Corneal topography in Ehlers-Danlos syndrome

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ABSTRACT

Purpose: To assess the use of corneal topography in conjunction with slitlamp biomicroscopy and retinoscopy to diagnose keratoconus in a large group of patients with Ehlers-Danlos syndrome (EDS).

Setting: Kresge Eye Institute, Wayne State University, Detroit, Michigan, USA.

Methods: Thirty-six patients (72 eyes) with genetically typed EDS had slitlamp biomicroscopy, retinoscopy, and videokeratography with the EyeSys instrument. The presence or absence of slitlamp keratoconus findings was correlated to a presumptive diagnosis based on corneal topography using derived topographic indexes associated with keratoconus. These topographic indexes included central corneal power, (CCP), difference in CCP, inferosuperior asymmetry (I-S) value, and asphericity (Q). Axial and profile difference maps were generated and analyzed for findings suggestive of keratoconus.

Results: In 72 eyes, no keratoconus was found using slitlamp biomicroscopy. No eye had an I-S value greater than 1.60 diopters (D), 2 eyes had a CCP greater than 46.50 D, and 2 eyes had a Q value less than −1.00. Eight of 36 pairs of eyes had an intereye CCP greater than 0.92 D. In both eyes of the patient with Q values less than −1.00, the profile difference maps were mildly abnormal.

Conclusions: Slitlamp biomicroscopy of the cornea was unremarkable in all patients. Only 1 patient had Q values and profile difference maps that were mildly suggestive of keratoconus. Even after adding topography to the examination, it appears that keratoconus in a known population of patients with EDS remains rare.
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Previous studies characterizing the corneal abnormalities associated with Ehlers-Danlos syndrome (EDS) have relied on slitlamp biomicroscopy, keratometry, and pachymetry. Most corneal abnormalities described were related to an alteration in corneal curvature, reduction in corneal thickness, or both.[1,2] These corneal curvature alterations include cornea plana, keratoconus, and keratoglobus. Most corneal changes were found in patients with EDS type VI. In patients who do not have EDS, the reported incidence of keratoconus (50 to 230 per 100,000 persons)[2,3] is variable and may be underreported because conventional keratometry may fail to detect small, inferiorly displaced cones that lie outside the central area sampled by the instrument.[1,4]

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Based on clinical experience, many corneal surgeons maintain that corneal ectasia, including keratoconus, is more common with EDS than in the general population.[2] Since these observations are, in part, anecdotal or based on studies published before digital videokeratoscopy, we questioned whether using this technique would uncover additional cases of subclinical keratoconus not detected by slitlamp findings in a genetically defined population of EDS patients.

Other investigators[2] have performed topographic analysis of the cornea using digital videokeratoscopy to identify preclinical keratoconus in the general population. Using the data derived from digital processing of the video image, Rabinowitz and McDonnell[5–7] published topographic indexes they believe to be sensitive indicators of subclinical keratoconus. Our study's use of these indexes is extrapolated from Rabinowitz and McDonnell's studies, which concentrated on identifying subclinical keratoconus in family members of patients with keratoconus.

The indexes used consisted of central corneal power (CCP), computed by placing the cursor at the center of the innermost ring; the intereye difference in CCP; the inferosuperior asymmetry (I-S) value. The I-S value is the difference between the average inferior corneal power and average superior corneal power computed at equal distances from the center of the cornea. The average inferior corneal power is the mean of corneal power readings at 5 points (210, 240, 270, 300, and 330 degrees) 3.0 mm from the center of the cornea. The average superior corneal power is the mean of corneal power readings at 5 corresponding points (30, 60, 90, 120, and 150 degrees) 3.0 mm from the center of the cornea. In 1997, Holladay[8] reported that an asphericity index (Q) is also a sensitive indicator of keratoconus. To assess their ability to predict keratoconus, the indexes and color-coded axial and profile difference maps for patients with EDS were compared with slitlamp findings.

Patients and Methods

Thirty-six patients (72 eyes) with EDS were evaluated: type I (7 patients), type II (7 patients), type III (17 patients), type IV (4 patients), and type VI (1 patient). All patients had slitlamp biomicroscopy performed by a fellowship-trained corneal specialist, central corneal pachymetry, retinoscopy, and digital videokeratoscopy. Slitlamp examination was used to detect keratoconus findings; no specific attempt was made to detect keratoglobus.

Corneal analysis was done using the EyeSys instrument (EyeSys Technologies). Version 3-1 software for the Holladay Diagnostic Summary was used to generate topographic maps. Axial and profile difference maps for all eyes were examined for corneal ectasia suggestive of keratoconus. Holladay's profile difference map[8] was used as it is helpful in diagnosing corneal diseases such as keratoconus, keratoglobus, and pellucid marginal degeneration in which the cornea changes its overall shape. This map compares the patient's actual cornea to the normal aspheric cornea. The actual refractive power of the patient at every point is compared with this ideal aspheric cornea. The difference between the two is plotted on a color-coded map. If the patient's cornea is steeper than the normal aspheric cornea, the difference is plus and is toward the red. In a keratoconic cornea, this map can easily delineate the extent and location of a cone. The CCP, intereye difference in CCP, and I-S value were computed using a custom software program developed by one of the authors (D.L.).[4–6] Asphericity was calculated using software included in the Holladay Diagnostic Summary, version 3-1.

Results

All slitlamp findings of the cornea were unremarkable. No eye showed evidence of prominent corneal nerves, Fleischer ring, Vogt's striae, breaks in Bowman's or Descemet's membrane, heightened endothelial reflex, apical thinning, or inferior cone formation. No scissoring of the reflex was observed on retinoscopy. Central corneal pachymetry showed no values less than 0.4 mm. Table 1 shows computer-assisted topographic indexes for all EDS types. To analyze the data, published values 2 standard deviations from normal were used as follows: CCP greater than 46.50 diopters (D)[5]; intereye difference in CCP 0.92[5]; I-S value greater than −1.60 D[5]; Q less than −1.00.[8]

These values were used to analyze the data in Table 1 (72 eyes). No eye had an I-S value greater than 1.60 D. In 2 eyes, the CCP exceeded 46.50 D (patients 23 and 26, left eyes). Of 36 pairs of eyes, 8 had an

Table 1. Computer-assisted topographic indexes for all EDS types.

Patient	EDS Type	Central Corneal Power			Inferosuperior Difference		Asphericity Index	
		OD	OS	Change	OD	OS	OD	OS
1	II	42.2	43.1	0.9	+0.08	+0.04	−0.43	−0.86
2	III	43.5	43.7	0.2	−0.04	−0.04	−0.16	−0.15
3	III	43.5	43.8	0.3	+0.03	+0.01	−0.11	+0.02
4	IV	41.8	42.1	0.7	+0.03	+0.02	−0.16	−0.19
5	III	42.2	41.5	0.7	−0.02	−0.02	−0.12	−0.21
6	III	42.3	41.7	0.5	+0.06	+0.03	+0.25	+0.26
7	IV	42.4	42.3	0.1	−0.15	−0.07	−0.32	−0.03
8	II	43.0	43.8	0.8	−0.07	−0.07	+0.06	−0.11
9	II	42.1	42.7	0.6	0.00	−0.03	+0.24	−0.08
10	III	44.9	42.4	2.5	−0.02	+0.06	−0.14	+0.10
11	III	43.3	42.2	1.1	−0.05	−0.03	−0.26	−0.22
12	III	42.4	42.8	0.4	−0.02	−0.01	−0.23	−0.20
13	II	42.7	43.2	0.5	−0.05	+0.05	+0.05	−0.05
14	III	41.7	40.3	1.4	−0.08	−0.05	−0.03	−0.12
15	VI	44.5	43.8	0.7	−0.09	0.00	−0.21	−0.07
16	II	42.6	43.1	0.5	+0.08	+0.02	−0.14	−0.22
17	II	42.7	43.3	0.6	+0.01	−0.01	−0.17	−0.16
18	I	44.8	45.5	0.7	−0.01	−0.05	−0.39	−0.49
19	I	44.1	44.2	0.1	−0.16	−0.13	+0.37	−0.23
20	III	43.0	43.0	0.0	−0.04	−0.07	−0.12	0.00
21	III	41.3	40.8	0.5	−0.08	−0.08	−0.14	−0.12
22	III	43.0	42.7	0.3	+0.69	+0.65	−0.21	−0.30
23	I	45.3	47.3	2.0	+0.02	−0.05	+0.13	−0.10
24	I	42.4	43.5	0.9	−0.06	−0.17	−1.16	−1.21
25	I	45.5	43.9	1.6	+0.05	+0.06	−0.74	−0.62
26	III	45.8	47.1	1.3	+0.07	−0.03	−0.25	−0.12
27	I	42.4	44.0	1.6	+0.12	+0.11	−0.10	−0.55
28	II	41.5	42.1	0.6	−0.04	−0.03	−0.23	−0.09
29	IV	42.5	42.4	0.1	−0.05	−0.86	−0.25	−0.19
30	III	43.6	43.6	0.0	−0.04	−0.06	−0.25	−0.17
31	III	42.7	43.3	0.6	+0.09	−0.04	−0.06	−0.10
32	IV	43.0	41.9	1.1	+0.01	−0.04	−0.33	−0.19
33	III	45.0	44.6	0.4	−0.03	+0.02	−0.08	+0.01
34	III	42.6	43.3	0.7	−0.01	−0.02	−0.12	−0.07
35	III	46.3	46.3	0.0	+0.03	+0.07	−0.33	+0.01
36	I	45.4	45.5	0.1	−0.01	+1.44	+0.07	+0.07

OD = right eye; OS = left eye

intereye difference in CCP greater than 0.92 D (patients 10, 11, 14, 23, 25, 26, 27, and 32). In 2 eyes (patient 24, both eyes), the Q value was less than −1.00. In that same patient, the profile difference maps were mildly suggestive of keratoconus (Figure 1).

Discussion

In this study, an isolated intereye difference in CCP exceeding 0.92 D appeared relatively nonspecific since 8 of 36 patients appeared to be keratoconus suspects. It

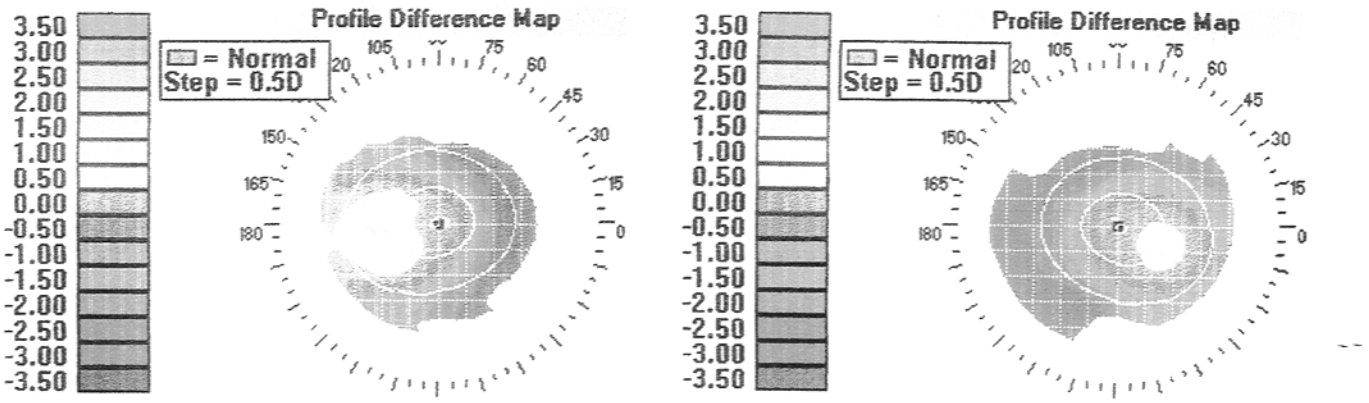

Figure 1. (McDermott) *Left:* Profile difference map of the right eye of Patient 24 (Q value = −1.16). Note the paracentral island suggestive of a plus difference from the normal aspheric cornea. *Right:* Profile difference map of the left eye of Patient 24 (Q value = 1.21). Note the similar appearance but greater magnitude when compared with the map at the left.

is unlikely these patients have keratoconus since the slitlamp examinations, I-S values, and Q values were normal and the profile difference maps were unremarkable. When the I-S values were computed, no eye had a value greater than the 1.60 D threshold. Although I-S values were calculated at 3.0 mm with the EyeSys system, they may represent slightly different values than those reported by Rabinowitz and McDonnell[5] using the CMS device with a different algorithm. In 1 case with a normal I-S value (patient 24, both eyes), both the profile difference map and Q values were mildly suggestive of keratoconus, despite negative slitlamp findings of keratoconus.

Our findings are somewhat surprising given the initial hypothesis; that is, in a group having a higher incidence of keratoconus than the general population, no definitive cases were uncovered, even with the addition of topography. It is possible that if a larger group of patients was collected or a prospective study of the present group undertaken, some patients may be found to have keratoconus. However, in this large cohort of 72 eyes, no definitive cases of keratoconus were seen.

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