African Vision and Eye Health
ISSN: (Online) 2410-1516, (Print) 2413-3183

A comparison of anterior and posterior central corneal powers in eyes with and without keratoconus

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Dates:
Received: 12 Aug. 2020
Accepted: 14 Oct. 2020
Published: 17 Dec. 2020

How to cite this article:
Chetty E, Rubin A. A comparison of anterior and posterior central corneal powers in eyes with and without keratoconus. Afr Vision Eye Health. 2020;79(1), a607. https://doi.org/10.4102/aveh.v79i1.607

Background: Keratoconus affects the anterior segment of the eye, which directly affects the refractive state of the eye. There are three components for the measurement of a corneal curvature or central corneal power (CCP) of the eye, namely, the power along the flat meridian, the power along the steep meridian and the axis of the flat meridian. Traditionally, CCP is analysed using univariate methods that processes each component separately; however, because of the trivariate nature of CCP, the use of multivariate methods and statistics may be beneficial.

Aim: The aim of this study was to compare the short-term variation of the anterior and posterior CCP in eyes with and without keratoconus using multivariate methods of analysis.

Setting: Data were extracted from a doctoral study by the first author. The group with keratoconus (KC) was obtained from patients attending a university-based contact lens clinic in Johannesburg, South Africa.

Methods: A total of 28 eyes with KC and 28 eyes of 28 healthy control eyes without KC were included in this prospective quantitative study. Measurements were taken with the Oculus Pentacam (Wetzlar, Germany) and data related to the anterior and posterior CCP were analysed using multivariate methods and analysis.

Results: For both KC and control groups, short-term variation of CCP of the anterior corneal surfaces was significantly greater than that for the posterior corneal surfaces. Whilst short-term variation was similar for both corneal surfaces in the KC group, variation of the posterior corneal surfaces was significantly different from that of the anterior corneal surfaces for the control group.

Conclusion: Multivariate analysis of short-term variation of CCP of both surfaces of the cornea in eyes with or without KC contributed towards a more complete understanding of the disease.

Keywords: keratoconus; cornea; multivariate analysis of dioptric power; central corneal power; Scheimpflug imaging.

Introduction

Between the late seventies and eighties of the 20th century, a combination of efforts from Long,[1] Keating[2,3,4] and Harris[5] led to the formalisation of a mathematically and scientifically meaningful representation of dioptric power via the concept of the symmetric, square 2 × 2 matrix. Over the last 30-odd years, much work in South Africa related to the effective analysis of dioptric power by Harris,[6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25] Harris et al.[26,27] and others elsewhere, such as Thibos et al.,[28] for example, developed the original concepts into what they are today. The matrix representation of dioptric power has enabled scientific methods of analysis to be conducted on critical optometric and ophthalmologic data that otherwise could not be properly understood either qualitatively or quantitatively. These methods include adding, averaging and squaring sphero-cylindrical powers in their entirety and calculating variances, standard deviations and a host of other univariate and multivariate statistical functions[6] that were once thought to be impossible for such data.[29] These methods of analysing refractive and keratometric data have been used very frequently in South Africa and elsewhere for the study of a multitude of clinical and research-oriented issues of critical importance to avoid, for example, unnecessary vision impairment and its consequences. These methods and their implications have been described in great detail elsewhere.[5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,30,31,32,33]

Refractive or dioptric power is made up of three components, namely sphere (*Fs* = S), cylinder (*Fc* = C) and axis (A). Similarly, corneal curvature measurements, from instruments such as the Oculus Pentacam (OP), are made up of three components as well, namely, the power along the flat meridian, the power along the steep meridian, and the axis of the flat meridian. Such quantities are used in many instruments to represent concepts such as *simulated keratometry*. Corneal curvature near the corneal apex or simulated keratometry can be more accurately described as central corneal power (CCP) and in this article will be referred to as such going forward.

Most studies that investigate CCP analyse each of the three components individually rather than as the holistic entity that they truly represent. In doing so, important information may be inadvertently overlooked and thus, here CCP will be analysed holistically in individuals with or without keratoconus (KC) using mainly multivariate methods. These methods are similar but not always identical to those described by Thibos et al.,[28] who advocated the use of power vectors (M, J_0 and J_{45}) to analyse refractive data. Some research has been performed to establish the difference in CCP between KC and control eyes[34,35,36,37,38] but, to the best of our knowledge, this is the first study that comprehensively compares both anterior and posterior CCP in KC and control eyes using multivariate methods of analysis. The results and discussion of this study will focus primarily on the differences between the anterior and posterior CCP in KC and in control eyes and less so on differences in CCP between eyes with KC and controls. Investigating the short-term variation of CCP in KC and healthy corneas may lead to a better understanding of the nature of the disease process in KC. This in turn may facilitate earlier diagnosis and perhaps improvements in treatment options for the disease, which could improve the quality of life for patients with KC.

Methods

This study formed part of the doctoral study of the first author.[39] This prospective quantitative study took place in the Optometry clinic at the University of Johannesburg, Doornfontein campus. The research group consisted of 28 KC eyes (18 participants) with a median age and quartile deviation of 22.0 (± 4.0) and 28 healthy control eyes (28 participants) with a median age and quartile deviation of 23.0 (± 1.0) years. Both male (five KC and nine controls) and female (13 KC and 19 controls) participants were included in this study. All patients who attended the specialty contact lens clinic and had been diagnosed with KC through routine preliminary tests (such as slit lamp and corneal topography) were invited to participate in this study. Control participants were recruited by means of convenience sampling from the student body at the university. Once participants had been suitably briefed and provided their informed consent, they were assessed for inclusion in this study by means of a questionnaire, slit lamp examination, ophthalmoscopy and single Pentacam measurements of both eyes (where possible) for participants in the KC group and only the right eye for controls. Only the right eyes of controls were included, but where possible, both eyes of those with KC were included. Exclusion criteria were current or recent contact lens wear, ocular pathology other than KC and recent eye surgery or any medication with possible ophthalmic side effects. The same exclusion criteria, as well as no ocular pathology, were applicable for control participants. Keratoconus participants with severely distorted corneas were also excluded because Pentacam measurements could not be acquired on these patients.

As mentioned before, this study formed part of a larger doctoral study,[39] which included measurements such as corneal pachymetry and refractive state that were taken with various instruments over two measuring sessions. For the purposes of this article, only the data from the OP at the first session were used. Forty consecutive OP (anterior and posterior) measurements for each of the 56 eyes were included here. Refer to Table 1 for basic demographic information. Measurements were taken according to the user manual for the OP and in the interest of measurement, independent participants were requested to reposition their heads after each of the 40 measurements. The time to obtain 40 measurements per eye with the OP varied across participants but was generally longer for those with KC and especially so where severity was greater and in many instances, otherwise suitable, participants had to be excluded because OP measurements were not possible because of disease severity. This was one of the reasons for inclusion of both right and left eyes for those with KC but only right eyes for those without KC. Overall time for 40 measurements per eye varied from approximately 10 min in controls to 30 min in eyes with KC.

Normality of samples was evaluated using skewness and kurtosis, and samples were generally not normally distributed; therefore, non-parametric statistical tests were used where necessary and non-parametric variables such as medians and quartile deviations have been included in the results such as box plots that follow.

With sphero-cylindrical power having its proper mathematical representation, any mathematical function possible with matrices becomes possible with refractive or keratometric data including, as mentioned, calculating means and variances that are two paramount statistics when comparing samples of data and making inferences for populations.[11] All the statistical methods discussed further are based on the dioptric power matrix. Harris, Malan and Rubin[26,27,40,41,42] have all contributed to the development of statistical and software methods using MATLAB that were specifically designed to convert such data into matrix

TABLE 1: Demographic information for eyes analysed.

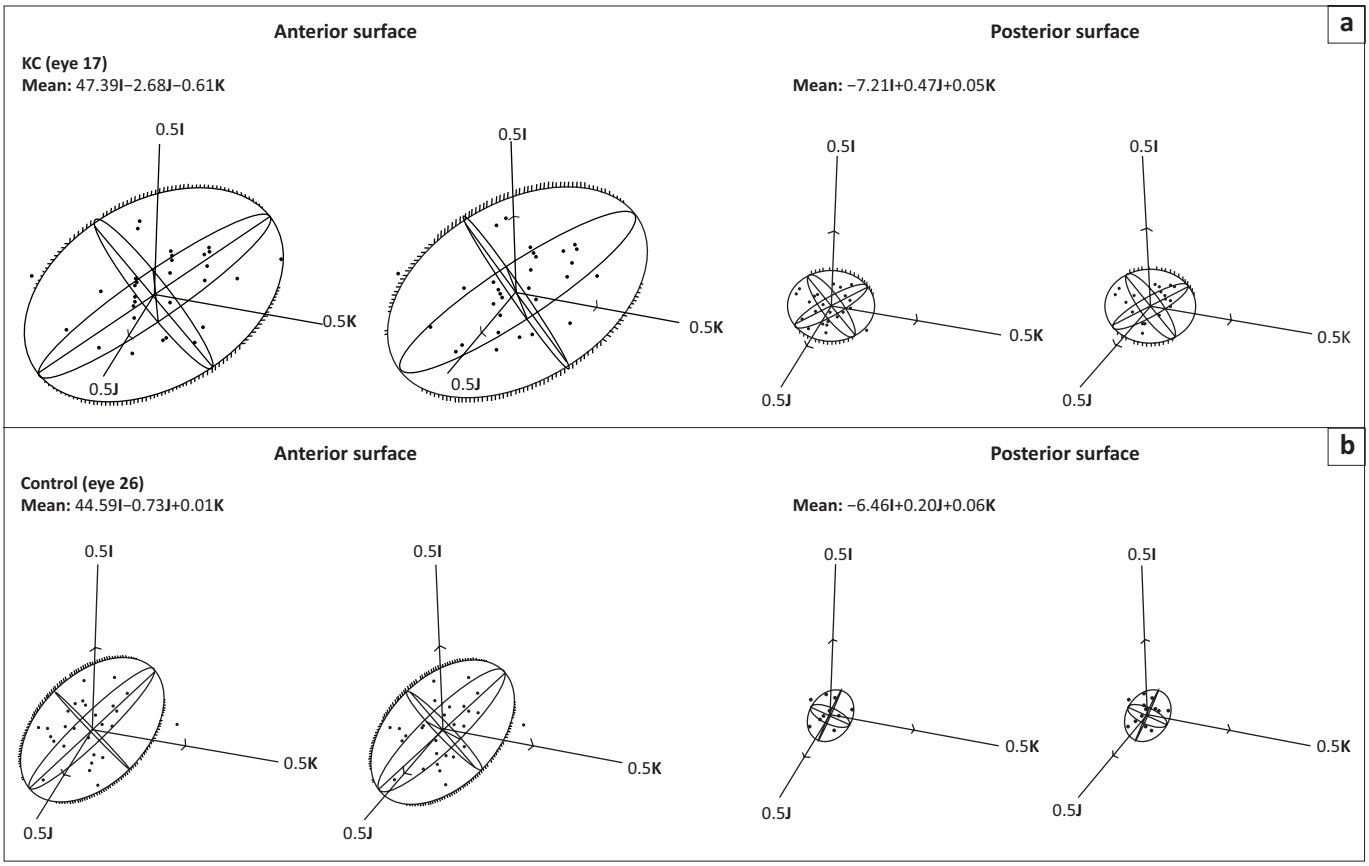
Group	Number of participants	Median age ± QD (years)	Number of eyes	Male/ Female	Right/ Left
Keratoconus	18	22.0 ± 4.0	28	5 / 13	14 / 14
Control	28	23.0 ± 1.0	28	9 / 19	28 / 0

QD, quartile deviation.

representations, which could then be used for multivariate statistical analyses. For the purposes of this study, these methods were used to convert the central raw keratometric data (radii of curvature along principal meridians) first into conventional powers and then into matrix representations. Refractive indices used for converting the anterior corneal surface measurements were 1.3375 for tears and 1.0 for air; for the posterior corneal surface, the refractive indices used were 1.376 for the cornea and 1.336 for the aqueous. Thereafter, all the statistical functions and methods (stereo-pair scatter plots with 95% distribution ellipsoids and variance-covariance matrices) required to analyse the data were carried out on the matrix equivalents. Univariate analyses of ellipsoid volumes and variances were also included and performed using Statistica (Tibco, version 13.3). Some analyses with MedCalc were also included.

Results

Multivariate statistical analyses of dioptric power are based on assumptions such as normality and equality of population variances, and if these assumptions are violated, then the inferences made for such data need to be treated with caution. However, if those data are represented graphically, then such statistical inferences can be validated and conclusions drawn are more meaningful.[15] Stereo-pair scatter plots provide an essential visual representation of dioptric power in its entirety and are constructed without any underlying assumptions, thus providing graphical substantiation to various statistical assertions made in this study. For the purposes of this study, each point in a stereo-pair scatter plot represents one OP corneal curvature reading that was converted to a symmetric matrix that is plotted in three-dimensional Euclidean space. Thibos[28] and others[34,43,44] use vectors in two dimensions to perform similar analyses but without stereo-pairs that in general enhance (and actually simplify) data visualisation and analysis. For example, instead of multiple plots for the various components of power (M, J_0 and J_{45}), only a single plot for a specific sample becomes necessary and given the fundamental three-dimensional nature of power, individual measurements can be properly localised and compared in the three-dimensional space (see Figure 1 for example). The three-dimensional percept of the stereo-pairs in Figure 1 can be appreciated by diverging the eyes to an imaginary point behind the page, that is, allow the eyes to drift outwards into an exo-position relative to the page. Alternatively, one can fuse to a point in front of the page, perhaps with the use of a pencil. Then, the eyes would be in an exo-posture and some explanations related to the plot may change slightly and not match that herein. For example, the origin becomes the closest point on the three axes to the viewer rather than the most distant point.



KC, keratoconus.

FIGURE 1: Stereo-pair scatter plots with 95% distribution ellipsoids for one randomly selected eye from the keratoconus group (eye 17) and the other from the control group (eye 26) for anterior and posterior central corneal power. The origin for each stereo-pair is placed at its sample mean as indicated above. Each stereo-pair has an axis length of 0.5 dioptre and a tick interval of 0.25 dioptre. Table 4 to follow includes the variances for these samples.

Ellipsoids of constant probability density (also referred to as distribution ellipsoids) have also been included in these stereo-pair scatter plots and, together with the data itself, provide a graphical representation of the spread of dioptric power in a sample. The size, shape and orientation of these distribution ellipsoids and the variances (see Table 5) characterise the nature of the variation of the population and provide a visual aid in making comparisons between populations.[16] For each sample, it is expected that 95% of keratometric measurements from the population from which the sample was taken will lie within the respective distribution ellipsoid. These distribution ellipsoids provide a visual indication of the nature of the variation of CCP within the sample and between samples. One is able to identify differences between anterior and posterior CCP in KC and control eyes by comparing the size, shape and orientation of the distribution ellipsoids generated for different samples.

Figure 1 provides stereo-pairs that represent both the anterior and posterior CCP for two randomly selected eyes from the KC and control groups. The stereo-pairs provide a clear indication that, as anticipated, variation of both the anterior and posterior CCP is greater in the eye with KC compared to the control eye and this is true for all cases within each group. However, the anterior CCP for both the eye with KC and the control eye is much greater than the respective posterior CCP. It is evident in Figure 1 that the data for both the KC and control eyes cluster closer to the mean of the sample for posterior CCP, whereas the points are more widely dispersed for the anterior surface. This indicates that the anterior CCP is more variable than the posterior CCP for both KC and control eyes.

This is further substantiated on inspection of the 95% distribution ellipsoid volumes for anterior and posterior CCP for both the KC and control groups (stereo-pair scatter plots and distribution ellipsoids were generated for all 56 eyes measured but are not included here) found in Table 2. The volumes for the 95% distribution ellipsoids were used to generate the box-and-whisker plots in Figure 2 and Table 3 provides the relative descriptive statistics.

As expected and irrespective of the surface (anterior or posterior) concerned, the median volumes for the KC group are much larger compared to those of the control group. The box-and-whisker plot in Figure 2 and standard deviations and quartile deviations in Table 3 show that the anterior surface of the cornea undergoes greater short-term variation in CCP in both KC and control eyes. On average (comparison of medians in Table 3), anterior CCP is approximately 12 times more variable than posterior CCP in control eyes and even more so in eyes with KC (approximately 48 times). On comparison of the 95% distribution ellipsoid volumes, the non-parametric Wilcoxon matched pair test showed that the anterior corneal surface exhibited significantly more variation than the posterior corneal surface for eyes with KC (comparison of medians in Figure 2a) ($p = 0.00$). The same was true for the controls (comparison of medians in Figure 2b) ($p = 0.00$).

TABLE 2: Distribution ellipsoid (95%) volumes for anterior and posterior central corneal power for 28 eyes with keratoconus and 28 control eyes. Maxima and minima are indicated in red and blue, respectively. Medians and quartile deviations (= 0.5 interquartile range) for ellipsoid volumes can be found in Table 3.

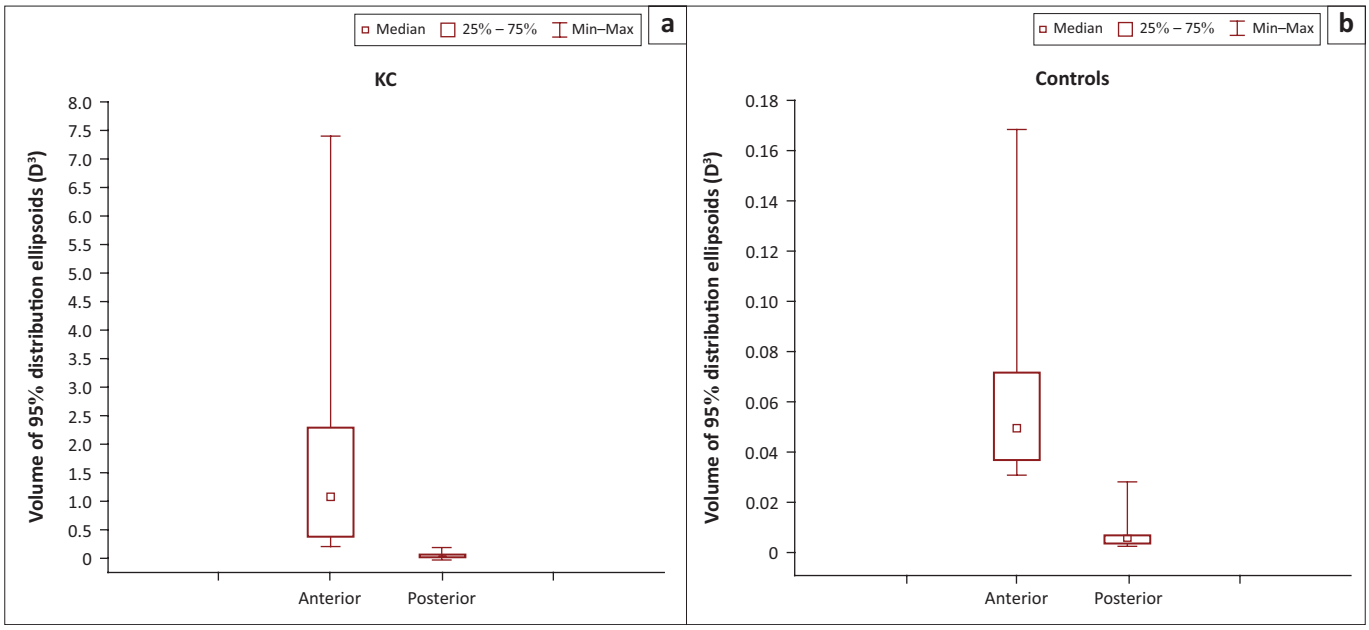
Eye	Keratoconus group		Control group	
	Anterior	Posterior	Anterior	Posterior
1	0.365	0.017	0.063	0.003
2	4.692	0.156†	0.048	0.004
3	0.330	0.009	0.031	0.003
4	2.324	0.069	0.070	0.007
5	2.207	0.111	0.071	0.005
6	0.408	0.003‡	0.034	0.002‡
7	0.897	0.010	0.065	0.005
8	0.718	0.066	0.046	0.004
9	0.581	0.010	0.040	0.006
10	0.380	0.014	0.041	0.004
11	1.527	0.029	0.033	0.003
12	3.060	0.022	0.101	0.006
13	2.046	0.018	0.038	0.002‡
14	0.510	0.013	0.037	0.002‡
15	1.910	0.022	0.168†	0.028†
16	1.222	0.029	0.031	0.003
17	0.257	0.011	0.046	0.004
18	1.234	0.027	0.049	0.006
19	0.701	0.022	0.030‡	0.002‡
20	0.478	0.023	0.079	0.006
21	2.591	0.045	0.063	0.013
22	7.369†	0.096	0.096	0.012
23	0.376	0.008	0.105	0.003
24	4.306	0.056	0.044	0.003
25	3.287	0.088	0.061	0.005
26	0.268	0.013	0.055	0.004
27	0.217‡	0.032	0.036	0.006
28	1.621	0.017	0.082	0.010

†, ‡, Maxima and minima are indicated in single dagger and double dagger, respectively.

To investigate the short-term variation of anterior and posterior CCP further, variances were extracted from the variance-covariance matrix for each of the 56 eyes tested and are included in Tables 4 and 5 for KC and control eyes, respectively. These values were then used to generate the box-and-whisker plots in Figure 3 (eyes with KC) and Figure 4 (control eyes).

For eyes with KC, the non-parametric Friedman analysis of variance (ANOVA) indicated that there were no significant differences in variances for the anterior corneal surface (comparison of medians in Figure 3a) nor for the posterior corneal surface (comparison of medians in Figure 3b). This indicates that there are similar amounts of stigmatic and anti-stigmatic variation on the anterior corneal surface as well as on the posterior corneal surface. The Friedman ANOVA also confirmed that both stigmatic and antistigmatic variations were significantly greater for the anterior corneal surface compared to the posterior corneal surface in eyes with KC (comparison of Figures 3a and 3b shows the differences in scales for the *y*-axes).

For control eyes, the Friedman ANOVA and associated *post-hoc* multiple comparison test indicated that there was significantly more stigmatic variation of anterior CCP than antistigmatic variation (comparison of medians in Figure 4a).



KC, keratoconus.

FIGURE 2: Box-and-whisker plots for 95% distribution ellipsoid volumes (D^3) for (a) eyes with keratoconus (n = 28) and (b) control eyes (n = 28) eyes for anterior and posterior central corneal power. Take note of the difference in the scale for the plots.

TABLE 3: Descriptive statistics for the box-and-whisker plots in Figure 2 for 95% distribution ellipsoid volumes. Units are D^3 throughout and all samples consisted of 28 eyes. Standard deviations and quartile deviations are included.

Variable	Means	SD	Medians	QD	Minima	Maxima
KC anterior CCP	1.639	1.679	1.060	0.936	0.217	7.369
KC posterior CCP	0.037	0.037	0.022	0.018	0.003	0.156
Control anterior CCP	0.059	0.030	0.049	0.017	0.030	0.168
Control posterior CCP	0.006	0.005	0.004	0.001	0.002	0.028

SD, standard deviation; QC, quartile deviations; KC, keratoconus; CCP, central corneal power.

For posterior CCP, it was found that there was statistically greater ortho-antistigmatic variation compared to stigmatic and oblique antistigmatic variation (comparison of medians in Figure 4b); however, there was no significant difference between stigmatic and oblique antistigmatic variation of posterior CCP. Similar to the KC group, control eyes also experienced statistically greater variation for the anterior corneal surface compared to the posterior corneal surface (comparison of Figure 4a and b again shows that the differences in scales for the y-axes are important in interpreting this finding).

Discussion

Previous studies have compared CCP between KC and control samples[34,35,36,37,38]; however, few have compared anterior and posterior CCP within the KC and control samples independently.[35,44] To the best of our knowledge, there are no studies that have used the multivariate methods of analysis as used in this article to compare anterior and posterior CCP in both KC and control eyes.

Tomidokoro et al.[34] conducted a retrospective observational study that compared 31 patients with KC with 18 patients without KC. Scanning slit videokeratography (Orbscan, Orbtek Inc., Salt Lake City, UT) was used and participants

TABLE 4: Variances (D^2) extracted from the variance-covariance matrices for anterior and posterior central corneal power for 28 eyes with KC where S_{II}, S_{JJ} and S_{KK} are the stigmatic and two antistigmatic variances; they relate to variances along the stigmatic and antistigmatic axes of stereo-pair scatter plots (such as in Figure 1), respectively. Maxima and minima for each column are indicated in red and blue, respectively. Medians and quartile deviations are also included.

Eye	Anterior			Posterior		
	S_{II}	S_{JJ}	S_{KK}	S_{II}	S_{JJ}	S_{KK}
1	0.011	0.037	0.007‡	0.001	0.004	0.002
2	0.174†	0.062	0.035	0.011	0.008	0.006†
3	0.026	0.009	0.010	0.001	0.004	0.001‡
4	0.038	0.037	0.070	0.004	0.004	0.005
5	0.029	0.083	0.047	0.003	0.013†	0.006†
6	0.015	0.026	0.011	0.000‡	0.001‡	0.001‡
7	0.020	0.020	0.030	0.001	0.002	0.002
8	0.024	0.030	0.014	0.007	0.007	0.002
9	0.017	0.015	0.025	0.002	0.001‡	0.001‡
10	0.010	0.015	0.021	0.002	0.003	0.001‡
11	0.027	0.048	0.041	0.002	0.002	0.003
12	0.050	0.072	0.101	0.002	0.002	0.003
13	0.105	0.052	0.031	0.004	0.003	0.001‡
14	0.009	0.015	0.033	0.002	0.002	0.002
15	0.024	0.042	0.077	0.002	0.002	0.003
16	0.015	0.031	0.052	0.002	0.006	0.004
17	0.009	0.013	0.015	0.001	0.002	0.002
18	0.028	0.043	0.021	0.006	0.004	0.003
19	0.020	0.027	0.018	0.001	0.003	0.002
20	0.013	0.014	0.019	0.002	0.006	0.001‡
21	0.043	0.073	0.039	0.003	0.004	0.003
22	0.058	0.155†	0.129†	0.005	0.008	0.005
23	0.016	0.015	0.011	0.001	0.001	0.001
24	0.123	0.034	0.099	0.006	0.002	0.005
25	0.121	0.085	0.031	0.012†	0.006	0.003
26	0.013	0.009‡	0.012	0.003	0.001	0.002
27	0.007‡	0.011	0.012	0.005	0.003	0.002
28	0.043	0.034	0.040	0.003	0.002	0.001‡
Medians	0.024	0.032	0.031	0.002	0.003	0.002
(QD)	(0.014)	(0.017)	(0.015)	(0.002)	(0.002)	(0.001)

QD, quartile deviations.

†, ‡, Maxima and minima are indicated in single dagger and double dagger, respectively.

TABLE 5: Variances (D^2) extracted from the variance-covariance matrices for anterior and posterior CCP for 28 control eyes where S_{II}, S_{JJ} and S_{KK} are the stigmatic and antistigmatic variances, respectively. Maxima and minima for each column are indicated in red and blue, respectively. Medians and QD are also included. Note that because of the small variances for controls, the values were rounded off to four places after decimal points.

Eye	Anterior			Posterior		
	S_{II}	S_{JJ}	S_{KK}	S_{II}	S_{JJ}	S_{KK}
1	0.0067	0.0038	0.0028	0.0021	0.0006	0.0002‡
2	0.0081	0.0027	0.0019	0.0010	0.0013	0.0004
3	0.0033	0.0033	0.0014‡	0.0009	0.0009	0.0002‡
4	0.0070	0.0033	0.0034	0.0010	0.0015	0.0008
5	0.0054	0.0032	0.0044	0.0003‡	0.0011	0.0012
6	0.0025‡	0.0024	0.0029	0.0004	0.0006	0.0007
7	0.0054	0.0031	0.0045	0.0006	0.0011	0.0012
8	0.0039	0.0024	0.0038	0.0008	0.0008	0.0013
9	0.0044	0.0020	0.0033	0.0014	0.0013	0.0004
10	0.0043	0.0016‡	0.0041	0.0008	0.0010	0.0005
11	0.0032	0.0027	0.0025	0.0007	0.0005	0.0005
12	0.0054	0.0046	0.0075†	0.0012	0.0011	0.0006
13	0.0031	0.0021	0.0037	0.0008	0.0007	0.0004
14	0.0039	0.0024	0.0025	0.0005	0.0012	0.0004
15	0.0142†	0.0059†	0.0053	0.0022†	0.0031†	0.0029†
16	0.0030	0.0023	0.0023	0.0008	0.0008	0.0004
17	0.0048	0.0030	0.0028	0.0005	0.0008	0.0008
18	0.0064	0.0020	0.0032	0.0009	0.0012	0.0006
19	0.0043	0.0019	0.0018	0.0004	0.0004‡	0.0005
20	0.0049	0.0036	0.0058	0.0008	0.0008	0.0009
21	0.0067	0.0050	0.0029	0.0012	0.0027	0.0014
22	0.0071	0.0057	0.0034	0.0007	0.0025	0.0014
23	0.0106	0.0047	0.0053	0.0004	0.0005	0.0007
24	0.0046	0.0023	0.0029	0.0005	0.0005	0.0006
25	0.0070	0.0046	0.0025	0.0013	0.0023	0.0003
26	0.0041	0.0033	0.0048	0.0006	0.0008	0.0005
27	0.0043	0.0034	0.0021	0.0012	0.0009	0.0006
28	0.0077	0.0058	0.0035	0.0007	0.0024	0.0010
Medians	0.0049	0.0032	0.0033	0.0008	0.0010	0.0006
(QD)	(0.0014)	(0.0009)	(0.0009)	(0.0003)	(0.0003)	(0.0003)

†, ‡, Maxima and minima are indicated in single dagger and double dagger, respectively.

were divided into three groups, namely, KC, KC suspects and normal controls. Data were analysed using Fourier series harmonic analysis, where dioptric power was transformed to trigonometric components in an attempt to analyse dioptric power holistically. This study showed that both the KC and KC suspects had significantly higher spherical power, greater regular and irregular astigmatism than the control group. It was also noted that KC affects the posterior corneal surface even in the early stages of the disease and this finding could possibly be used as a diagnostic factor. Most researchers and clinicians have not emphasised the posterior corneal surface and so possibly greater attention is suggested to better understand the role of this surface in KC.

Piñero et al.[35] placed their 71 subjects in one of the four groups, that is, 18 in the keratoconus 2 group (grade II), 19 in the keratoconus 1 group (grade I), 14 in the subclinical group and 20 in the control group. Participants in the grade II group had more severe KC than the participants in the grade I group. Corneal assessment was performed using Scheimpflug imaging with the OP. Corneal volume, pachymetry and keratometric and refractive states were investigated. Keratometric and refractive states were analysed without taking into account the specific meridian along which the dioptric power lies. This study revealed that there was a strong correlation between the anterior and posterior corneal curvature in the normal (controls) and subclinical groups but weaker correlations in the KC 1 and 2 groups, which conversely had a higher correlation between anterior and posterior astigmatism than did the normal and subclinical groups. The subclinical group did not have significant differences between anterior and posterior curvatures, but they were found to be distinctly different from the normal group with their significantly higher amounts of posterior astigmatism. It was also found that the two keratoconus groups had significantly higher spherical equivalents and cylinder values compared to the normal controls.

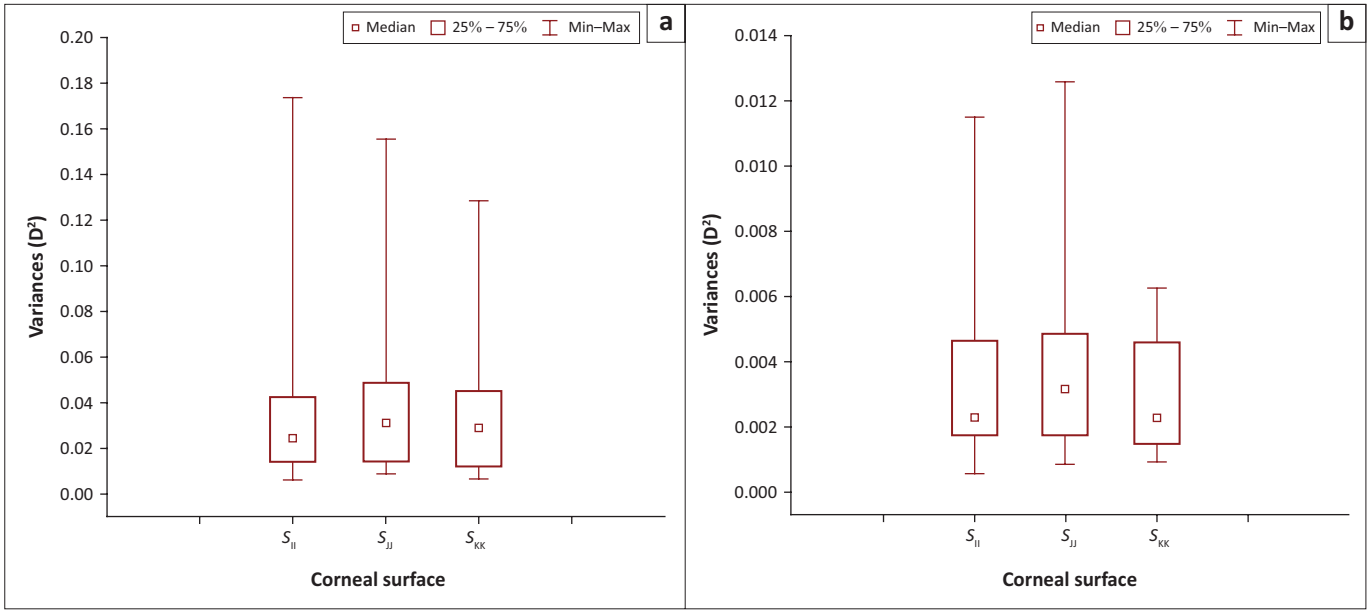


FIGURE 3: Box-and-whisker plots for stigmatic and antistigmatic variances of anterior and posterior central corneal power for 28 eyes with (a) Keratoconus: Anterior corneal surface, (b) Keratoconus: Posterior corneal surface.

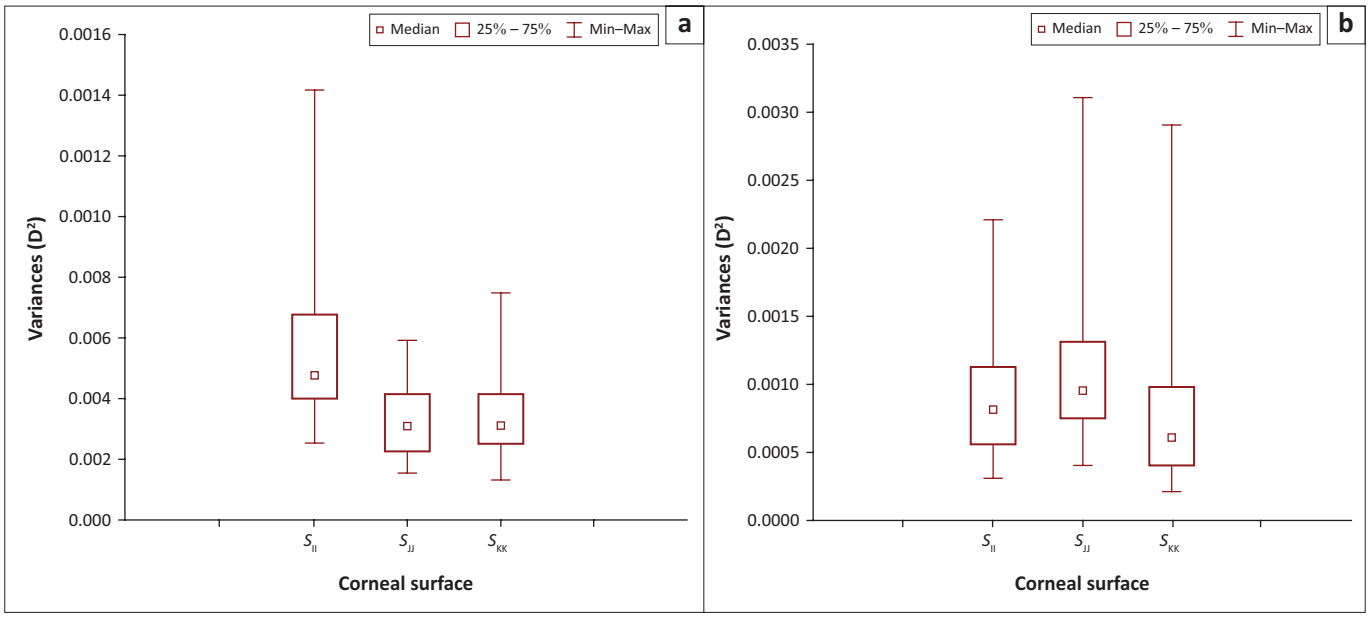


FIGURE 4: Box-and-whisker plots for stigmatic and antistigmatic variances of anterior and posterior central corneal power for 28 control eyes. Note the difference in scales on the *y*-axes when comparing with eyes with keratoconus in Figure 3. (a) Controls: Anterior corneal surface, (b) Controls: Posterior corneal surface.

A retrospective evaluation[37] of 164 patients (of which 68 were keratoconic) was assessed using a Galilei dual Scheimpflug Analyzer (Ziemer Group, Switzerland), which were grouped as KC, early KC and normal control eyes. Reddy et al.[37] also investigated pachymetry and keratometric and refractive states and analysed the keratometric and refractive data similar to Piñero et al.[35] In addition to omitting axes in their analysis, they also used the averaged refractive and keratometric values. They found that corneal structural parameters such as pachymetry and anterior and posterior corneal curvature were significantly different in keratoconic eyes when compared to normal eyes and corneal aberration measurements were particularly useful in differentiating early keratoconus from normal eyes. Other studies[36,38] that were conducted in a similar manner arrived at similar conclusions.

With the use of measurements taken with the Sirius (CSO, Italy) on 161 participants (61 of which had KC), Montalbán et al.[44] analysed data different from those mentioned above in that they compared the anterior and posterior corneal surfaces within the KC and control groups and then between the groups. This was carried out by calculating an antero-posterior *k*-ratio within each study group. The *k*-ratio was calculated by dividing the mean anterior corneal radii by the mean posterior corneal radii in each group. They found that although there were significant differences in corneal curvatures between the KC and control eyes, there was no statistical significant difference in the *k*-ratio between the groups and thus, the ratio was found to be a poor predictor in the diagnosis of KC.

A limitation in some of the above mentioned studies is that keratometric and refractive data were not analysed holistically; sometimes important factors such as axis orientation for cylinder powers were ignored and keratometric and refractive values were averaged for principal meridians. One other study made use of the multivariate methods used herein to evaluate a single moderately keratoconic cornea. In his study, Gillan[45] evaluated a single eye with KC in detail in much the same way as we have for this article. As in our article, he found greater variation in CCP for the anterior corneal surface compared to the posterior corneal surface in the eye with KC. Gillan[45] also found that for both anterior and posterior corneal surfaces, the variation along the ortho-antistigmatic axis was greater than the stigmatic and oblique antistigmatic axes.

A total of 40 measurements each for the anterior and posterior corneal surfaces of 56 eyes were analysed holistically using multivariate methods for this article. Stereo-pair scatter plots (such as in Figure 1) provide a simple but vital and fundamental visual representation of each CCP measurement taken on each KC and control eye. They demonstrate the manner in which variation occurs over time as regards the parameters of concern, for example, here anterior and posterior CCP. They allow for identification of patterns or trends in the data, possible outliers or departures from data normality. The type and magnitude of variation can be determined and compared with other samples or the same sample over time or in relation to many variables of concern. They allow one to visualise and understand keratometric and refractive behaviour and they are free of assumptions or conditions that might limit the use of other statistical methods. Furthermore, they provide essential methods to visualise sample means (example, centroids or centres of the surfaces of constant probability density) and variances. Measures of central tendency (such as means and medians) and of dispersion such as variances are two of the most critical or fundamental statistics necessary for any analysis of data and stereo-pairs allowing such statistics to be studied

and understood in the context of any experiment involving dioptric power.

The spread of the data points in Figure 1 illustrates clearly that whilst there is unsurprisingly more short-term variation of CCP in the KC eye compared to the control eye (for both surfaces), the anterior surfaces of both the eye with KC and the control eye exhibited more variation of CCP than their respective posterior surfaces. On comparison of the 95% distribution ellipsoid volume for the control eye (eye 26, Table 2), the anterior volume (0.055 D^3) is 14 times greater than the posterior volume (0.004 D^3), whereas for the KC eye (eye 17, Table 2), the anterior volume (0.257 D^3) is 23 times greater than the posterior volume (0.011 D^3).

The box and whisker plots for the volumes of the 95% distribution ellipsoids for CCP (Figure 2) and the associated statistics (Table 3) provide an overall view of all eyes measured in this study. The anterior volumes were approximately 48 times (1.060 D^3 vs 0.022 D^3) and 12 times (0.049 D^3 vs 0.004 D^3) greater than the posterior volumes for KC and control eyes, respectively (comparison of medians in Table 3). An interesting point to note is that the anterior surface of healthy corneas undergoes twice as much short-term variation in CCP relative to the posterior corneal surface of eyes with KC (0.049 D^3 vs 0.022 D^3). As mentioned before, the short-term variation of CCP measurements has rarely been analysed previously in other papers using the methods used herein, and therefore, it is difficult to compare our findings with other studies. However, the distinct differences found when comparing the KC and control groups (eyes with KC display approximately 22 times greater anterior variation and six times greater posterior variation compared to control eyes) are analogous to other studies that have shown that there are significant differences in CCP between the two groups.[34,35,36,37,38,44]

The box and whisker plots in Figure 3 (KC group) and Figure 4 (control group) are used to provide a visual representation of the nature of the observed variation in CCP. The quantities S_{II}, S_{JJ} and S_{KK} are variances with respect to the stigmatic, ortho-antistigmatic and oblique antistigmatic axes (see Figure 1), respectively. Both KC and control groups had significantly greater stigmatic and antistigmatic variation of CCP for their anterior corneal surface when compared to their respective posterior surfaces. For the KC group, there were minor differences found for the stigmatic and anti-stigmatic variation of CCP for the anterior corneal surfaces, that is, eyes with KC undergo similar amounts of stigmatic and antistigmatic variation on the anterior surface of the cornea. The same was found for the posterior surface as well. Although there are similar amounts for both stigmatic and antistigmatic variation, the ortho-antistigmatic variation is slightly greater than the stigmatic and oblique antistigmatic variation (compare medians in Table 4), which is well comparable with the finding of Gillan.[45] Control eyes experience significantly greater stigmatic variation (S_{II} = 0.0049 D^2) than antistigmatic variation (S_{JJ} = 0.0032 D^2 and S_{KK} = 0.0033 D^2) for the anterior corneal surface, whilst there was significantly greater ortho-antistigmatic variation (S_{JJ} = 0.0010D_2) than stigmatic (S_{II} = 0.0008 D^2) or oblique anti-stigmatic (S_{KK} = 0.0006 D^2) variation for the posterior surface. This indicates that although eyes with KC experience similar amounts of stigmatic and antistigmatic variation for both corneal surfaces, healthy eyes experience greater stigmatic variation for the anterior corneal surface and greater ortho-antistigmatic variation for the posterior corneal surface. This finding is also related to the study conducted by Piñero et al.[35] where it was also found that KC 1 and 2 groups had a higher correlation between anterior and posterior astigmatism than did the normal and subclinical groups. They also found that control eyes had significantly higher amounts of posterior astigmatism than for the anterior corneal surface.

Whilst it may be a limitation of the OP that the data obtained from the back surface of the cornea via Scheimpflug imaging are based on computer algorithms, which use arithmetic assumptions and extrapolated data,[46] such data still provide valuable insight into further understanding keratoconus. The greater variation noted for the anterior corneal surface for both the KC and control groups could be that the anterior surface of the cornea is more susceptible to external factors such as blinking and a poor tear layer, whilst the posterior surface is surrounded by a fairly stable internal environment.

Conclusion

The primary aim of this study was to compare the short-term variation (behaviour) of the anterior and posterior CCP in eyes with and without keratoconus using multivariate methods of analysis. Such analysis occurs both within and across eyes and groups. Whilst it is well known that eyes with KC exhibit greater variation in corneal power measurements than those of healthy eyes without KC, the nature of variation has not been fully evaluated before and especially not using the methods used herein. Thus, this study provides new information and knowledge through a comprehensive analysis of variation of CCP using predominantly multivariate methods and statistics for further investigation using univariate methods and statistics where necessary.

Acknowledgements

Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

All authors contributed equally to this work.

Ethical consideration

Permission to conduct the study was provided by the Research Ethics Committee, Faculty of Health Sciences of the University of Johannesburg, South Africa (ethical clearance number: REC-241112-035).

Funding information

This study was funded by the Thuthuka grant (TTK160519165562) from the National Research Foundation in South Africa.

Data availability statement

Data sharing is not applicable to this article.

Disclaimer

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the authors.

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