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Corneal parameters and their correlations with refractive error, axial length, anterior chamber depth and lens thickness in black South Africans

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南非黑人角膜参数与屈光不正、眼轴长度、前房深度和晶状体厚度的相关性

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摘要

目的:收集南非健康黑人的角膜直径(CD)、曲率(ACC)和角膜中央厚度(CCT)的数据并探讨其与屈光不正等效球镜(SE)、眼轴长度(AL)、前房深度(ACD)、晶状体厚度(LT)的相关性,及三个角膜参数之间的相关性。

方法:选取 600 例受试者,包括 305 例男性和 295 例女性(平均年龄:28.15±13.1y,年龄范围:10~66y)接受全面的眼科检查,包括验光,裂隙灯和眼底镜检查。Oculus Keratograph 4 检测 CD 和 ACC,ivue-100 光学相干断层扫描检测 CCT。Nidek AR-310A 自动验光仪和主观验光检测屈光不正。Nidek US-500 A 超检测 AL,ACD 和 LT。

结果:由于左右眼参数评估的差异无统计学意义,此处只显示右眼的结果。角膜各项参数平均值如下:CD=11.77±0.32 mm(10.30-13.70 mm),ACC=7.88±0.29 mm(7.13~8.88 mm),CCT=493.05±33.2 μm(412~590 μm)。CD 与 SE 无相关性(r=0.05,P=0.24)。CD 与 AL(r=0.58,P=0.00)、ACD(r=0.63,P=0.00)显著相关,但与 LT(r=-0.40,P=0.00)呈负相关。ACC 与 SE(r=-0.03,P=0.48)无显著相关性。ACC 与 AL(r=0.40, P=0.00)呈正相关。ACC 与 ACD(r=0.04,P=0.56)、LT(r=-0.03,P=0.88)无显著相关性。CCT 与角膜以外其他参数间无显著相关性。角膜各项参数的相关性表明,CD 与 ACC(r=0.71,P=0.00)、CCT(r=-0.68,P=0.00)相关。

结论:CD 与 AL、ACD、LT 相关,ACC 与 AL 相关。CCT 与角膜以外其它参数无相关性,是一个独立的因素。在角膜各项参数中,CD 与 ACC、CCT 相关。

关键词:角膜直径;角膜曲率;角膜中央厚度;等效球镜;眼轴长度;前房深度;晶状体厚度;南非黑人

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Abstract

• AIM: To establish profiles of corneal diameter (CD), curvature (ACC), corneal central thickness (CCT) and investigate their correlations with refractive errors' spherical equivalent (SE), axial length (AL), anterior chamber depth (ACD) and crystalline lens thickness (LT) in black South Africans with healthy eyes. We also investigated the intercorrelation among the three corneal parameters.

• METHODS: Eyes of six hundred subjects that included 305 males and 295 females (mean age: 28.15±13.1y, range: 10-66y) underwent a complete ophthalmic examination including refraction, slit lamp and ophthalmoscopy. CD and ACC were measured using the Oculus Keratograph 4 (OCULUS Optikgeräte GmbH), and the CCT was measured with the iVue-100 (Optovue, Inc.) optical coherence tomography. Refractive errors were assessed with the Nidek AR-310A auto-refractor and then subjective refraction. The AL, ACD and LT were measured with the Nidek US-500 A-scan ultrasound device.

• RESULTS: There are no statistically significant between the parameters of the right and left eyes assessed, and therefore only the results of the right eyes are presented here. The mean corneal parameter values were: CD=11.77±0.32 mm (range=10.30-13.70 mm), ACC=7.88±0.29 mm (range=7.13-8.88 mm) and CCT=493.05±33.2 μm (range=412-590 μm). CD did not correlate with SE (r=0.05, P=0.24). However, CD was correlated significantly with AL (r=0.58, P=0.00) and ACD (r=0.63, P=0.00) but inversely correlated with LT (r=-0.40, P=0.00). There was no significant correlations between ACC and SE (r=-0.03, P=0.48). ACC correlated positively with AL (r=0.40, P=0.00). There were no significant correlations between ACC and ACD (r=0.04, P=0.56), and LT (r=-0.03, P=0.88). Also, there was no correlation between CCT and other ocular dimensions assessed. However, correlations among corneal parameters showed that CD correlated with ACC (r=0.71, P=0.00) and CCT (r=-0.68, P=0.00).

• CONCLUSION: While CD correlated with AL, ACD and LT, the ACC correlated with AL. CCT did not correlate with any of the metrics studied here, suggesting that it is an independent factor unrelated to other ocular dimensions. Among corneal parameters, CD correlated with ACC and CCT.
• KEYWORDS: corneal diameter; corneal curvature; central corneal thickness; spherical equivalent; axial length; anterior chamber depth; lens thickness; black South Africans
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INTRODUCTION

Accurate assessments of ocular dimensions are important in the management of many ocular disorders and anomalies. For example, accurate assessments of corneal diameter (CD) are important to diagnose and manage ocular diseases, such as microcornea, macrocornea, relative microphthalmus, corneal dystrophies, and congenital glaucoma[1-3]. The precise measurements of CD is also mandatory for haptic size calculation in anterior chamber or sulcus - implanted intraocular lenses (IOLs), and when calculating IOL power in cataract surgery[4-6]. In addition, there has been increasing interest in measuring corneal curvature (ACC) due to its importance in corneal refractive surgery, ocular aberration analysis, diagnosing and managing keratoconus, contact lens fitting and detecting higher astigmatism[7-8]. Furthermore, the measurement of central corneal thickness (CCT) plays an important role in both the diagnostic and therapeutic assessment of glaucoma and corneal diseases, in evaluating contact lens use, and in refractive surgery[9-11].

Intraocular pressure (IOP) measurements using applanation tonometry have been reported in several publications to be affected by biometric variables, such as CD, ACC, CCT and axial length (AL)[12-13]. Hosny *et al*[14] reported that CD correlated significantly with anterior chamber depth (ACD), which has implications for glaucoma. Previous investigations have also shown that eyes with longer ALs are associated with wider CD[3,14] and flatter ACCs[3]. Chen *et al*[15] found no significant correlation between CCT and AL. ACC and CCT have been shown not to correlate with ACD[14], and ACC has been reported not to correlate with refractive error[14-15]. Wei *et al*[16] reported a negative correlation between CCT and refraction degree.

Corneal parameters and their correlations have been shown in many published studies to vary between races and ethnicities. Therefore, data from different areas and ethnicities should be studied. There is currently a paucity of information on these parameters and their correlations in South Africans which makes it difficult to develop treatment or interventions that address their specific needs. The present study was carried out to determine the average values of CD, ACC and CCT and to investigate their correlations with SE, AL, ACD, LT in a black South African population with healthy eyes. In addition, we investigated the correlations among CD, ACC and CCT. Such data provide important and valuable information about the pathophysiology, diagnosis and management of ocular diseases.

SUBJECTS AND METHODS

An observational cross-sectional design was adopted that included 600 participants, selected through stratified random cluster sampling in six districts of Durban, a major City in the Kwa-Zulu Natal Province of South Africa. The study was carried out in a University Eye clinic. All participants had to meet a minimum uncompensated or compensated visual acuity (VA) criterion of 20/20 or better monocularly. The following exclusion criteria were used during participants' recruitment: non black South Africans, presence of any visual condition not correctable by refraction, a history of contact lens wear, signs of any eye diseases, injury or systemic diseases associated with ocular pathology. In addition, those with corneal anomalies, or had undergone refractive or cataract surgery, presence of colour vision deficiencies, any other systemic conditions (such as rheumatoid arthritis, hypertension, diabetes mellitus *etc.*) or ocular findings (such as infections, encroached pterygium, dystrophies, ectasias *etc.*) that may influence values to be collected were excluded. Those with abnormal intraocular pressure (IOP) and visual fields, on medication or eye drops (such as corticosteroids that are likely to affect corneal integrity), with nystagmus, strabismus, pregnant and on contraceptive drugs, and who were unable or unwilling to give informed consent were excluded. All participants included in the study reported having good health. To identify participants who met the inclusion criteria, a comprehensive ocular examination was performed, which included a refraction, funduscopy, slit lamp biomicroscopy, intra-ocular pressure measurement, and the administration of a brief questionnaire.

Height was measured with a tape measure with the subjects standing up without shoes and recorded in centimetres. Both autorefraction (with the Nidek AR-310A) and subjective refraction were performed on all participants to determine their refractive status. Autorefraction was performed to obtain the baseline refractive error that was subsequently refined using subjective refraction, the results being used to determine the relevant spherical equivalents (SEs). All participants who met the inclusion criteria underwent CD, ACC, CCT, AL, ACD and LT measurements. CD and ACC were measured with the Oculus Keratograph 4 (OCULUS Optikgeräte GmbH), with participants being instructed to blink completely between each scan to evenly spread the tear film over the cornea[17]. CCT measurements were taken with the iVue-100 OCT, between 2 and 8 pm, with all subjects having been awake for at least two hours before the measurements were taken. A trained and experienced operator performed the CCT measurements according to the analysis protocol and variables. The measurements were taken with a CAM lens attached; the quality of the image being displayed after each scan, this being based on the intensity of the reflected light. This is described as the signal strength index (SSI), and ranges from near 0 (no signal) to approximately 90 (very strong signal). Only the scans with a SSI of 45 and higher were used for analysis, as per the manufacturer's recommendations[18].

AL, ACD and LT were measured with Nidek US-500 Echoscan, which was placed perpendicular to the cornea at 1.5 mm temporally from the reflex of the fixation light. Measurements were taken following instillation of one drop of 0.4% oxybuprocaine hydrochloride and twenty seconds duration allowed for the anaesthetic to take effect. Participants were instructed to fixate at a distant target at all times to minimise accommodation-related changes in ACD and LT. The Echoscan probe was sterilized with hydrogen peroxide before use and between measurements on each participant. The measurements were taken in a room with constant illumination level as measured with a light meter, and all the equipment were calibrated before each measurement was taken. All corneal parameters (CD, ACC and CCT), AL, ACD and LT measurements were performed by the same examiner, with three valid repeated measurements made and then averaged. A pilot study was conducted among 60 participants who did not form part of the final study. This was undertaken to critically evaluate the execution of the field and clinical work, and perform preliminary data analysis. The pilot also indicated areas of improvement in the logistical and operational aspects of the study.

The University of KwaZulu-Natal's Biomedical Research and Ethics Committee approved the research proposal and the study was conducted in accordance with the tenets of the Declaration of Helsinki for research involving human subjects. Informed consent and accent was obtained from each participant after the nature of the study procedures had been explained to them.

When data was entered into the database, each participant was allocated a unique identity number to ensure confidentiality of information. The data was captured into STATA (version 13.1, USA) which was also used for the statistical analyses. Test for normality of distribution was performed with the Kolmogorov-Smirnov tests. Descriptive statistics was used to calculate the range, mean and standard deviations. Paired samples t-test was used to analyzed ocular variables between right and left eyes. Pearson correlation and linear regression analysis were used to assess the relationships between corneal parameters and variables of age, SE, AL, ACD, and LT. Intercorrelation among CD, ACC and CCT were assessed with Pearson correlation coefficients.

RESULTS

A total of 600 individuals with an age of 28.15±13.1y (range: 10-66y) participated in this study, of whom 305 were males and 295 were females. There were no significant differences between right and left eyes in the t-test for the parameters assessed (all P>0.05). Kolmogorov-Smirnov test results showed that the corneal parameters assessed were essentially normally distributed. Table 1 shows the descriptive statistics of the measured variables. Males were on average taller than females.

Table 1 Statistics of measured variables from all participants

Variable	Mean±SD	Range
Age (a)	28.15±13.1	10-66
CD (mm)	11.77±0.3	10.30-13.70
ACC (mm)	7.88±0.3	7.13-8.88
CCT (μm)	493.05±33.2	412-590
SE (D)	-0.46±1.5	-7.00-3.00
AL (mm)	23.05±1.0	20.42-27.28
ACD (mm)	3.21±0.4	2.38-4.13
LT (mm)	3.69±0.3	2.24-4.66

CD: Corneal diameter; ACC: Anterior corneal curvature; SE: Spherical equivalent; AL: Axial length; ACD: Anterior chamber depth; LT: Lens thickness; SD: Standard deviation.

Sex *vs*. Ocular Parameters Males had significantly wider CD, flatter corneas and greater AL, ACD and LT than their females counterparts (all P<0.05). However, there was no significant difference in the mean values of SE and CCT in a gender comparison (all P>0.05).

Age *vs*. Ocular Parameters Age was strongly positively correlated with LT (r=0.77, P=0.00) and moderately inversely correlated with AL (r=-0.54, P=0.00), CD (r=-0.47, P=0.00) and strongly inversely correlated with ACD (r=-0.72, P=0.00). Figure 1 is a graphical representation of the regression of CD on age. A linear model best described this relationship, CD (mm) = -0.0233×Age+12.247; R^2 = 0.239; (r=-0.47, P=0.00). There was no significant correlation between ACC and age (r=-0.04, P=0.98) and CCT (r=0.07, P=0.14).

Corneal Parameters *vs*. Other Ocular Parameters The correlation coefficient and P-values between corneal parameters and other ocular biometric values are presented in Table 2.

Pearson correlation showed that the CD was significantly positively correlated with AL (r=0.58, P=0.00) and ACD (r=0.63, P=0.00) of the eye. The regression of CD *vs*. AL and CD *vs*. ACD are plotted in Figure 2 and 3. Figure 4 is a scatter plot showing the relationship of ACC and AL (r=0.40, P=0.00). For CCT, it was not correlated with SE, AL, ACD or LT (P>0.05 for all).

Correlations among Corneal Parameters An analysis of corneal parameters showed that the strongest correlations were found between CD and ACC (r=0.71, P=0.00), followed by CD and CCT (r=-0.68, P=0.00). The correlation between ACC and CCT, however, was not statistically significant (r=0.16, P=0.08).

DISCUSSION

In the present study, CD, ACC and CCT were measured to establish their distribution and their correlations with SE, AL,

Table 2　Correlation matrix of corneal parameters with other ocular parameters measured

Parameters	SE		AL		ACD		LT	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*
CD	0.05	0.24	0.58	0.00	0.63	0.00	-0.40	0.00
ACC	-0.03	0.48	0.40	0.00	0.04	0.56	-0.03	0.88
CCT	0.05	0.25	-0.06	0.38	-0.01	0.74	0.06	0.15

CD: Corneal diameter; SE: Spherical equivalent; AL: Axial length; ACD: Anterior chamber depth; LT: Lens thickness; ACC: Anterior corneal curvature; CCT: Central corneal thickness.

ACD and LT in a black South African population with healthy eyes. This information has never been reported previously in this population, and is important to enable appropriate eye care services to be provided. These parametersand their correlations are important to monitor congenital glaucoma, ocular aberration analysis, cataract and refractive surgery as well as to diagnose corneal diseases[1-11].

Males had wider, flatter corneas, longer AL, deeper ACD and thicker lenses than females. Previous investigators[15,19] have suggested that the gender differences in these parameters could be due to the fact that men are generally taller (and have correspondingly larger eyes) than women, which were also observed in the present study. Our study suggests that black South African women may be more at risk of developing acute angle closure glaucoma because of their smaller eyes and steeper corneas compared to their male counterparts.

The mean CD in this study (11.77±0.32 mm, range=10.30-13.70 mm) compares well with those reported in other ethnic groups[1,2,20]. However, the variability in the age cohorts, instruments used and the selection of participants in these studies prevent a direct comparison. Our findings suggests that CD values less than 10.30 mm and greater than 13.70 mm may be considered as microcornea and macrocornea respectively in this population group.

The decrease in CD with age may be due to alterations in the corneal architecture and other biomechanical properties as suggested by Elscheikh *et al*[21]. We established that CD was significantly but mildly related to age and was represented by the equation: CD = -0.0233×Age + 12.247 (Figure 1). According to this equation, a 10-year increase in age leads to approximately a 0.23 mm decrease in CD. The increase of 0.23 mm is small and may therefore not be clinically significant. No correlations were found between CD and SE, while Hosny *et al*[14] reported that CD decreased with hyperopia and increased with myopia. Our study included participants with a low range of SE, and this could have influenced the results. Zha *et al*[2] have shown that eyes with myopia of -3 D and lower had lower CD values. In addition, Martin *et al*[6] found that eyes with moderate (between 6.00D and 12.00D) and high (>12.00D) degrees of myopia had lower CD than eyes with low SE myopia (<6.00D). Further studies are therefore, required to investigate the relationship between higher refractive errors and CD in this population.

CD was significantly but moderately related to AL and was represented by the equation: CD = 0.2868×AL + 5.157 (Figure 2). Based on this equation, a 2 mm increase in AL would lead to approximately a 0.57 mm increase in CD. The relationship between a large AL and an increase in CD can be explained as part of the emmetropization process in eyes with large ALs, which tend to be myopic, the cornea might elongate to increase the radius of curvature and shift towards hyperopia to compensate for myopia[22]. CD correlated strongly with ACD (r = 0.63, P = 0.01), indicating that when CD is larger, the ACD is deeper. Hosny *et al*[14] also found that the relation of CD to ACD was significant (r = 0.74, P = 0.00), denoting a strong and significant linear relation. We found a mild negative correlation between CD and LT (r = -0.40, P = 0.00) suggesting that this relationship may be clinically insignificant in this population.

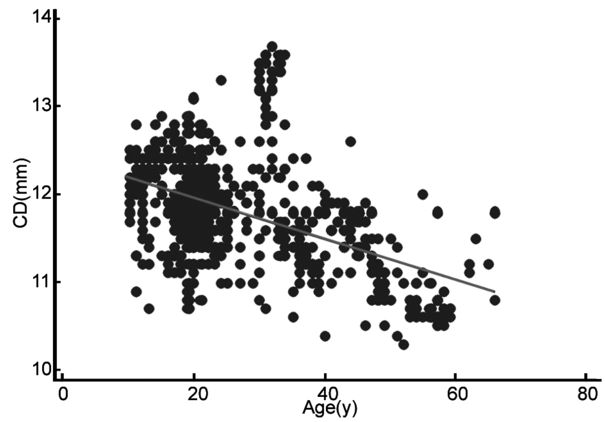

Figure 1　Correlation between the average corneal diameter (CD) and age　The regression equation is Y = -0.0233X + 12.247; R^2 = 0.239.

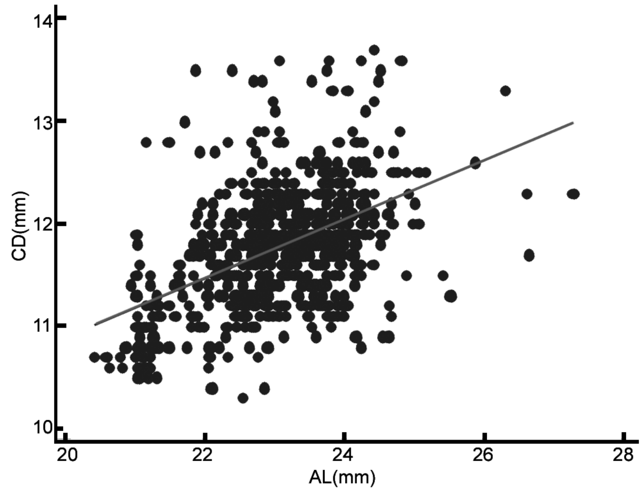

Figure 2　Regression and correlation between corneal diameter (CD) and axial length (AL)　Regression between AL (X) and CD (Y) yielded: Y=0.2868X + 5.1570; R^2 = 0.225.

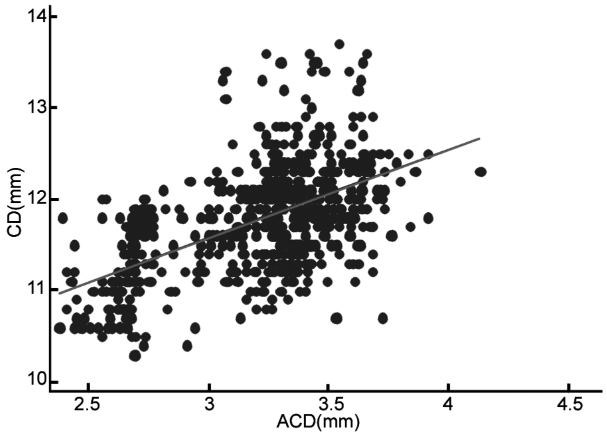

Figure 3 Scatterplots between average corneal diameter (CD) and anterior chamber depth (ACD) Regression between ACD (X) and CD (Y) in the study population yielded: Y=0.9642X + 8.6752; R^2=0.280.

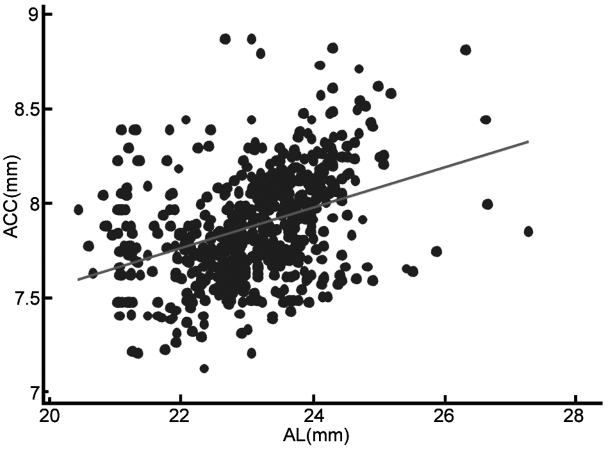

Figure 4 Relation between corneal curvature (ACC) and axial length (AL), (n=600, r=0.40, P=0.00) Regression between AL (X) and ACC (Y) yielded: Y=0.1053X + 5.4517; R^2=0.142.

The ACC in our study (7.88±0.29 mm) (range=7.13–8.88 mm); is close to the results of Iyamu and Eze[23], which reported ACC value of 7.85 mm±0.35 from 95 Nigerian individuals aged 20 to 69y old using a keratometer. Although general overall comparisons between these results cannot be made due to differences in age groups, measurement methods, and instrument, our results suggest that ACC values outside this range can be regarded as abnormal in this population when measured with the Oculus Keratograph 4. The relationship between ACC and refractive error has been the subject of an ongoing debate. For example, some researchers[24] have demonstrated no relationship between the ACC and refractive error, whereas other authors[25-26] have found that as the mean refractive error decreases, the cornea steepens. We did not find any correlation between ACC and SE; and again, this could be due to our relatively low range of SE. A significant positive but mild correlation was found between ACC and AL, which suggests that on average, longer eyes have flatter corneas. Guggenheim *et al*[27] and Scheiman *et al*[28] also reported that ACC and AL were correlated in their studies (r=0.54 and r=0.57, respectively). Guggenheim *et al*[27] suggested that specific genetic variants influence this relationship and environmental factors may play a role in changing the coordinated growth of these components in ametropic eyes. ACC and ACD are important in phakic and refractive phakic IOL implantation and inaccurate estimation of these parameters contribute 22% and 42% of the error in predicted refraction of an IOL using optical biometry[29]. No correlation between ACC and ACD was found, which is consistent with a study by Carney *et al*[30]. The authors[30] also found that eyes with flatter corneas had higher LT values, which was not observed in the current study (r=−0.03, P=0.88).

The average CCT in our study was 493.05±33.2 μm (range=412 μm to 590 μm), with other studies among different ethnic groups[20,23,31-33] reporting different values. Although it is difficult to compare findings of these studies, as the age cohorts, methods and instruments varied, ethnic variations in CCT exist and have been reported previously[20,23,31-33]. CCT values below 412 and above 590 μm can be considered abnormal when measured with the iVue-100 OCT in a black South African population. Our findings also suggest that black South Africans have thinner CCTs than those of other ethnicities[20,23,31-33]. These results have significant clinical implications in glaucoma detection and management. For example, the accuracy of tonometry has been reported to be more precise in patients having an average CCT of between 500 and 550 μm[34] and eyes with thinner than average corneas may underestimate the true IOP[35]. Therefore, black South Africans have thinner corneas which compound the underestimation of IOP readings during Goldmann applanation tonometry. The under-reading of IOP may contribute to delay in diagnosis and appropriate IOP target setting for glaucoma therapy in this population.

CCT did not correlate with age or SE, which agreed with previous studies[31-32]. Differences in ages, races, sample sizes and measurement methods and techniques could explain the discrepancies in these studies. For example, the difference between our study and others that showed a correlation between CCT and refractive error may be due to the current study not using cycloplegic refraction, whereas that was used in the previous studies.

The correlation between CCT and AL is inconsistent as contradictory results have been reported in the literature. For example, Chang *et al*[36] have demonstrated that thinner CCTs were associated with greater AL possibly due to the fact that as the surface area of the cornea increases, the corneal stroma becomes thinner. However, Iyamu *et al*[37], found no associations between CCT and AL, which was also reported in the present study. It is well known that the eyeball elongates and the sclera thins during the development of myopia[27]. In addition, the components of the sclera and cornea, such as collagen, glycosaminoglycan, elastin and hydration, vary between them[28]. It is therefore possible that CCT may be unaffected by the scleral thinning that occurs during axial elongation[15]. In our study, there was no correlation between CCT and ACD, which could also partly explain the lack of association of CCT and AL mentioned above. As previously reported by Ehlers *et al*[38], CCT did not correlate with LT.

Larger corneas had flatter surfaces ($r = 0.71$, $P = 0.00$). These findings are important clinically in terms of the choice of the microkeratome suction ring because there appears to be a higher risk of free cap with flatter corneas in keratorefractive surgery and a larger suction diameter should be chosen to create a larger flap in such cases[39]. The strong negative correlation between CD and CCT found in our study concurs with other authors' findings that larger corneal diameters are associated with thinner corneas. As earlier stated, the presence of thin corneas in black South Africans may increase their susceptibility to glaucoma compared to other races.

Possible limitationsof this study include the low range of spherical equivalent considered and few participants above 60y of age. Therefore, it is recommended that future studies use a wider range of spherical equivalents and eyes of older subjects.

In conclusion, a population profile of CD, ACC and CCT was established in a black South Africans for the first time. These parameters are comparable to some studies but differ from others. CD was positively correlated with AL and ACD while ACC was positively correlated with AL. CCT was found to be independent of AL, ACD and LT. Intercorrelation among corneal parameters showed that CD positively correlated with ACC and negatively correlated with CCT. Findings of this study can be used as a reference for diagnostic and clinical purposes.

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