

Oculomotor Status, Binocular Vision, and Stereoacuity in a Series of Keratoconus Subjects

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PURPOSE. A group of keratoconus subjects (KG) and a control group (CG) were evaluated for sensory and motor status. We tried to clarify the factors (best-corrected visual acuity [BCVA]), heterophorias, fusional amplitude, anisometropia, astigmatism) that may be associated with a binocular disturbance.

METHODS. BCVA (logMAR) was measured. Binocular vision was checked using cover tests, striate Maddox, and a 6^A base-down prism (simultaneous perception), a prism bar (fusion and fusional convergence break point), and Titmus Fly Test (stereopsis).

RESULTS. Fifty-four subjects of the KG, 27 men (median 16 years), and 29 of the CG, 15 men (median 20 years), were evaluated. In the KG, 8 (15%) subjects had strabismus. Those whose BCVA in the worse eye was logMAR ≥ 0.7 had a significantly higher frequency of strabismus and absence of simultaneous perception. Spherical equivalent anisometropia ≥ 1.0 diopter (D) was significantly different in both groups as was the frequency of gross stereopsis. In comparing fine and gross stereopsis in both the KG and the CG, there was a significant difference in the frontal astigmatism between eyes in the KG ($P = 0.03$) and CG ($P = 0.01$).

CONCLUSIONS. In our study, the KG presented a higher frequency of strabismus and impaired binocular vision. Frontal astigmatism was different between groups with gross and fine stereopsis, in both the CG and KG. Future studies are needed to elucidate or reinforce the factors associated with the loss of binocularity in keratoconus. Testing for stereopsis may be helpful to consider in the treatment guidelines for keratoconus.

Keywords: keratoconus, binocular vision, anisometropia, strabismus, visual acuity

Keratoconus is a progressive corneal ectasia, characterized by progressive thinning and protrusion of the cornea. Its etiology is possibly multifactorial, involving genetic and environmental factors.^{1,2} Epidemiologic studies show a prevalence of 0.4 to 86 cases per 100,000.³ As an important cause of low vision in young people, it interferes greatly with their quality of life, which is why corneal transplantation is often indicated.⁴ The clinical suspicion of keratoconus is due to a history of progressive low vision, more intensely in the second and third decades of life, associated with the prescription of increasing degrees of astigmatism and myopia. Corneal tomography is the gold standard for diagnostic confirmation.^{4,5}

Among the unclear aspects in keratoconus are the issues of vision development and maintenance of binocularity. Although keratoconus is frequently associated with decreased vision and anisometropia, which are conditions commonly associated with reduced binocular performance,^{6,7} there are still few studies that have evaluated keratoconus' patients sensory status.^{8–10} This is an important issue, as we know that binocular collaboration between the eyes maintains eye alignment¹¹ and is directly related to the performance of certain motor skill functions.¹²

Classically, the binocular functions can be graded, according to their performance, as “first” degree (simultaneous perception), “second” degree (fusion and fusional amplitudes),¹³ and “third” degree of binocularity (stereopsis, measured by

stereograms).¹⁴ Stereopsis is the capability of perceiving depth due to retinal disparities.¹⁵ The Titmus test is one of the commonly used tests to measure stereoacuity, and it can measure disparities ranging from 3500 to 40 arcsec.¹¹

There are many doubts regarding the best optical prescription in keratoconus patients due to anisometropia and visual acuity differences. In cases of anisometropia,¹⁶ the optical correction might lead to visual discomfort related to aniseikonia or prismatic effects in different positions of the eye, or may or may not be associated with impaired stereopsis associated with amblyopia or impaired vision.^{17–19} The goal of this study was to clarify whether keratoconus is associated with binocular impairment and to try to identify the possible factors (such as visual acuity, heterophorias, fusional amplitude, anisometropia, corneal astigmatism) that may be associated with a binocular disturbance in these subjects.

SUBJECTS AND METHODS

The study was approved by the local Ethics Committee and followed the tenets of the Declaration of Helsinki.

Keratoconus subjects who were under the care of a corneal ambulatory clinic were included in this study and comprised the keratoconus group (KG).



For the control group (CG), we included relatives of subjects with keratoconus. We also included other individuals with high refractive errors (astigmatism and/or myopia), to investigate if high ametropias would lead to stereopsis impairment. In the CG, the right eyes were chosen to be compared to the keratoconus subjects' better eyes, and the left eyes were compared to the keratoconus subjects' worse eyes. The rationale for choosing to include in the CG those with refractive errors was to demonstrate that refractive error per se does not cause loss of stereopsis in a similar age- and sex-distributed group of subjects.

Corneal tomography confirmed or rejected the keratoconus diagnosis in both groups, based on the global consensus on keratoconus and ectatic diseases, in which abnormal posterior corneal ectasia, abnormal spatial distribution of corneal thickness, and noninflammatory corneal sharpening were mandatory for the diagnosis confirmation.²⁰ Both groups were also classified according to the Belin et al. classification,²¹ which takes into account clinical and tomographic parameters that are graded separately. Corneal tomography images were obtained using the principle of Scheimpflug (Pentacam HR; Oculus Optikgeräte GmbH, Wetzlar, Germany), on the same day as sensory evaluation, by a trained technician. The images were captured in the automatic mode, and data were automatically extracted from Pentacam to a Microsoft Excel spreadsheet (Microsoft, Redmond, WA, USA).

Both groups were evaluated for binocular vision and extraocular muscle motor function with or without best-corrected visual acuity (BCVA) with the glasses they routinely wore. None of them were contact lens wearers. Visual acuity was measured using the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at 4 m and recorded in logMAR units. In the KG, we defined the best eye as the one with the better BCVA.

Manifest refractometry and binocular sensory and motor status assessments were performed by an experienced ophthalmologist examiner, and they determined the optical prescription for each subject. None of these subjects had contact lenses as the optical prescription. Most of the subjects used glasses. In a second evaluation, the examiner performed the sensory testing. Three additional data sets were collected for the KG: the age at which impaired vision was first noticed, the age at which the subject started using glasses, and the age at diagnosis of keratoconus.

All subjects were evaluated in the same room with lights on. A fixation target of approximately 15 W matte light was used for fixation. Binocular vision status for distance (4 m) was checked using a simple cover test (to detect tropia) and an alternate cover test (to check for heterophoria), red striate Maddox and a 6^Δ base-down prism (for simultaneous perception), and a prism bar (to determine fusion and fusional convergence break point). Simultaneous perception tests were performed in the two following ways: (1) by placing the Maddox striated test in front of the worse eye (striates horizontal so the patient could see a red vertical line); and (2) by placing a 6^Δ base-down prism in front of the worse eye. Fusional convergence break point was measured using a horizontal prism bar (4 m away from light focus), as described previously.²² The base-out prisms were gradually increased, starting with 1^Δ, until the subject indicated horizontal diplopia. Stereopsis was measured using the Titmus Fly Test at a distance of 40 cm. For stereopsis, subjects were divided into two groups: those with fine stereopsis (stereopsis equal to or better than 60 arcsec) and those with gross/no stereopsis (stereopsis varying from 80 arcsec to stereoblind).

Subjects with previous surgical procedures (intrastromal rings, corneal transplantation, or strabismus surgeries), contact lens wearers, or individuals who could not understand the

sensory checkup were excluded from this study, as well as those with other corneal conditions that could alter tomographic data, including disorders such as pterygium or herpes.

The D'Agostino and Pearson normality test was used to search for normality data. Nonparametric data were expressed in median and range values. *P* values < 0.05 were considered statistically significant. Mann-Whitney test was used for nonparametric unpaired data and the Wilcoxon test was used for nonparametric paired tests. The Fisher exact test was used for categorical data. The Spearman coefficient was used for correlation analysis. All analyses were performed using Graph-Pad Prism version 7.0 (San Diego, CA, USA).

RESULTS

Figures 1 and 2 summarize KG and CG motor and sensory status.

KG and CG: Demographic, Tomographic, and BCVA Data

Fifty-four subjects from the KG, with a median age of 16 (9–38) years and a female:male ratio of 27:27, and 29 subjects from the CG, with a median age of 20 (9–39) years and a female:male ratio of 15:14, were evaluated. Some demographic and tomographic data are shown in Table 1. Table 2 shows their ABCD classification,²³ their oculomotor and sensory status, and the spherical equivalent of both eyes of the KG.

The median age at which subjects of the KG started having impaired vision was 12 (5–28, *n* = 48); the median age at which they started using glasses was 12 (7–29, *n* = 45) years, and the median age at which they had the diagnosis of keratoconus was 14 (9–38, *n* = 48). Median difference between the age at which they manifested impaired vision and the age at the diagnosis of keratoconus was 2 years (*P* < 0.0001, Wilcoxon test). Median difference between the age at which they started using glasses and the age at the diagnosis of keratoconus was 1 year (*P* < 0.0001, Wilcoxon test).

Median BCVA in both eyes of the CG was logMAR 0 (right eyes: −0.1 to 0.2; left eyes: −0.1 to 0.3). In the KG, median BCVA of the better eye was logMAR 0.1 (−0.2 to 0.6) and of the worse eye was logMAR 0.4 (−0.1 to 1.1).

In the CG, 9 out of 29 (31%) subjects had manifest astigmatism between 4.0 and 6.0 cylinder diopters. Three out of 29 (10%) had spherical equivalent anisometropia varying between 1.0 and 2.25 diopters (D). In the KG, manifest astigmatism equal to or higher than 4.0 cylinder diopters was present in 9 out of 53 (17%) better eyes and in 11 out of 51 (22%) worse eyes.

In the CG, the median spherical equivalent was −0.81 (−9 to +1.25) for the right eyes and −1.25 (−11.25 to +1.25) for the left eyes. In KG, the median spherical equivalent was −1.25 in the best eyes (−7.5 to +3.25) and −2.25 (−20.25 to +5.75) in the worse eyes. Considering spherical equivalent, the KG and CG were not significantly different.

Table 3 shows the median differences between BCVA and uncorrected visual acuity (uVA), in better and worse eyes of 47 subjects who used an optical correction (glasses) in the KG. With glasses, visual acuity improved 2 logMAR lines in better eyes and 3 logMAR lines in worse eyes.

KG and CG: Frequency of Strabismus and Heterophorias

Eight out of 54 subjects presented with strabismus on the simple cover test, 7 exotropic (1 with intermittent exotropia) and 1 esotropic. None of the subjects of the CG was strabismic

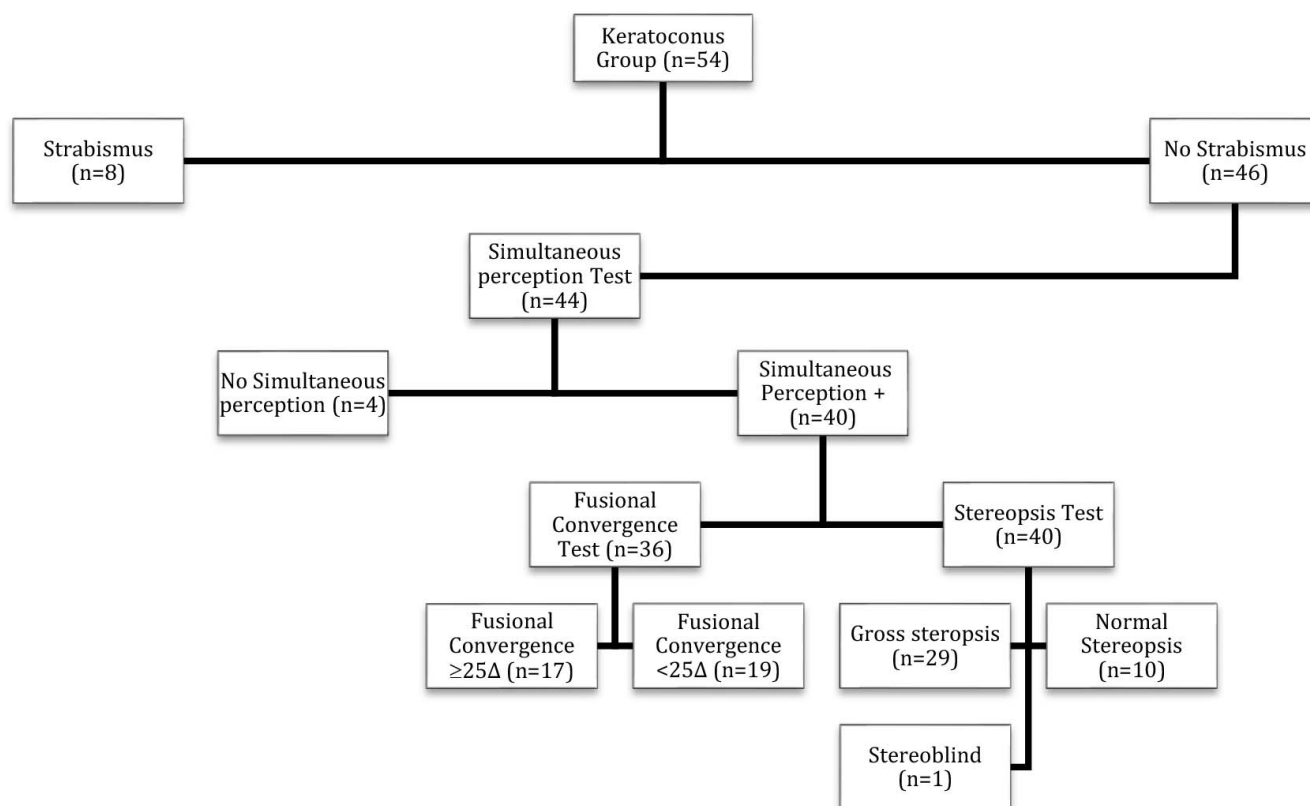


FIGURE 1. KG motor and sensory status. The total number of keratoconus subjects and their motor and sensory status are described in a schematic format.

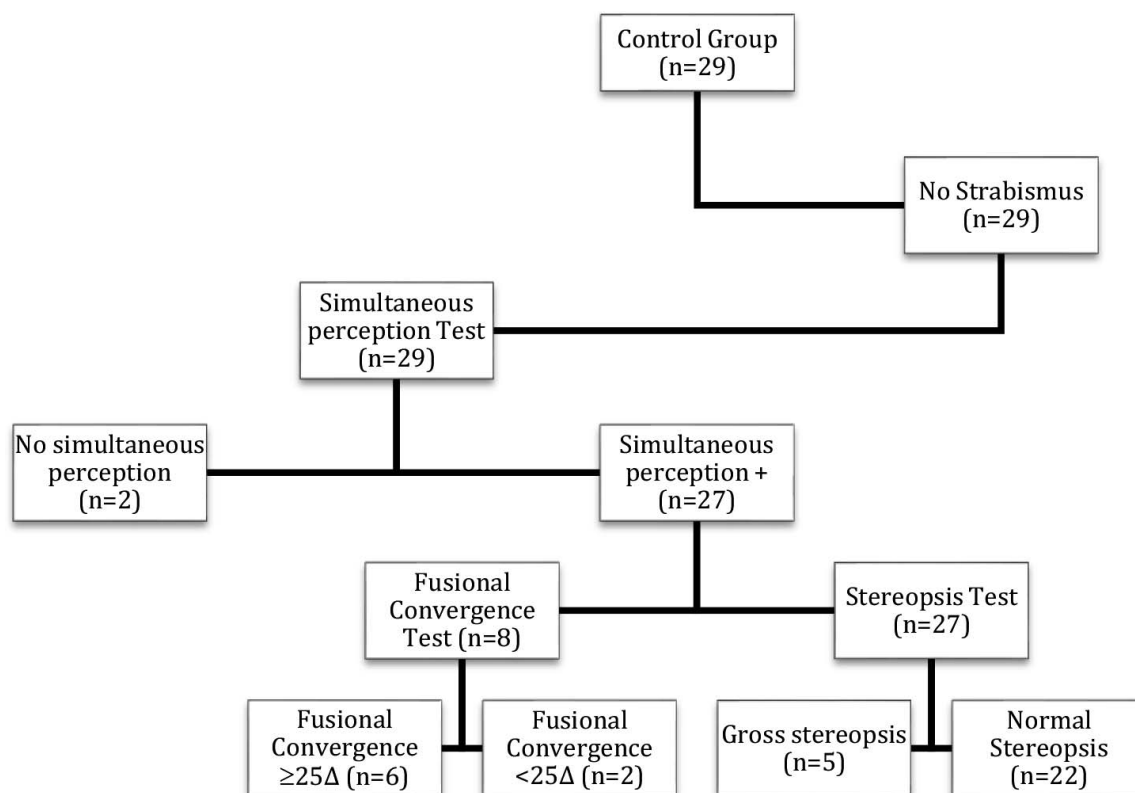


FIGURE 2. CG motor and sensory status. The total number of control subjects and their motor and sensory status are described in a schematic format.

TABLE 1. KG and CG: Demographic, Tomographic, and BCVA (logMAR) Data

| Characteristics | CG, <i>n</i> = 29 | KG, <i>n</i> = 54 | <i>P</i> |
|---------------------|-----------------------|-----------------------|----------|
| Age | 20, 9 to 39 | 16, 9 to 38 | 0.2 |
| Sex, F:M | 15:14 | 27:27 | – |
| K1 | 43.0, 40.2 to 47.1 | 45.2, 39.3 to 56.4 | 0.0009 |
| K2 | 45.5, 40.6 to 51.9 | 48.9, 43.4 to 61.5 | <0.0001 |
| Kmax | 46.2, 40.9 to 52.5 | 53.6 | <0.0001 |
| Pachymetry | 533, 493 to 583 | 460, 193 to 558 | <0.0001 |
| BCVA, better eyes | 0, –0.1 to 0.2 | 0.1, –0.2 to 0.6 | 0.0001 |
| BCVA, worse eyes | 0, –0.1 to 0.3 | 0.4, –0.1 to 1.1 | <0.0001 |
| Δ BCVA | 0 | 0.35 | <0.0001 |
| Sph eq, better eyes | –0.81, –9.00 to 1.25 | –1.25, –7.50 to 3.25 | 0.36 |
| Sph eq, worse eyes | –1.12, –11.25 to 1.25 | –2.25, –20.25 to 5.75 | 0.09 |

Data of the KG better eyes were compared with the CG right eyes for K1, K2, Kmax, and pachymetry. BCVA and spherical equivalent (Sph eq) of KG were also compared with the CG. Data of the KG worse eyes were compared with the CG left eyes. Δ BCVA, difference between better BCVA and worse BCVA eyes. Mean and range of values, statistical analysis by Mann-Whitney test; $P < 0.05$ was considered significant.

($P = 0.04$; odds ratio [OR] infinity; 95% confidence interval [CI] 1.2 to infinity). Median horizontal heterotropia in strabismic subjects was an exotropia of 18^Δ ($n = 8$, ranging from an exodeviation of 60^Δ to an esodeviation of 1^Δ), and median horizontal heterophoria in nonstrabismic subjects was orthophoria ($n = 46$, ranging from an exophoria of 12^Δ to an esophoria of 2^Δ). There were no differences in the amount of horizontal heterophoria between subjects with fine or gross stereopsis.

Subjects from the KG whose BCVA in the worse eye was logMAR ≥ 0.7 had a significantly higher frequency of strabismus ($P = 0.0002$; OR 33.2; 95% CI 4.2–380; Table 4).

KG Without Strabismus and CG: Simultaneous Perception Evaluation

Forty-four out of 46 subjects of the KG without strabismus and 29 subjects of the CG were evaluated for simultaneous perception. Forty out of 44 (91%) of the KG and 27 out of 29 (93%) subjects of the CG demonstrated simultaneous perception with both the Maddox striate test and 6^Δ base-down prism ($P > 0.05$, Fisher test). Subjects from the KG whose BCVA in the worse eye was logMAR ≥ 0.7 had a significantly higher frequency of no simultaneous perception ($P = 0.01$; OR 21; 95% CI 2.4–276.7; Table 5).

KG and CG Without Strabismus and With Simultaneous Perception: Fusional Convergence Break Point Evaluation

Thirty-six out of 40 subjects from the KG with simultaneous perception were tested for fusional convergence break point. Nineteen out of 36 (53%) had a fusional convergence break point smaller than 25^Δ . Among these 19 subjects, median fusional convergence break point was 18^Δ (ranging from 1^Δ to 22^Δ). Eight subjects with simultaneous perception were evaluated in CG, and two (25%) demonstrated fusional convergence break point worse than 25^Δ . There was no difference between the CG and KG ($P = 0.24$, Fisher test). There was no correlation between the amount of horizontal heterophoria and the fusional convergence break point ($r = -0.22$, $P = 0.19$, Spearman test).

KG and CG Without Strabismus and With Simultaneous Perception: Stereopsis Measurement

Forty subjects of the KG and 27 subjects of the CG without strabismus and with simultaneous perception completed the

Titmus Fly Test. Five out of 27 (19%) of the CG and 30 out of 40 (75%) of the KG had gross/no stereopsis. This showed a significantly higher frequency of gross stereopsis in the KG when compared to the CG ($P = 0.0001$; OR 13.2; 95% CI 3.7–40.1; Table 6). Figure 3 shows the stereopsis values for both groups.

The CG was composed of 17 keratoconus subjects' relatives (1 out of 17 had gross stereopsis) and 12 subjects with refractive errors that raised the suspicion of keratoconus, a diagnosis that was discarded by corneal tomography. Of these 12 subjects, 2 did not have simultaneous perception, and 4 had gross stereopsis. These six subjects had astigmatism higher than 3.5 cylinder diopters in both eyes.

If we add the patients with gross stereopsia ($n = 30$) to the ones with strabismus ($n = 8$) and those without simultaneous perception ($n = 4$), we have 42 out of 54 (78%) subjects in the KG and 7 out of 29 (24%) subjects in the CG who either had gross stereopsis or were stereoblind ($P < 0.0001$; OR 11; 95% CI 3.8–29.9).

Thirty-eight subjects in the KG (from the group without strabismus and with simultaneous perception) had their stereopsis measured with and without their glasses, and it was not significantly different ($P = 0.48$, Wilcoxon test).

KG and CG: Frequency of Anisometropia

Data from 54 patients of the KG and 29 of the CG were analyzed. Spherical equivalent anisometropia equal to 1.0 spherical diopters or greater was significantly different in the KG and CG ($P = 0.01$; OR 5.5; 95% CI 1.4–18.7; Table 6). In subjects with spherical equivalent anisometropia equal to or greater than 1.0 spherical diopters, 3 out of 23 had fine stereopsis, and among those with anisometropia smaller than 1.0 diopter, 7 out of 17 had fine stereopsis ($P = 0.06$; OR 4.7; 95% CI 1.1–18.6).

To assess anisometropia due to corneal curvature, we compared Km (diopters) differences between right and left eyes of each subject in the KG and CG. We found in the KG with fine stereopsis median -3.25 (-6.5 to 0.1), in the KG with gross stereopsis median -3.2 (-17.4 to 7.9), in the CG with fine stereopsis median 0.05 (-0.7 to 1.1), and in the CG with gross stereopsis median 0.1 (-0.3 to 0.7). Km differences between eyes were not significantly different when comparing CG with fine and gross stereopsis or the KG with fine and gross stereopsis ($P = 0.5$, Wilcoxon test).

We also analyzed the amount of frontal astigmatism in both groups. This differed significantly when comparing the CG with gross (median -3.7 [-4.9 to -0.7]) and with fine stereopsis (median -0.9 [-6.1 to 1.0]) ($P = 0.01$, Mann-

TABLE 2. KG: Demographic Data, Oculomotor and Sensory Status, ABCD Classification, and Spherical Equivalent of Both Eyes

| Age | Sex | Oculomotor Status | Simultaneous Perception | Fusional Convergence ≥ 25 ^A | Stereopsis | ABCD | | Spheric Equivalent | |
|-----------------------|-----|-----------------------|----------------------------|--|------------|---------------|--------------|-----------------------|--------------|
| | | | | | | Better Eye | Worse Eye | Better Eye | Worse Eye |
| Strabismic subjects | | | | | | | | | |
| 12 | M | 1 ^A ET | NP | NP | - | A0B2C1D0 | A1B1C0D2 | +2.5 | +5.75 |
| 12 | F | 10 ^A XT | NP | NP | - | A4B4C3D2 | A4B4C3D3 | -7.25 | -9.25 |
| 12 | M | 25 ^A XT | NP | NP | - | A4B4C2D1 | A4B4C3D4 | -4.5 | NP |
| 14 | F | 20 ^A XT, H | NP | NP | - | A4B4C4D1 | A4B4C4D4 | -0.37 | -2 |
| 14 | M | 60 ^A XT | NP | NP | - | A2B4C1D1 | A4B4C1D2 | -3.75 | -2.5 |
| 17 | F | 30 ^A XT, H | NP | NP | - | A1B2C2D1 | A2B3C2D1 | -0.5 | -4.5 |
| 31 | F | 14 ^A XT | NP | NP | - | A1B2C1D1 | A0B0C1D3 | NP | NP |
| 32 | F | 16 ^A XT, H | NP | NP | - | A0B0C1D1 | A2B2C2D3 | -0.25 | NP |
| Orthotropic subjects: | | | | | | | | | |
| gross stereopsis | | | | | | | | | |
| 9 | M | 2 ^A X | Yes | No | 140 | A0B1C0D1 | A2B2C0D2 | -2 | -7.25 |
| 10 | M | O | Yes | NP | 200 | A2B2C0D1 | A3B4C2D2 | -0.5 | -3.5 |
| 13 | M | O | Yes | No | 3500 | A4B4C2D1 | A2B4C4D2 | -5.75 | -3.5 |
| 13 | F | O | NP | NP | NP | A4B4C3D2 | A4B4C3D2 | -2 | -3 |
| 14 | M | 2 ^A X | Yes | No | 3500 | A1B2C1D0 | A2B2C1D1 | -2.5 | -0.75 |
| 14 | M | 6 ^A X, H | Yes | No | 3500 | A0B1C1D0 | A2B4C2D2 | -2 | 0 |
| 14 | M | O | Yes | Yes | 100 | A2B2C1D0 | A2B4C1D1 | -0.75 | -1 |
| 14 | M | O | Yes | Yes | 100 | A2B2C2D1 | A2B4C2D2 | 0 | 1.25 |
| 14 | F | O | Yes | No | 100 | A1B2C1D0 | A2B3C2D1 | -0.05 | -0.5 |
| 15 | F | 2 ^A E | Yes | No | 100 | A2B2C1D0 | A2B4C3D1 | 1 | 1.25 |
| 15 | F | O | No | NP | NP | A2B2C1D2 | A2B2C1D2 | -1 | -5.75 |
| 15 | M | O | Yes | Yes | 400 | A1B4C2D2 | A2B2C0D2 | -1.25 | -0.5 |
| 15 | F | O | Yes | NP | 400 | A4B4C1D1 | A2B4C3D1 | -2.75 | 3.25 |
| 15 | M | O | Yes | Yes | 400 | A4B4C2D1 | A2B4C3D1 | -1 | 0.63 |
| 15 | M | O | No | NP | NP | A0B0C1D0 | A2B3C2D3 | 3.25 | -5.5 |
| 15 | F | O | Yes | No | 400 | A0B0C0D0 | A0B4C3D2 | -0.37 | -2.5 |
| 16 | F | 6 ^A X | Yes | No | 140 | A1B2C0D0 | A2B3C1D2 | -3 | -20.25 |
| 16 | F | O | Yes | Yes | 400 | A0B0C0D0 | A4B4C0D3 | -0.75 | -4 |
| 16 | M | O | Yes | No | SB | A0B0C2D1 | A4B4C3D3 | -1.5 | -3 |
| 16 | F | O | Yes | Yes | 100 | A2B4C3D0 | A4B4C2D2 | -1.25 | -5 |
| 16 | M | O | Yes | No | 400 | A2B2C1D1 | A4B4C3D3 | -0.67 | -1 |
| 17 | M | O | Yes | Yes | 140 | A3B4C2D2 | A0B4C3D0 | -1.25 | -14.75 |
| 18 | F | 12 ^A X | NP | NP | - | A2B4C3D1 | A3B4C3D2 | -0.5 | -1 |
| 19 | F | O | Yes | No | 200 | A2B2C2D1 | A4B4C3D2 | -3.75 | -5 |
| 20 | M | H | Yes | Yes | 400 | A0B2C1D0 | A3B4C0D2 | -5 | -0.75 |
| 20 | M | O | Yes | No | 100 | A2B4C3D1 | A4B4C3D2 | -1.37 | -0.5 |
| 21 | M | O | Yes | NP | 400 | A2B3C1D2 | A2B3C1D2 | -2 | 0 |
| 23 | M | 20 ^A X, H | Yes | No | 100 | A2B3C2D1 | A2B2C2D2 | -1.5 | -2.25 |
| 23 | F | O | No | NP | NP | A2B2C1D1 | A4B4C3D3 | -1.25 | -1 |
| 25 | M | 2 ^A X | Yes | Yes | 200 | A2B3C2D0 | A2B4C2D1 | -1.25 | -2.5 |
| 25 | M | O | Yes | No | 3500 | A0B2C1D0 | A2B4C1D0 | -0.5 | -5.75 |
| 26 | M | O | Yes | No | 200 | A0B2C0D0 | A3B4C1D2 | 0 | -1.75 |
| 28 | F | 3 ^A X | Yes | No | 400 | A3B4C1D1 | A4B4C1D1 | -5.25 | -1.25 |
| 29 | F | O | Yes | No | 400 | A2B4C1D1 | A4B4C1D1 | -1.25 | -4.25 |
| 34 | F | O | No | NP | NP | A2B2C1D0 | A4B4C1D2 | -4 | -3 |
| 38 | F | O | Yes | Yes | 100 | A1B2C2D0 | A2B4C2D2 | -3.37 | -2.5 |
| Orthotropic subjects: | | | | | | | | | |
| fine stereopsis | | | | | | | | | |
| 12 | F | O | Yes | No | 60 | A4B4C0D1 | A4B4C1D2 | -1.25 | -4.5 |
| 14 | M | 2 ^A X | Yes | No | 40 | A2B2C1D0 | A2B4C3D1 | -0.87 | -1.5 |
| 14 | M | 1 ^A X | Yes | Yes | 60 | A0B2C2D0 | A2B4C3D2 | -0.5 | -1 |
| 15 | F | O | Yes | Yes | 50 | A2B3C0D0 | A2B2C1D2 | -1.25 | -1 |
| 16 | F | 4 ^A X | Yes | Yes | 50 | A2B3C1D1 | A4B4C1D2 | -1.75 | -4.5 |
| 20 | M | O | Yes | Yes | 60 | A0B1C1D0 | A3B4C2D1 | -0.5 | 0 |
| 22 | F | O | Yes | Yes | 50 | A0B0C0D0 | A1B4C2D0 | 0 | -0.25 |
| 24 | F | 3 ^A X | Yes | NP | 40 | A2B3C2D0 | A2B3C2D1 | -3.87 | -3.5 |
| 24 | F | O | Yes | Yes | 60 | A4B4C2D1 | A4B4C2D1 | -7.5 | -7 |
| 30 | M | O | Yes | Yes | 50 | A2B3C0D0 | A2B3C1D0 | -1 | -2 |

M, male; F, female; XT, exotropia; ET, esotropia; O, orthophoria; E, esophoria; X, exophoria; H, hyperphoria (up to 4^A); NP, not performed; SB, stereoblind. ABCD classification: A0 < 46.5, A1 < 48.0, A2 < 53.0, A3 < 55.0, A4 > 55.0; B0 < 57.25, B1 < 59.25, B2 < 65.5, B3 < 68.5, B4 > 68.5; C0 > 490 μ m, C1 > 450 μ m, C2 > 400 μ m, C3 > 300 μ m, C4 \leq 300 μ m; D0 logMAR 0 to -0.2, D1 logMAR > 0, D2 logMAR > 0.3, D3 logMAR > 0.6, D4 logMAR > 1.1.

TABLE 3. KG: Median Differences Between BCVA and Uncorrected Visual Acuity (uVA) (logMAR) in Better and Worse Eyes (Wilcoxon Test)

| KG, <i>n</i> = 47 | Δ , BCVA – uVA | <i>P</i> |
|-------------------|-----------------------|----------|
| Better eye | –0.2 | <0.0001 |
| Worse eye | –0.3 | <0.0001 |

Whitney test). Values of frontal astigmatism for the KG eyes were also significantly different: In the KG with fine stereopsis, median was –3.0 [–8.2 to 4.3] and with gross stereopsis median was –5.0 [–11.3 to 7.9] ($P = 0.03$, Mann-Whitney test).

KG: Stereopsis Measurement, Considering BCVA Values in Both Eyes

Data from 40 subjects with simultaneous perception were analyzed. In the KG, among subjects with a logMAR ≤ 0.3 in both eyes, 7 out of 28 had fine stereopsis. Among those in whom at least one eye had a BCVA of logMAR > 0.3 , 3 out of 12 had fine stereopsis. Subjects with BCVA in both eyes of logMAR ≤ 0.3 (logMAR 0.3 to –0.1) did not have a better stereopsis performance than subjects with at least one eye with a BCVA of logMAR > 0.3 (logMAR 0.4–1.1) ($P > 0.05$, Fisher test).

KG: Stereopsis Measurement, Considering Anisometropia and BCVA

Data from the CG and KG subjects with simultaneous perception were analyzed relative to manifest anisometropia and BCVA. Five out of 11 subjects from the KG without strabismus, with simultaneous perception, and a spherical equivalent anisometropia of < 1.0 spherical diopters and BCVA in both eyes equal to logMAR ≤ 0.3 (logMAR 0.3 to –0.1) were not different from subjects of the CG with the same characteristics, among whom 21 out of 26 subjects had fine stereopsis ($P = 0.05$, OR 5.0; 95% CI 1.1–19.7, Fisher test).

KG With Fine Stereopsis, KG With Gross Stereopsis, CG With Fine Stereopsis, and CG With Gross Stereopsis, With Spherical Equivalent Anisometropia < 1.0 Spherical Diopters and BCVA in Both Eyes Equal logMAR ≤ 0.3

To assess anisometropia due to corneal curvature, we again compared Km differences between right and left eyes of each subject in the CG with fine stereopsis (median 0.3 [0–1.1]) or

TABLE 4. KG: Frequency of Strabismus ($P = 0.0002$; OR 33.2; CI 95% 4.2–380, Fisher Test)

| KG, <i>n</i> = 54 | No Strabismus | Strabismus |
|----------------------------------|---------------|------------|
| BCVA worse eye logMAR ≥ 0.7 | 8 | 7 |
| BCVA worse eye logMAR < 0.7 | 38 | 1 |

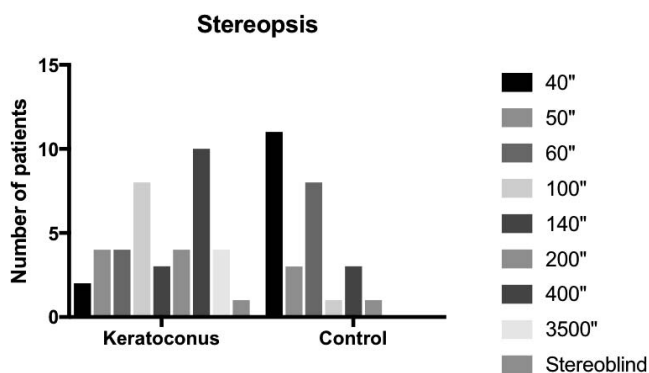
gross stereopsis (median 0.2 [0.1–0.7]), and each subject in the KG with fine stereopsis (median 2.0 [1.1–5.4]) or gross stereopsis (median 2.65 [1.8–4.0]). CG fine and gross stereopsis were not different ($P = 0.7$). KG fine and gross stereopsis also were not significantly different ($P = 0.7$) (Mann-Whitney test).

DISCUSSION

Our data show that the KG has a higher frequency of strabismus when compared to the general population^{24–26} and to the CG. Besides binocular alignment, simultaneous perception is also a prerequisite for the third degree of binocularity (stereopsis). We observed that among 44 orthotropic subjects in the KG, suppression responses were observed in 4 (9%) subjects, contributing to impaired stereopsis in this group. This also happened in two subjects with high ametropia in the CG, suggesting that the suppression response may be triggered by the presence of high astigmatism.

The KG and CG were not different relative to the first and second degrees of binocular vision (simultaneous perception, fusion, and fusional convergence). As simultaneous perception is a prerequisite for fusion, the number of subjects evaluated for fusional convergence was 40, that is, the ones that demonstrated simultaneous perception with both striate Maddox and 6^A base-down prism tests. Although the KG and CG were not different relative to first and second degrees of binocularity, our data demonstrate that there was an association between good visual acuity and simultaneous perception, as subjects from KG whose BCVA in the worse eye was logMAR ≥ 0.7 were associated with a higher frequency of strabismus and a higher chance of having absence of simultaneous perception (Tables 4, 5).

As in anisometropia with amblyopia, one of the factors associated with an increased frequency of strabismus or impaired binocular vision is the difference in visual acuity between the two eyes. Our data show decreased visual acuity in both eyes in the KG and a difference in visual acuity between the better and worse eye of logMAR 0.35 in the KG. Although careful refractometry improved at least two lines of vision in the better eye and almost three lines in the worse eye in the KG (Table 3), relevant differences between BCVA from both eyes remained, and were associated with impaired binocular vision, as occurs in amblyopia associated with strabismus and anisometropia.^{6,16} Optical correction with glasses of the refractive errors did not change the KG stereopsis performance, similar to that seen by Lee et al.²⁷ None of the GC or KG subjects were contact lens wearers. One

**FIGURE 3.** Stereopsis: KG and CG without strabismus and with simultaneous perception. Frequency of stereopsis according to Titmus Fly Test.**TABLE 5.** KG: Simultaneous Perception Evaluation, Using Both Maddox Striate Test and a 6^A Base-Down Prism ($P = 0.01$; OR 21; CI 95% 2.4 – 276.7, Fisher Test)

| KG, <i>n</i> = 44 | SP | No SP |
|----------------------------------|----|-------|
| BCVA worse eye logMAR ≥ 0.7 | 5 | 3 |
| BCVA worse eye logMAR < 0.7 | 35 | 1 |

TABLE 6. Spherical Equivalent Anisometropia: KG and CG ($P = 0.01$; OR 5.5; 95% CI 1.4–18.7, Fisher Test)

| Sph Equiv | CG ($n = 29$) | KG ($n = 54$) |
|--------------|-----------------|-----------------|
| ≥ 1.0 D | 26 | 33 |
| < 1.0 D | 3 | 21 |

Sph equiv, spherical equivalent.

possibility is that the adaptation of hard contact lenses, which improves the irregularities of the anterior corneal surface, reduces aniseikonia, and improves visual acuity, might improve their sensory status.

Regarding the third degree of binocular vision (stereopsis), the KG subjects without strabismus but with simultaneous perception still show a significantly impaired stereoscopic performance (Fig. 3). Although studies of stereopsis and its prevalence in the general population have much bias (such as the choice of nonnaïve observers, observers with clinical characteristics that could influence the results, or the use of nonstandardized stereopsis tests and/or nonstandardized methods for exclusion of participants),¹¹ Heron et al.²⁸ showed that in an adult population, about 85% of the observers had a stereoacuity equal to or better than 50 arcsec. In our data, however, only 10 (18%) subjects in the KG demonstrated stereopsis equal to 60 arcsec or better, while stereopsis was present in 22 (76%) of the CG subjects. Our study agrees with others that described impaired binocular vision in keratoconus subjects. In 2000, Brahma et al.⁸ also found gross stereopsis in keratoconus subjects. After penetrating keratoplasty in one eye of keratoconus subjects, he found median stereopsis of 360 arcsec, although the logMAR visual acuity median of the operated eyes was 0.07. There were no data about the visual acuities of the nonoperated eyes. In 2001, Sherafat et al.⁹ studied 20 subjects with keratoconus who used rigid contact lenses in the worse eye. He found only 1 patient with a stereopsis of 60 arcsec, and 13 out of 20 had stereopsis equal to 480 arcsec or worse. Their visual acuities ranged from logMAR 0 to 1.0. These data agree with the hypothesis that improvement of visual acuity, either with contact lenses or with corneal transplantation, was not sufficient to allow stereopsis to recover in these subjects to 60 arcsec or better.

Although low vision in one eye was associated with an increased frequency of strabismus and the absence of simultaneous perception, we did not find a correlation between BCVA of logMAR > 0.3 in at least in one eye and a higher frequency of impaired stereopsis, showing that some other factors may be contributing to impaired stereopsis.

We also examined whether anisometropia was associated with stereopsis performance of the keratoconus subjects, as other studies have already demonstrated reduced stereoacuity observed experimentally^{29,30} or clinically.³¹ Astigmatism occurs mostly in the surface of the anterior cornea, which is also true in keratoconus subjects. In the absence of keratoconus, prescription of the cylindrical degree is similar to the values found in corneal tomography. In keratoconus, however, this does not occur in the same way. Corneal tomography scans show fairly high irregular astigmatism values that are incompletely corrected by cylindrical lenses. Consequently, keratoconus subjects frequently do not get complete visual acuity improvement and usually cannot use all the cylinder correction. For this reason, anisometropia in keratoconus subjects was estimated both based on the manifest refractometry chosen subjectively by them (spherical equivalent anisometropia was calculated based on their subjective manifest refractometry) and also based on objective measurements such as Km (mean of the flat [K1] and the steep [K2]

meridians) and frontal astigmatism of the anterior cornea surface, both obtained by corneal tomography.

Considering subjective manifest refractometry, although spherical equivalent anisometropia ≥ 1.0 spherical diopters equivalent was more frequent in the KG than in the CG ($P = 0.01$; Table 6), we did not find an association between spherical equivalent anisometropia < 1.0 spherical diopters and a better stereopsis performance ($P = 0.06$) in the KG. Lee et al.,²⁷ on the other hand, found worse stereopsis and a greater proportion subjects with gross stereopsis in the anisometric group. However, he studied non-amblyopic children. The nonsignificance of our data might be explained by the fact that the CG was composed of approximately 40% (11 out of 29) of subjects with myopia and/or astigmatism equal to or greater than 3.5 cylinder diopters in both eyes, and 3 also had anisometropia between 1.0 and 2.25 spherical equivalent. These characteristics also increased the frequency of impaired stereopsis in the CG to a frequency of 24% (7 out of 29 subjects in the CG had gross stereopsis). It is important to remember that, as already mentioned, keratoconus was discarded in the CG by corneal tomography.

All refractometries were performed by a single experienced ophthalmologist. However, these values are still highly subjective in keratoconus subjects. For this reason, we also analyzed two other objective parameters, Km and frontal astigmatism. Although Km values were not different between eyes in the CG and KG, we found that frontal astigmatism was significantly different in the eyes of the CG (gross and fine stereopsis, $P = 0.01$), as well as in the eyes of the KG (gross and fine stereopsis, $P = 0.03$). In other words, no matter which subject group was examined (CG or KG), the amount of frontal astigmatism was significantly higher in the groups with gross stereopsis. The distortion caused by irregular high astigmatism on the frontal corneal surface may explain the disruptive effect on the ability to perform stereopsis tests, as observed by Asaria et al.³² in subjects with epiretinal membranes.

Our data agree with other studies, in which experimentally induced^{29,30} or clinically observed³¹ astigmatism was associated with stereopsis reduction. Increasing the number of subjects with astigmatism in both the KG and CG might give us clues to determine the amount of astigmatism at which stereopsis becomes impaired. Looking back to the CG, 12 out of 29 subjects had astigmatism equal to or higher than 3.5 cylinder diopters and, curiously, 6 out of 7 subjects with gross stereopsis had astigmatism higher than 3.5 cylinder diopters. These data reinforce the need for more studies in order to improve our knowledge on the effect of astigmatism on stereoacuity. It is possible that one-meridian amblyopia in highly astigmatic subjects in both groups may explain this finding, depending on their age when they started using their optical correction.³³

Although the age reported as the onset of the impaired vision was 12 years old, it is difficult to know at which age the ectasia and its consequences on the binocular system began to develop, since keratoconus is a disease with asymmetric progression. This information, on the other hand, reinforces the importance of a closer follow-up of teenagers with a family history of keratoconus, strabismus, atopy, anisometropia, and poor eyesight.

In our study, no patient complained of diplopia, contrary to what Khan and Al-Shamsi described in 2008.¹⁰ He described seven subjects with strabismus and keratoconus, who were referred for treatment of diplopia after a surgical procedure meant to improve the vision of the worse eye. This difference in findings may be explained by the fact that Khan series was obtained from subjects with diplopia who were referred to an outpatient strabismus clinic. In our series, the KG subjects were followed up after the diagnosis of keratoconus in a

corneal service. They did not have diplopia, and some of them were not even aware of their ocular deviation.

There are some limitations to our study. First, this was a cross-sectional study, and new assessments could alter the results. The ability to perceive smaller angles of stereopsis using different approaches may be possible, since it is known that the contour-based stereoscopic tests overestimate stereopsis due to monocular cues.³⁴ Second, refractometry was not performed under cycloplegia due to peripheral aberrations in the KG. Although the examiner had significant experience with refractometry, this fact may have influenced the data collected. Third, axial lengths were not measured, so corneal refractive errors could not be separated from axial errors. Fourth, we do not know the exact time period when these subjects developed keratoconus and the exact period when they started using optical correction, nor do we know its influence on stereopsis over time, including in the CG. Fifth, impaired stereopsis may be associated with convergence insufficiency, and this issue was not investigated in our subjects. However, it is possible that convergence insufficiency could be a cause or consequence of impaired stereopsis.

In conclusion, keratoconus subjects using their best optical correction (glasses) had a higher frequency of strabismus and absence of simultaneous perception. This was associated with low vision at least in one of the eyes. Stereopsis performance was also significantly different in keratoconus subjects when compared to controls. Anisometropia did not appear to cause a deterioration of stereopsis in the studied groups. Frontal astigmatism was significantly higher in both CG and KG subjects with gross stereopsis. Improvement in the early diagnosis of keratoconus, through corneal tomography, as well as a better understanding of factors that help in the stereoscopic perception of space, may help us better understand the factors associated with stereoscopic impairment.

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