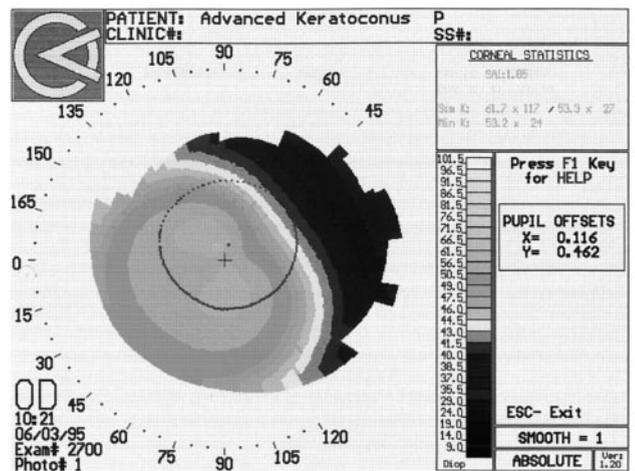
To determine how useful the KISA% index is for detecting eyes with early keratoconus and keratoconus suspects, data from 20 eyes were extracted from the database of study participants in the Keratoconus Genetics Research Program at Cedars-Sinai Medical Center. The KISA% index was calculated for each eye. This was an independent group of study participants, none of whom had been used in the analysis for calculating the KISA%



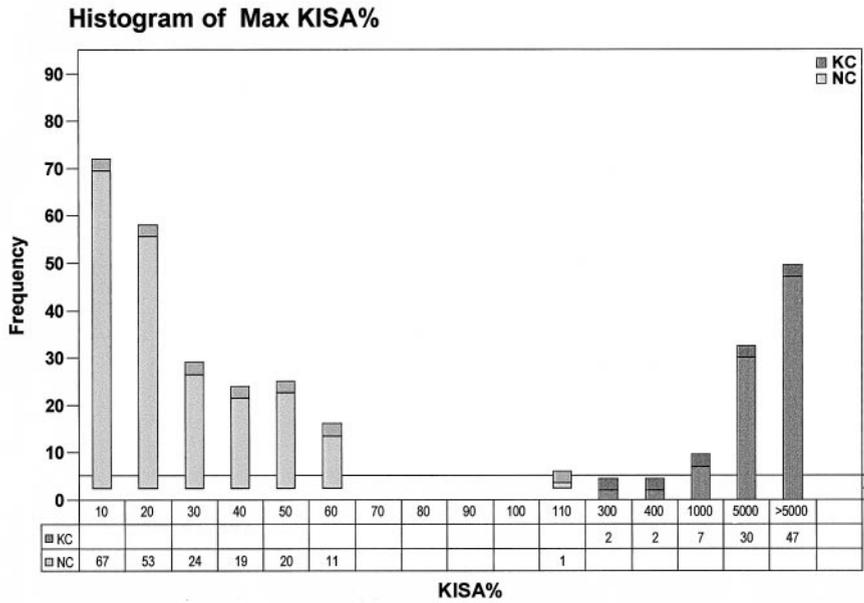
**Figure 4.** (Rabinowitz) Early keratoconus; the steepest radius above the horizontal meridian is at 30 degrees; the steepest inferior radius is at 273 degrees. The SRAX, therefore, is 63 degrees. The other indices are as follows: K = 46.32 D; I-S = 2.46 D; AST = 3.70 D. The KISA% is, therefore, as follows:  $(1 \times 2.46 \times 3.7 \times 63) \times 100/300 = 191.1\%$ .

index using patients with keratoconus and normal control eyes as described earlier in this section.

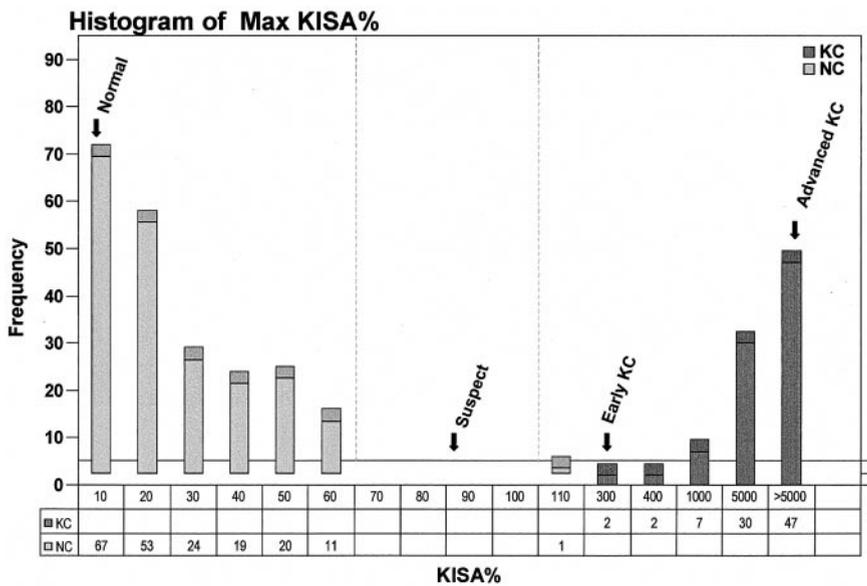
Of these 20 eyes, 12 had early keratoconus and 8 had keratoconus-suspect corneal topography. For this study, *early keratoconus* was defined as an eye that had no slitlamp findings of keratoconus (i.e., thinning, Vogt's striae, or Fleischer ring) and appeared normal on slitlamp evaluation but had scissoring of the red reflex on



**Figure 5.** (Rabinowitz) Advanced keratoconus; The steepest radius above the horizontal meridian is at 160 degrees; the steepest inferior radius is at 249 degrees. The SRAX, therefore, is 91 degrees. The other indices are as follows: K = 57.64 D; I-S = 8.76 D; AST = 8.40 D. The KISA% is, therefore, as follows:  $(10.4 \times 8.76 \times 8.4 \times 91) \times 100/300 = 23305.6\%$ .



**Figure 6.** (Rabinowitz) A histogram of Max KISA% index of the normal control versus the keratoconus patients shows minimal overlap between the 2 groups. The X-axis values represent the upper limit of the bin range.



**Figure 7.** (Rabinowitz) The same histogram as in Figure 6, showing a range between 60% and 100% that can be used to designate suspects and illustrating (arrows) where patients with normal topography (Figure 2), keratoconus-suspect topography (Figure 3), early keratoconus (Figure 4), and advanced keratoconus (Figure 5) fall relative to the study group. The patient with the suspect topography is from the keratoconus group and has obvious keratoconus in the fellow eye. The X-axis values represent the upper limit of the bin range.

dilated retinoscopy and a videokeratography pattern consistent with keratoconus. An eye was designated keratoconus suspect if it was the fellow eye of a patient with clinical keratoconus, had no slitlamp findings of keratoconus, had a normal red reflex on dilated retinoscopy, and had a videokeratography pattern showing a well-defined circumscribed localized area of corneal steepening. The definition of *suspect* used in this study was devised solely to confirm that the abnormal topography in the normal appearing fellow eye was a result of keratoconus and not other pathology. In this analysis, individual eyes were used, not the Max KISA% of both eyes.

## Results

### Max KISA% in Normal Eyes and Eyes with Clinical Keratoconus

The mean Max KISA% in the normal control group was  $20.44 \pm 16.89$  (SD) and in the keratoconic group,  $10382 \pm 11206$ . There was minimal overlap between the 2 groups, as seen in the frequency distribution histogram in Figure 6. The eye with the smallest KISA% with definite clinical signs of keratoconus on clinical examination had a KISA% value of 103, as described in the Methods section. (The fellow eye had a KISA% of

**Table 1.** Correct classification rates using the Rabinowitz/McDonnell, Klyce, and KISA% indices; n (%).

Classification Index	False Negatives (n = 86)	False Positives (n = 195)	Total (n = 281)
Max CK > 47.2 D	9 (10.5)	0 (0)	9 (3.2)
Max I-S > 1.4 D	2 (2.3)	10 (5.1)	12 (4.3)
CK > 47.2 D or I-S > 1.4 D	2 (2.3)	10 (5.1)	12 (4.3)
Max KISA% > 60%	0 (0)	4 (2.1)	4 (1.4)
Max KCI > 0%	0	7 (3.6)	7 (2.5)
Max KPI > 0.23	0 (0)	16 (8.2)	16 (5.7)

562.) The highest KISA% value in the normal control group was 107; this eye had mild topographic features that might be considered suspect but had no subtle or overt clinical signs of keratoconus. All other eyes in the normal control group had a KISA% of 60 or less (Figure 5). The relative positions of the normal control (Figure 2), a patient with keratoconus-suspect topography (Figure 3), a patient with early keratoconus (Figure 4), and 1 with advanced keratoconus (Figure 5) are shown on the modified histogram (Figure 7), which also shows an area between 60 and 100 that could be designated as the suspect range with no overlap with the keratoconus population and minimal overlap with normal controls (1 of 195).

Table 1 shows the false positive and false negative classification rates using each index individually and when the K and I-S indices are used together. The Max KISA%, Max KCI%, and Max KPI correctly classified all keratoconic patients. Using the Max KISA% with a cutoff point of 100%, only 1 normal eye was misclassified (0.4% misclassification rate). The false positive rates with the Max KCI% and the Max KPI were substantially higher. Table 2 shows the results of a statistical comparison of the Max KISA% and the Max KCI% using the McNemar test. The Max KISA% with a cutoff

of 60% produced significantly less false positives than the Max KPI or Max KCI%.

### *KISA% Index in Early Keratoconus and Keratoconus Suspect Eyes*

Table 3 shows the calculation of the KISA% index for the eyes with keratoconus-suspect corneal topography and those with early keratoconus; the K-value, I-S value, and Klyce KCI% are included for comparison. Eleven of 12 eyes (92%) with early keratoconus had a KISA% of 100 or more, and 6 of 8 suspect eyes (75%) were in the 60 to 100 range.

## Discussion

Since Amsler's original Placido disk studies in the early 1900s, we have known that early forms of keratoconus can be detected in the absence of clinical signs by studying the anterior topography of the cornea.<sup>17,18</sup> With the advent of computer-assisted corneal topographic analysis, the challenge has been to reliably quantify the minimal topographic criteria necessary for the diagnosis of keratoconus that clinicians can use universally and reproducibly. This has become particularly relevant for ruling out early keratoconus when screening candidates for refractive surgical procedures and for use in complex computerized segregation analysis, an analytical technique that could advance our understanding of the genetics of keratoconus.<sup>13,14</sup>

With Placido-disk-based videokeratoscopes, there are 2 potential ways to determine the subtle transition from normal topography to keratoconus suspect and early keratoconus: pattern recognition or the use of quantitative indices generated by these devices. In a previously reported study using this same database of normal controls, we showed that 1 topographic pattern was found in only 1 of 390 eyes (i.e., asymmetric bow tie

**Table 2.** Comparison of false positive rates obtained by the KISA%, KPI, and KCI using the McNemar test (N = 195).

Indexes	Misclassified by Both Indices	Misclassified by Max KISA% Only	Misclassified by (Index) Only	Misclassified by Neither Index	McNemar Test (Chi-Square)	P Value (Alpha = .05)
Max KPI versus Max KISA% (cutoff 60%)	1	0	15*	179	15.0	.0001
Max KCI versus Max KISA% (cutoff 60%)	1	0	5†	189	5.0	.0253

\*Max KPI only

†Max KCI only

**Table 3.** KISA% index in eyes with early keratoconus and with keratoconus-suspect corneal topography.

Patient	K-Value (D)	I-S Value (D)	KISA%	KCI%	Diagnosis
1	44.90	1.20	33.25	0	Keratoconus suspect
2	43.11	2.11	53.51	13	Keratoconus suspect
3	44.84	3.16	60.72	31	Keratoconus suspect
4	43.63	2.12	70.53	22	Keratoconus suspect
5	42.03	2.18	74.69	0	Keratoconus suspect
6	44.16	2.2	81.40	28	Keratoconus suspect
7	42.84	2.51	89.45	21	Keratoconus suspect
8	47.42	2.71	89.56	0	Early keratoconus
9	45.15	2.56	93.61	19	Keratoconus suspect
10	46.78	4.02	107.49	30	Early keratoconus
11	46.78	4.35	108.12	37	Early keratoconus
12	45.13	2.39	114.27	35	Early keratoconus
13	45.56	3.75	115.91	27	Early keratoconus
14	48.86	3.54	128.27	33	Early keratoconus
15	45.47	2.84	140.48	26	Early keratoconus
16	45.66	3.61	189.75	68	Early keratoconus
17	47.86	2.34	196.41	60	Early keratoconus
18	45.87	6.20	217.87	67	Early keratoconus
19	45.15	4.28	271.11	50	Early keratoconus
20	47.80	5.11	365.03	47	Early keratoconus

with skewing of the radial axis above and below the horizontal meridian, AB/SRAX).<sup>15</sup> This pattern was found in virtually 100% of topographic patterns of the patients studied who had clinical keratoconus. This pattern, similar to the skewing seen on retinoscopy, could represent the earliest sign of irregular astigmatism and might be a reasonable cutoff point in the transition from normal topography to keratoconus. This patient was the only one in the normal control group who had a KISA% greater than 60 (KISA% 107). Our ongoing longitudinal studies of normal fellow eyes of patients with unilateral keratoconus and family members of patients with keratoconus will, over time, clearly define which patterns ultimately lead to keratoconus and may lend support to this hypothesis.

The use of quantitative videokeratography-derived indices potentially represents a more reproducible way of quantifying keratoconus and its early phenotypes. It may also enable us to determine an accurate transition from normal to suspect and subsequent keratoconus topography.

We initially described the central K- and I-S values that quantified both nipple- and oval-type cones.<sup>6</sup> Subsequently, we introduced a new index, the SRAX, to quantify the irregular astigmatism occurring in eyes with keratoconus.<sup>10</sup> Using a combination of 4 indices—K, I-S value, AST (Sim K1 – Sim K2), and SRAX—we demonstrated that we could distinguish 40 keratoconus patients from a group of 195 normal controls with low false positive (1 of 195; 0.5%) and false negative (1 of 40; 2.5%) rates.<sup>10</sup>

Maeda and coauthors<sup>7</sup> devised an expert system classifier, a rule-based system that determines the presence or absence of keratoconus based on the analysis of 8 numerical topographic indices derived from the TMS videokeratoscope. The system combines a classification tree with a linear discriminant function derived from discriminant analysis. The linear discriminant function yields a single composite discriminant value for each map: the KPI. The division between keratoconus and nonkeratoconus patterns is the cutoff value. Maps with a KPI value greater than the optimum cutoff are classified

as keratoconus, whereas maps with a KPI value less than the optimum cutoff value are classified as nonkeratoconus. The expert system classifier determines whether a keratoconus-like pattern is seen in a particular map using the binary classification tree and, if so, reports a value between 1% and 100% (the KCI) in proportion to the linear discriminant function to quantify the severity of keratoconus or 0% to report no detectable keratoconus-like pattern.

Maeda and coauthors<sup>8</sup> compared this system to the modified K-value ( $>47.2$  D) and modified I-S value ( $>1.4$  D) and found the sensitivity of this test for detecting keratoconus was 96% compared with 98% for the expert system; the specificity was 85% compared with 99% for the expert classifier. This system was not designed to identify keratoconus suspects. Smolek and Klyce<sup>9</sup> subsequently designed a neural network approach that could reliably distinguish their definition of suspect topography from keratoconus and keratoconus-like topography.

All the preceding keratoconus detection systems have several drawbacks. First, they are derived from several complex indices, all of which must be integrated into a decision process, limiting their clinical utility. The Rabinowitz system uses 4 indices, while the Maeda/Klyce system uses 8 indices, and a neural network system for suspects may be available in the future. Second, no index bears a clinical correlation to the clinical severity of keratoconus. For example, a patient with frank keratoconus may have a KCI of 55%, while an eye with suspect topography with no clinical signs of disease may have a KCI of 30% or more. Third, these systems are designed so they are system specific (i.e., can currently only be used on the TMS). Fourth, none of the systems adequately addresses the issue of suspects.

Clearly, the most useful index for videokeratography screening for refractive surgery would be a single index with excellent clinical correlation to disease severity that clearly differentiates keratoconus eyes from normal eyes and provides a range for potential keratoconus suspects with minimal overlap with the normal population. The KISA% index achieves this goal. Furthermore, it is more accurate and specific than any previously described keratoconus detection systems for differentiating keratoconus from normal eyes.

When the KISA% has a value of 100 or more in an eye with no other pathology, the patient almost always

has clinically detectable keratoconus. As the severity of the disease increases, so does the numerical value of the index. Using this index set at 100%, there is clear separation between normal eyes and those with keratoconus, with almost no overlap. Values ranging from 60% to 100% could be used to designate or label patients as keratoconus suspects with minimal fear of significant overlap with the normal population ( $<0.5\%$ ), making the index useful for clinical keratoconus screening of refractive surgical candidates. These suspect patients could be followed over time to see whether they develop keratoconus, and an individual decision could be made whether to exclude them from refractive surgical procedures.

As the KISA% index has an excellent clinical correlation, it is highly likely that an eye with a topographic map with a KISA% index over 100% has keratoconus, and the patient should be alerted to the potential risks of having refractive surgery.<sup>19,20</sup> If no clinical signs were detected before topography was done, a value greater than 100% should alert the clinician to the possibility of keratoconus and to look for scissoring of the red reflex on dilated retinoscopy or perform pachymetry to rule out corneal thinning and verify the presence of early keratoconus. Because this is a single index with good clinical correlation, it will also be useful for complex computerized segregation analysis that might improve our understanding of the genetics of keratoconus.<sup>21,22</sup> The KISA% index must be verified by independent observers using different sets of normal control eyes and keratoconus patients. However, if verified, its simplicity will allow it to be used on a universal basis for topographically diagnosing keratoconus using different videokeratoscopes. The studies described here were performed using the TMS-2 with sagittal algorithms. Work is currently in progress to determine cutoff points for tangential algorithms and other topographic devices, including the Alcon EyeMap. This could enhance the utility of this algorithm and may make it universally acceptable for topographically diagnosing keratoconus.

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*Accepted for publication May 6, 1999.*

*From the Cornea-Genetic Eye Institute (Rabinowitz, Rasheed), Division of Ophthalmology, Department of Surgery (Rabinowitz, Rasheed), Burns and Allen Research Institute, Cedars-Sinai Medical Center, and Departments of Ophthalmology (Rabinowitz) and Medicine & Pediatrics (Rabinowitz), UCLA School of Medicine, Los Angeles, California, USA.*

*Presented in part at the annual meeting of the Association for Research and Vision in Ophthalmology, Fort Lauderdale, Florida, USA, May 1996.*

*Supported by NIH Grant EY09052 and The Eye Birth Defects Research Foundation, Inc.*

*Dr. Rabinowitz is a paid consultant to Alcon Laboratories, Inc., and owns the copyrights for the computer program described.*

*David MacLellan, senior engineer, Tomey Co. USA, provided technical assistance.*